CJHP JCPH

The Canadian Journal of Hospital Pharmacy
Le Journal canadien de la pharmacie hospitalière

Vol. 58, Supplement 2 (AGM), August 2005
Vol. 58, Supplément 2 (AGA), Août 2005

58th AGM & Educational Sessions • 58e AGA et séances éducatives

Ottawa 150 1855-2005 Come celebrate with us! Venez célébrer avec nous!

A Capital Destination / Une destination capitale
CSHP/SCPH AGM/AGA 2005 Ottawa

Publications Mail Agreement 40036323 / PAP 9787

Canadian Society of Hospital Pharmacists
Société canadienne des pharmaciens d'hôpitaux

LIPITOR*: Hitting targets.

LIPITOR is an HMG-CoA reductase inhibitor (statin). LIPITOR is indicated as an adjunct to lifestyle changes, including diet, for the reduction of elevated total cholesterol, LDL-C, TG and apolipoprotein B in hyperlipidemic and dyslipidemic conditions (including primary hypercholesterolemia, combined (mixed) hyperlipidemia, dysbetalipoproteinemia, hypertriglyceridemia and familial hypercholesterolemia) when response to diet and other non-pharmacological measures alone has been inadequate.

LIPITOR also raises HDL-cholesterol and therefore lowers the LDL-C/HDL-C and Total-C/HDL-C ratios (Fredrickson Type IIa and IIb).

NEW § LIPITOR is indicated to reduce the risk of myocardial infarction in adult hypertensive patients without clinically evident coronary heart disease, but with at least three additional risk factors for coronary heart disease such as age ≥55 years, male sex, smoking, type 2 diabetes, left ventricular hypertrophy, other specified abnormalities on ECG, microalbuminuria or proteinuria, ratio of plasma total cholesterol to HDL-cholesterol ≥6, or premature family history of coronary heart disease.

Less than 2% of patients discontinued therapy due to adverse experiences. Most common adverse effects were constipation, diarrhea, dyspepsia, flatulence, nausea, headache, pain, myalgia and asthenia.

LIPITOR is contraindicated: During pregnancy and lactation; active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal; hypersensitivity to any component of this medication.

Lipid levels should be monitored periodically and, if necessary, the dose of LIPITOR adjusted based on target lipid levels recommended by guidelines.

Caution should be exercised in severely hypercholesterolemic patients who are also renally impaired, elderly, or are concomitantly being administered digoxin or CYP 3A4 inhibitors.

Liver function tests should be performed before the initiation of treatment, and periodically thereafter. Special attention should be paid to patients who develop elevated serum transaminase levels, and in these patients, measurements should be repeated promptly and then performed more frequently.

EFFICACY ➢ **Power to start with a *FLEXIBLE FIRST DOSE*™ at 10 mg, 20 mg, 40 mg[††]**
† When a >45% LDL-C reduction is required, patients may be started at 40 mg o.d.[1]

EXPERIENCE ➢ **More than 76 million patient-years of experience[2‡‡]**

EVIDENCE NEW ➢ **ASCOT[£] demonstrated LIPITOR's efficacy in reducing the risk of myocardial infarction in adult hypertensive patients without clinically evident CHD, but with at least three additional risk factors for CHD[1§]**

LIPITOR has a leading edge clinical research program exploring new areas that may extend beyond lipid control[3]

¥ Based on Pfizer's analysis of IMS Health data.[2]
‡ A patient-year represents the total time of exposure to LIPITOR as defined by the sum of each patient's time on LIPITOR.[2]
£ ASCOT = Anglo-Scandinavian Cardiac Outcomes Trial

*LIPITOR atorvastatin calcium tablets

***power** you can **trust**™*

10 mg 20 mg 40 mg 80 mg

Pfizer
Life is our life's work

PMAB R&D

Dear Colleague:

It is with great pleasure that we invite you to join us to "A Capital Destination" in the Nation's Capital Ottawa, Ontario, on August 13th to 16th, 2005, for the Canadian Society of Hospital Pharmacists 58th Annual General Meeting and Educational Sessions.

The Educational Services Committee, chaired by Judy Chong, has assembled a fantastic educational program that will include A Pharmacists' Role in Peacekeeping, Electronic Health Record-Based Drug Information Systems in Canada, Challenges of the Special Access Programme with perspectives from a Regulator and a Hospital Pharmacist. This year's workshops will include a special CHPRB Residency workshop and a workshop addressing the Hospital Pharmacy Management Crisis: Development of Strategies and Solutions.

Included in our vendor exhibit program this year is the annual booth decoration. This year our participating exhibitors will decorate their booth as a capital city of the world. Members can participate in the host committee events and win great prizes while networking and seeing the latest products and services. Please take time to visit and gain from their expertise and acknowledge the tremendous support they offer to our event.

The 2005 Annual General Meeting is scheduled for Sunday, August 14th at 3:00 PM. The AGM will provide all members with the chance to hear about the many important initiatives that have helped advance hospital pharmacy in the past year. Reports from CSHP Council will include important updates on patient safety, CSHP's strategic plan, advocacy, education, and networking. The Wine and Chat immediately following the AGM offers an informal opportunity to continue the discussion with Council and staff of CSHP. It's important to make time in your busy AGM schedule to participate in the Wine and Chat as Council needs to hear from you, our members.

This year's social events kick off on Saturday, August 13th, with the Tenth Annual CSHP Research and Education (R&E) Foundation Fundraising Golf Tournament, to be held at Emerald Links Golf Course. All profits from this event will be donated to the R&E Foundation, supporting and promoting the research and education initiatives of CSHP's members.

The Ottawa Host Committee, chaired by Kelly Babcock, has organized social activities, including an early morning Fun Run/Walk, Fun Night at the Honest Lawyer, and our annual Past Presidents' Dinner and Dance at the National Arts Centre. The efforts of this year's Committee guarantee a memorable time.

AGM 2005: A Capital Destination. We look forward to seeing you and sharing the fun.

Régis Vaillancourt,
PharmD, FCSHP
CSHP President

Myrella Roy,
Pharm.D., FCCP
Executive Director

Cher collègue,

C'est avec un immense plaisir que nous vous invitons à vous joindre à nous vers une « destination capitale », à l'occasion de la 58e Assemblée générale annuelle (AGA) de la Société canadienne des pharmaciens d'hôpitaux et de ses séances éducatives qui auront lieu du 13 au 16 août 2005 dans la Capitale nationale, la ville d'Ottawa en Ontario.

Sous la direction de Judy Chong, le comité des services éducatifs vous a préparé un programme éducatif sensationnel. Ainsi, vous aurez l'occasion d'entendre parler du rôle du pharmacien dans une opération de maintien de la paix, des systèmes d'information sur les médicaments intégrés dans le dossier de santé électronique au Canada et des défis posés par le programme d'accès spécial de Santé Canada avec les points de vue d'un membre d'un organisme de réglementation et d'un pharmacien d'hôpital. Cette année, vous pourrez aussi assister à un atelier spécial sur la résidence organisé par le CCRPH ainsi qu'à un atelier traitant de la crise qui touche la direction de la pharmacie hospitalière : élaboration de stratégies et recherche de solutions.

Cette année encore, le programme d'exposition des fournisseurs inclura un volet décoration des stands. Cette année, les exposants qui participeront à l'événement décoreront leur stand à l'image des capitales du monde. Les membres peuvent participer aux événements préparés par le comité d'accueil et gagner de magnifiques prix tout en se constituant un réseau de contacts et en jetant un oeil aux dernières nouveautés en matière de produits et services. Veuillez prendre le temps de visiter les exposants afin de pouvoir profiter de leurs compétences particulières et de les remercier par la même occasion pour l'immense soutien qu'ils offrent à notre événement.

L'assemblée générale annuelle 2005 se tiendra à quinze heures, dimanche le 14 août. L'AGA offre aux membres l'occasion d'entendre parler de plusieurs initiatives importantes qui ont contribué à faire avancer la pharmacie d'hôpital au cours de la dernière année. Les comptes-rendus du Conseil de la SCPH porteront sur d'importantes mises à jour concernant la sécurité des patients, sur le plan stratégique de la SCPH, la communication des intérêts, la formation et le réseautage. Tout de suite après l'AGA, un vin vous sera servi, ce qui vous donnera l'occasion de continuer la discussion sans cérémonie avec les membres du Conseil et le personnel de la SCPH. Il est essentiel que vous preniez le temps, malgré l'horaire chargé de l'AGA, d'assister à cette rencontre et de bavarder avec les membres du Conseil. Ceux-ci ont besoin de connaître l'opinion des membres.

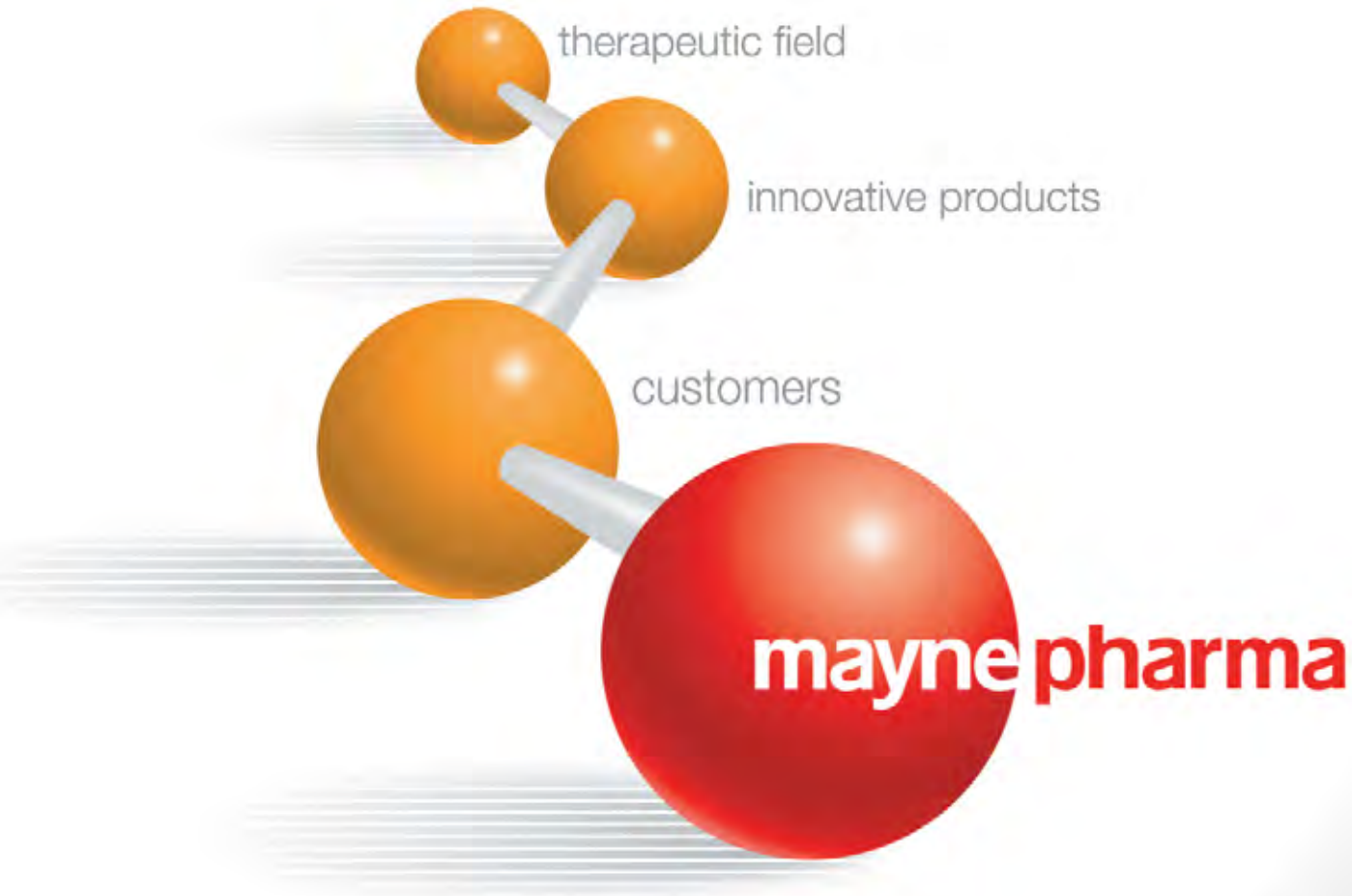
Cette année, les activités sociales commenceront le samedi 13 août par le 10e tournoi de golf annuel de la SCPH destiné au financement de la Fondation pour la Recherche et l'Éducation, qui aura lieu au Club de golf Emerald Links. Tous les profits de cet événement seront remis à la Fondation pour la Recherche et l'Éducation en soutien et promotion de recherche et d'éducation de membres de la SCPH.

Le comité d'accueil d'Ottawa, sous la présidence de Kelly Babcock, a préparé plusieurs activités sociales dont une promenade/course matinale amicale, une soirée d'agrément au restaurant récréatif « The Honest Lawyer », et le dîner dansant annuel des anciens présidents qui aura lieu au Centre national de arts. Les efforts déployés par le comité d'accueil de cette année vous garantissent un séjour mémorable.

AGA 2005 : Une destination capitale. Nous espérons vous y voir et nous y amuser avec vous.

Régis Vaillancourt,
Pharm. D., FCSHP
Président de la SCPH

Myrella Roy,
Pharm. D., FCCP
Directrice exécutive



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Welcome/Bienvenue 1

With Thanks/Remerciements

CSHP Corporate Members/
Entreprises membres de la SCPH 8

CSHP Sponsors 2005/2006/
Commanditaires de la SCPH 2005/2006 8

CSHP/SCPH

Educational Services Committee/
Comité des services éducatifs 3

Host Committee/Comité d'accueil 3

Executive and Council/Bureau et Conseil 4

CSHP Staff/Personnel de la SCPH 4

PPC 2006 Call for Abstracts/
Sollicitation de résumés pour le CPP 2006 37

Registration Information/
Renseignements sur l'inscription

Where to stay at AGM 2005/Où loger durant l'AGA 2005 . . . 10

Flight Arrangements/Dispositions de vol 10

Continuing Education Credits/
Crédits de formation continue 10

AGM 2005 at a Glance/L'AGA 2005 d'un coup d'œil 12

Upcoming Events/Événements à venir 12

AGM Social Activities/Activités sociales de l'AGA 12

Program/Programme

Program of Events/Programme des événements 15

Speakers Abstracts/Résumés des conférenciers 18

Poster Abstracts/Résumés des affiches 29

Faculty/Conférenciers 36

Exhibitor List/Liste des exposants 40

Index of Advertisers/Index des annonceurs

Amgen – Aranesp 39

CATIE – Canadian AIDS Treatment Information Exchange. 13

EPS Inc. – Corporate. 14

Genpharm – Venofer . . . . . IBC

Hospira – Corporate. 41

Mayne Pharma – Corporate 2

Novopharm – Corporate 5

Ortho Biotech – Velcade 6/7

Pfizer Canada – Lipitor . . . . . IFC

PPC – Corporate . . . . . OBC

Sabex – Corporate 11

Sanofi Aventis – Plavix 9

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Our commitment to hospital pharmacy is really starting to show.

At Novopharm, we're making great strides in Hospital Pharmacy, because we know how important it truly is.

With the recent acquisition of Sicor Pharmaceuticals, Novopharm now has access to the largest number of injectable products on the market as well as new dosage forms and innovative IV delivery systems. As a result, Novopharm has several new exciting product launches on the horizon, the first of which is the release of Novopharm Propofol. Propofol is an established product in the Sicor product line resulting in a consistent supply to the Canadian market. With our Diamond Support of the CSHP and our renowned customer service, our commitment to hospital pharmacy has never been stronger.

Introducing new Novopharm Propofol, available in 20, 50 and 100 mL.

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STRENGTH LIKE NO OTHER™

VELCADE achieved:

- **28% overall response rate in high-risk patients**
  (n=188, 95% C.I. 21,35)[1]
- **12-month median duration of response**
  (n=188, Kaplan-Meier Estimate, 95% C.I. 224,NE)[1]
- **16-month median overall survival**
  (n=202, 95% C.I. 471,NE)[1]

The effectiveness of VELCADE is based on response rate. There are no controlled trials demonstrating a clinical benefit such as an improvement in survival.

The most commonly reported adverse events were asthenia (including fatigue, malaise, weakness, fatigue aggravated and lethargy) (65%), nausea (64%), diarrhea (including loose stools) (55%), appetite decreased (including anorexia) (43%), constipation (43%), thrombocytopenia (43%), peripheral neuropathy (including peripheral sensory neuropathy and peripheral neuropathy aggravated) (37%), pyrexia (36%), vomiting (36%), and anemia (32%). 14% of patients experienced at least one episode of Grade 4 toxicity, with the most common toxicity being thrombocytopenia (3%) and neutropenia (3%).

† VELCADE, indicated for the treatment of multiple myeloma patients who have relapsed following front-line therapy and are refractory to their most recent therapy, has been issued marketing authorization with conditions, pending the results of studies to verify its clinical benefit. Patients should be advised of the nature of the authorization.

The safety and effectiveness of VELCADE in children and adolescents have not been established.

1 Open-label, single-arm, multicentre clinical trial of 202 patients, 183 patients with relapsed and refractory myeloma, who had received at least 2 prior lines of treatment and who were progressing on their most recent treatment. An IV bolus injection of VELCADE 1.3 mg/m²/dose was administered twice weekly for 2 weeks, followed by a 10-day rest period (21-day treatment cycle) for a maximum of 8 treatment cycles. Overall response rate made up of complete response (100% disappearance of the original monoclonal protein from blood and urine on at least 2 determinations at least 6 weeks apart by immunofixation and <5% plasma cells in the bone marrow on at least 2 determinations for a minimum of 6 weeks, stable bone disease and calcium) and partial response (≥50% reduction in serum myeloma protein and ≥90% reduction of urine myeloma protein on at least 2 occasions for a minimum of at least 6 weeks, stable bone disease and calcium).

† Clinical significance unknown. Reference: 1. VELCADE Product Monograph, Janssen-Ortho Inc., January 2005.

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DIVISION OF JANSSEN-ORTHO INC.

Member R&D PAAB MILLENNIUM*

Indicated for the treatment of multiple myeloma patients who have relapsed following front-line therapy, and are refractory to their most recent therapy.†

**INHIBIT THE PROTEASOME^
DISCOVER A UNIQUE TARGET IN MULTIPLE MYELOMA**

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It's the Clot that Kills.[1,2]

PLAVIX protects long-term against further atherothrombotic events.[2,3,4]

For patients with: • MI • Stroke • Peripheral arterial disease • Non-Q-wave MI • Unstable angina

In CAPRIE, PLAVIX provided an 8.7% RRR in combined stroke, MI and vascular death over 3 years* vs ASA in stroke, MI or PAD patients ($p = 0.045$). Absolute outcomes: PLAVIX 9.78%, ASA 10.64%. PLAVIX 75 mg o.d. (n = 9,599); ASA 325 mg o.d. (n = 9,586).[3] In CURE, PLAVIX + ASA provided a 20% RRR in combined stroke, nonfatal MI and CV death over 1 year vs placebo + ASA in patients with UA or non-Q-wave MI ($p = 0.00009$). Absolute outcomes: PLAVIX + ASA 9.3%, placebo + ASA 11.4%. PLAVIX 300 mg loading dose, then 75 mg o.d. (n = 6,259) or placebo (n = 6,303) plus ASA 75 - 325 mg o.d.[4]

* The long-term comparative clinical significance of these findings over 3 years is unknown.

MI, Stroke or Established Peripheral Arterial Disease (PAD). PLAVIX (clopidogrel bisulfate) is indicated for secondary prevention of atherothrombotic events (MI, stroke and vascular death) in patients with atherosclerosis documented by MI, stroke or established PAD.[5]

Acute Coronary Syndrome. PLAVIX, with ASA, is indicated for early and long-term secondary prevention of atherothrombotic events (MI, ischemic stroke, cardiovascular death and/or refractory ischemia) in patients with acute coronary syndromes without ST-segment elevation (unstable angina or non-Q-wave MI). These benefits were shown only when patients were concomitantly treated with ASA plus other standard therapies. These benefits were seen in medically managed patients and those managed with percutaneous coronary intervention (with or without stent) or CABG (coronary artery bypass graft).[5]

PLAVIX is contraindicated in patients with hypersensitivity to the drug substance or any product component, patients with active bleeding such as peptic ulcers or intracranial hemorrhage, and patients with significant liver impairment or cholestatic jaundice.[5]

PLAVIX should not be used in patients who have active gastrointestinal lesions with a propensity to bleed.[5]

PLAVIX should be used with caution in patients who may be at risk of increased bleeding from recent trauma, surgery or other pathological conditions, patients with severe or moderate renal impairment, and patients with moderate hepatic impairment who may have bleeding diatheses.[5]

In CAPRIE, the most common side effects were headache, flu-like symptoms and pain (7.6%, 7.5%, 6.4%).[3]

In CURE, major bleeding: PLAVIX + ASA 3.7%; placebo + ASA 2.7% ($p = 0.001$). Minor bleeding: PLAVIX + ASA 5.1%; placebo + ASA 2.4% ($p < 0.001$).[5]

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Bristol-Myers Squibb Pharmaceutical Group

Plavix® clopidogrel 75mg

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Continuing Education Credits/ Crédits de formation continue

C.C.C.E.P.
Canadian Council on Continuing Education in Pharmacy

The Educational Services Committee

The Educational Services Committee (ESC) of CSHP has been working in conjunction with the local host committee and the national office for approximately 10 months on the content and format of AGM 2005. The ESC is comprised of a core committee of 10 hospital pharmacists as well as 8 corresponding members from the CSHP branches.

Goal and Objectives for the 2005 AGM Program

Goal:
To provide registrants with quality educational sessions

Objectives:
- To provide registrants with educational sessions which inform, educate and motivate clinical practitioners and managers
- To provide leadership in hospital pharmacy practice by presenting sessions on innovative pharmacists' roles, pharmacy practice and pharmacy programs
- To promote life-long learning skills through active participation in problem-based workshops
- To provide registrants with networking and sharing opportunities through the exhibits program and poster sessions
- To provide an opportunity for Pharmacy Specialty Networks to meet

But et objectifs du programme de l'AGA 2005

But :
Présenter des conférences éducatives de qualité aux participants.

Objectifs :
- Présenter aux personnes inscrites des conférences éducatives susceptibles d'informer, d'instruire et de motiver les cliniciens et les gestionnaires
- Orienter l'exercice de la pharmacie d'hôpital en présentant des conférences sur les nouveautés touchant le rôle du pharmacien, l'exercice de la pharmacie et les programmes de pharmacie
- Favoriser des aptitudes d'apprentissage permanent par une participation active à des ateliers de formation centrés sur des problèmes
- Donner aux participants l'occasion d'établir des réseaux et d'échanger grâce au salon des exposants et aux séances d'affichage
- Donner l'occasion aux réseaux de spécialistes en pharmacie de se réunir

How to Get to AGM / Comment se rendre à l'AGA

Air Canada has been appointed the official airline for CSHP's Annual General Meeting and Educational Sessions 2005. Please quote Reference Number **CV053414** when making your travel arrangements.

As an AGM 2005 registrant, you will be offered the best available fare on all flights booked through Air Canada Convention Sales. Be sure to tell your travel agent to refer to **CV053414** in reference to your ticket and you could receive up to 50% off. Remember you will continue to accumulate your travel plan points while assisting CSHP.

You can book your flight in three convenient ways:

1. Through UNIGLOBE PREMIERE TRAVEL at 1-800-267-9372 or
2. Directly through Air Canada Convention Sales at 1-800-361-7585 or
3. Through your preferred travel agent quoting the Reference Number.

By ensuring **CV053414** appears on your ticket, you help support your organization-in advance, we thank you.

Ground Transportation/Transport terrestre

Via Rail is the official ground transportation for AGM 2005. Travel is valid from August 9th through August 19th, 2005. The CSHP discount is 35% off the full adult economy class, minimum fare $15.00 OR 5% off the full adult VIA-1 first class and/or sleeper fare. The discount fare applies to a maximum of two passengers per purchase. Please refer to CSHP's promo number **10524**. For schedule/fare information and reservations please call 1-888-842-7245. Taxis are readily available outside the terminal to the Westin Ottawa.

Where to Stay for AGM?/ Où loger durant l'AGA?

The Westin Ottawa

CSHP is pleased to offer a special room rate of $149.00 – Single or Double occupancy at The Westin Ottawa. All CSHP official conference related meetings will take place at this property. The Conference rate of $149.00 will be guaranteed until July 9, 2005. Don't miss out – make your reservation early. You may make your reservations by telephoning the hotel directly at (613) 560-7000. When doing so, please remember to make reference to **CSHP AGM 2005** for your conference rate.

How can a new company have already made a lasting impression?

Find out in September 2005.

AGM 2005 at a Glance / L'AGA d'un coup d'oeil

Educational Sessions

Sunday, August 14	08:30-15:00
Monday, August 15	08:30-16:30
Tuesday, August 16	08:30-16:00

Annual General Meeting

Sunday, August 14	15:00-17:00

Registration

Saturday, August 13	15:00-17:30
Sunday, August 14	07:30-17:00
Monday, August 15	07:30-17:00
Tuesday, August 16	08:00-16:00

Exhibits

Sunday, August 14	10:00-15:00
Monday, August 15	10:00-15:00

Lunch with Exhibitors

Sunday, August 14	12:00-14:00
Monday, August 15	12:30-14:30

Posters

Presentations:

Sunday, August 14	12:00-14:00
Monday, August 15	12:30-14:30

Viewing:

Sunday, August 14	10:00-10:30
Monday, August 15	10:00-10:30

Social Events at a Glance / Activités sociales d'un coup d'oeil

In order to provide accurate dinner numbers to our host facilities, we encourage registrants to purchase tickets for both the Fun Night at the Honest Lawyer on Sunday and the Past Presidents Dinner on Monday prior to your arrival at AGM 2005. Ticket sales are included on the AGM 2005 Registration Form. Tickets may be available on-site. Absolutely no tickets will be sold after 17:00 on Saturday, August 13. Thank you for your co-operation.

Saturday, August, 13

Research and Education Foundation Fundraising Golf Event
07:00-16:00; Breakfast 06:00
The Emerald Links Golf Course
Limit: 80 golfers

CHPRB Residency Mentorship Program Reception
17:30-19:30
The Westin Ottawa, Governor General Room

Opening Reception
19:00-23:00
The Westin Ottawa, Provinces Ballroom

Sunday, August 14

Fun/Run Walk Event
06:30-08:00
The Westin Ottawa Lobby

Wine and Chat
17:00-18:00
The Westin Ottawa, Les Saisons

Fun Night
Honest Lawyer Restaurantainment
18:00-24:00

Monday, August 15

Past Presidents Dinner and Dance
National Arts Centre (NAC)
18:00-01:00

Satellite Symposia / Symposiums satellites

Monday, August 15 – breakfast
Hosted by: LEO Pharma Inc.
Provinces Ballroom II
06:15-08:00

Upcoming Events / Événements à venir

Professional Practice Conference (PPC) 2006
Jan. 28 to Feb. 1, 2006
The Westin Harbour Castle
Toronto, ON

Professional Practice Conference (PPC) 2007
Jan. 27-31, 2007
The Westin Harbour Castle
Toronto, ON

Professional Practice Conference (PPC) 2008
February 2-6, 2008
The Westin Harbour Castle
Toronto, ON

Professional Practice Conference (PPC) 2009
Jan. 31 to Feb. 4, 2009
The Westin Harbour Castle
Toronto, ON

Professional Practice Conference (PPC) 2010
Jan. 30 to Feb. 3, 2010
The Westin Harbour Castle
Toronto, ON

Annual General Meeting (AGM) 2006
August 12-15, 2006
Le Centre Sheraton
Montréal, QC

Annual General Meeting (AGM) 2007
August 11-14, 2007
Delta Regina
Regina, SK

Annual General Meeting (AGM) 2008
August 9-12, 2008
Saint John Hilton & Convention Centre
Saint John, NB

Annual General Meeting (AGM) 2009
August 8-11, 2009
TBA
Winnipeg, MB

Ottawa 150 1855-2005

Bob Chiarelli
Mayor / Maire

On behalf of Members of Council and the 840, 000 residents of the City of Ottawa, it gives me great pleasure to extend a very warm welcome to all those participating in the **58th Annual General Meeting and Educational Sessions** of the **Canadian Society of Hospital Pharmacists**, and taking place in the nation's capital from **August 13th to 16th 2005**.

I would also like to take this opportunity to congratulate the Canadian Society of Hospital Pharmacists, volunteers, sponsors as well as the delegates from across Canada, who have committed their time, energy and talents to the successful organization of this important meeting of national scope.

As Mayor of the host city and in celebration of Ottawa's 150th anniversary, I invite visitors to explore the numerous civic as well as national treasures and historic sites, which Canada's capital has to offer.

Allow me to wish you all a most pleasant stay.

Au nom des membres du Conseil municipal et des 840 000 résidents d'Ottawa, c'est avec grand plaisir que je souhaite chaleureusement la bienvenue aux participants de la **58e Assemblée générale annuelle et des séances d'information de la Société canadienne des pharmaciens d'hôpitaux** et qui auront lieu dans la capitale nationale **du 13 au 16 août 2005**.

Je tiens également à féliciter la Société canadienne des pharmaciens d'hôpitaux, les bénévoles, les commanditaires ainsi que les délégués de partout au Canada, qui ont consacré temps, énergie et compétences à l'organisation réussie de cette réunion importante d'envergure nationale.

En tant que maire de la ville hôte et en célébration du 150e anniversaire d'Ottawa, j'invite les visiteurs à découvrir les nombreux trésors municipaux et nationaux ainsi que les nombreux lieux historiques qu'abrite la capitale nationale.

Permettez-moi de vous souhaiter à tous un séjour des plus agréables.

Bob Chiarelli
Mayor/Maire

FROM ONE TO ONE MILLION

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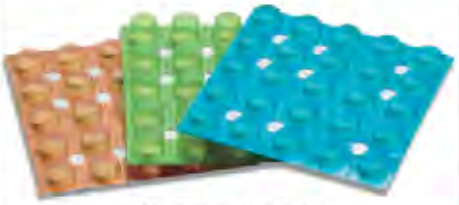

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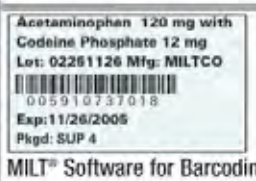

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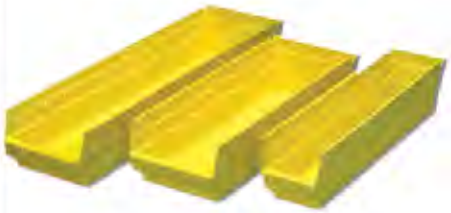

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CSHP 58th AGM and Educational Sessions/
58e Assemblée générale annuelle et séances éducatives de la SCPH

Saturday, August 13 • Samedi le 13 août

07:00-16:00 **Research & Education Foundation Fundraising Golf Event**
Tournoi de golf de la Fondation pour la recherche et l'éducation

Emerald Links Golf Club (bus departing from the Westin). Have some fun and help raise funds for the R&E Foundation.

Come out for a casual round of golf using a best ball format, shotgun start. We encourage everyone to participate, golfers or not. Buses will return around 4:00 pm

15:00-17:30 **Registration/Inscription**

COAT CHECK/VESTIAIRE

17:30-19:30 **CHPRB Residency Mentorship Program Reception/**

Réception du programme de mentorat de la SCPH pour les résidents

GOVERNOR GENERAL/GOUVERNEUR GÉNÉRAL

19:00-23:00 **Opening Reception/**
Réception d'ouverture

PROVINCES BALLROOM/SALLE DES PROVINCES

Dress: Casual

Reconnect with friends and colleagues and meet new ones while gambling someone else's money away. This team event will allow you to play Blackjack, Roulette, Craps and Texas Hold 'em in the presence of "Dignitary Dealers". This, combined with the cash bar, will provide the perfect environment for you to catch up on all of the "gossip". All of your points will go towards your team. The teams that gain the most points will win some great prizes!

Sunday, August 14 • Dimanche le 14 août

06:30-08:00 **Fun Run/Walk Event/**
Course/promenade pour amateurs

MEET – HOTEL LOBBY

You won't be able to skate on the Rideau Canal, but it is the perfect route to run, walk, or limp. Following your morning workout, everyone is invited back to the hotel for a hot buffet breakfast. You'll receive a souvenir T-shirt for your effort.

07:30-17:00 **Registration/Inscription**

COAT CHECK/VESTIAIRE

08:30-08:45 **Opening Remarks/**
Remarques préliminaires

CONFEDERATION BALLROOM I/
SALLE DE LA CONFÉDÉRATION I

08:45-09:15 **Plenary Session/Séance plénière**

CONFEDERATION BALLROOM I/
SALLE DE LA CONFÉDÉRATION I

Pharmacists' Role in Peacekeeping

Régis Vaillancourt, PharmD, FCSHP
Canadian Forces Health Services
Ottawa, ON

09:15-10:00 **The Evolution of Electronic Health Record-Based Drug Information Systems in Canada**

Kurtis Bishop
Canada Health Infoway
Toronto, ON

10:00-10:30 **Break/Posters/Pause/Affiches**

CONFEDERATION BALLROOM II/III/
SALLE DE LA CONFÉDÉRATION II/III

10:30-11:15 **Concurrent Session/**
Sessions concomitantes

PROVINCES BALLROOM I/SALLE DES PROVINCES I

1. **Malpractice Insurance: How to Protect Yourself and Your Patients**

   Patricia McLean, RN, BN, LL.B
   Canadian Nurses Protective Society
   Ottawa, ON

2. **Short and Snappies/En un clin d'oeil**

   PROVINCES BALLROOM II/SALLE DES PROVINCES II

   TNT: Blasting LDL to Lower Targets

   Lynn Yang, BScPhm, ACPR
   The University of Ottawa Heart Institute
   Ottawa, ON

   Use of Proton Pump Inhibitors and the Incidence of *Clostridium difficile* diarrhea: Is There a Link?

   Shelita Dattani, PharmD
   Queensway Carleton Hospital
   Ottawa, ON

   Drotrecogin Alfa (activated) for the Treatment of Severe Sepsis: Piecing together the ENHANCE Study

   Salmaan Kanji, PharmD
   The Ottawa Hospital
   Ottawa, ON

11:15-12:00 **Concurrent Sessions/**
Sessions concomitantes

PROVINCES BALLROOM I/SALLE DES PROVINCES I

1. **Pharmacy Technician Delegation: Opportunities and Challenges**

   Michael Tierney, BScPhm, MSc
   CCOHTA
   Ottawa, ON

   Anne-Marie Dugal
   The Ottawa Hospital
   Ottawa, ON

PROVINCES BALLROOM II/SALLE DES PROVINCES II

2. **Use of Old Drugs for Neuropathic Pain in Palliation – Methadone, Ketamine, Lidocaine**

   Sally Tierney, BScPhm
   Sisters of Charity of Ottawa Health Services
   Ottawa, ON

12:00-14:15 **Lunch/Exhibitors/Poster/**
Déjeuner/Kiosques/Affiches

CONFEDERATION BALLROOM II/III/
SALLE DE LA CONFÉDÉRATION II/III

14:15-15:00 **Plenary Session/Séance plénière**

CONFEDERATION BALLROOM I/
SALLE DE LA CONFÉDÉRATION I

Challenges of the Special Access Programme (SAP) – A Regulator and a Hospital Pharmacist's Perspectives

Joanne Garrah, BSc, MSc
Health Canada
Ottawa, ON

Darcy Nicksy, BScPhm, RPh
The Hospital for Sick Children
Toronto, ON

15:00-17:00 **Annual General Meeting/ Assemblée générale annuelle**

CONFEDERATION BALLROOM I/ SALLE DE LA CONFÉDÉRATION I

17:00-18:00 **Wine & Chat/Vin et causette**

LES SAISONS

18:00-24:00 **Fun Night at the "Honest Lawyer"/ Soirée d'agrément au « Honest Lawyer »**

OFFSITE: HONEST LAWYER

Dress: Casual

Honest Lawyer (Honest Pharmacists for the Day!), located in the famous Byward Market, will host the fun night. This bar atmosphere is within walking distance of the hotel. Join us for an evening of fun games (e.g. pool, bowling, pinball, etc.), great food and other surprises, complimented by a renowned musician from the Ottawa area. As is tradition, creativity at a night like this may help out your team.

Monday, August 15 • Lundi le 15 août

06:15-08:00 **Satellite Symposium (breakfast included)/ Symposium satellite (petit déjeuner inclus)**

PROVINCES BALLROOM II/SALLE DES PROVINCES II

Thrombosis – Anticoagulation in Special Populations

Hosted by: LEO Pharma Inc.

07:30-17:00 **Registration/Inscription**

COAT CHECK/VESTIAIRE

08:15-08:30 **Announcements/Annonces**

CONFEDERATION BALLROOM I/ SALLE DE LA CONFÉDÉRATION I

08:30-09:15 **Plenary Session/Séance plénière**

CONFEDERATION BALLROOM I/ SALLE DE LA CONFÉDÉRATION I

Strategic Thinking for Practice: Application of Critical Thinking to the Practice of Pharmacy

Cleo Boyd, MA
University of Toronto at Mississauga
Mississauga, ON

09:15-12:30 **CHPRB Residency Workshop/ Atelier sur la résidence du CCRPH**

ONTARIO

Giving & Receiving Constructive Feedback

Helen Roberts
Providence Health Care
Delta, BC

09:15-10:00 **Concurrent Sessions/ Sessions concomitantes**

PROVINCES BALLROOM I/SALLE DES PROVINCES I

1. **Drugs are technologies too: An Overview of Health Technology Assessment at the Canadian Coordinating Office for Health Technology Assessment (CCOHTA)**

   Don Husereau, BScPhm, MSc
   CCOHTA
   Ottawa, ON

PROVINCES BALLROOM II/SALLE DES PROVINCES II

2. **Metabolic Disturbances Associated with Atypical Antypsychoic Use**

   Barbara Thomas, BScPhm
   Healthcare Corporation of St. John's
   St. John's, NL

10:00-10:30 **Break/Posters/Pause/Affiches**

CONFEDERATION BALLROOM II/III SALLE DE LA CONFÉDÉRATION II/III

10:30-12:30 **Workshops/Ateliers**

QUEBEC/QUÉBEC

1. **So you want to be an Infectious Diseases Pharmacist**

   Margaret Gray, BSP
   Capital Health
   Edmonton, AB

   Rosemary Zvonar, BScPhm
   The Ottawa Hospital
   Ottawa, ON

PROVINCES BALLROOM II/SALLE DES PROVINCES II

2. **Complete Care of Patients with Diabetes**

   Derek Jorgenson, PharmD
   Saskatoon Health Region
   Saskatoon, SK

LES SAISONS

3. **The 10-minute Neurological Exam for Pharmacists of all Ages**

   Rakesh Patel, MSc, PharmD, MD
   The Ottawa Hospital
   Ottawa, ON

4. **PSN Session – Cardiology/Geriatrics – Cholesterol and the Elderly/ Session RSP – Cardiologie/Gériatrie – Cholestérol et la personne âgée**

   PROVINCES BALLROOM I/SALLE DES PROVINCES I

   An Age Old Issue

   Ross Tsuyuki, PharmD, FCSHP
   University of Alberta
   Edmonton, AB

   What's the Risk? What Every Pharmacist Needs to Know

   Susan Bowles, PharmD, FCSHP
   Queen Elizabeth II Health Sciences Centre
   Halifax, NS

12:30-14:30 **Lunch/Exhibitors/Poster/ Déjeuner/Kiosques/Affiches**

CONFEDERATION BALLROOM II/III SALLE DE LA CONFÉDÉRATION II/III

14:30-15:30 **Plenary Session/Séance plénière**

CONFEDERATION BALLROOM I/ SALLE DE LA CONFÉDÉRATION I

Challenges in Education-Future Practice

Monique Richer, PharmD
Université Laval
Québec, QC

15:30-16:30 **Concurrent Sessions/ Sessions concomitantes**

PROVINCES BALLROOM I/SALLE DES PROVINCES I

1. Medication Reconciliation: A New Patient Safety Goal

Ann Nickerson, BScPhm
South-East Regional Health Authority
Moncton, NB

PROVINCES BALLROOM II/SALLE DES PROVINCES II

2. Solid Organ Transplant 101 for Pharmacists

Nilu Partovi, PharmD, FCSHP
Vancouver Hospital & Health Sciences Centre
Vancouver, BC

18:00-01:00 **Past Presidents' Dinner and Dance/ Dîner dansant des anciens présidents**

OFFSITE: NATIONAL ARTS CENTRE/ CENTRE NATIONAL DES ARTS

Dress: Business Casual

This gala event will honour the past presidents of CSHP. The NAC is within walking distance and overlooks the Rideau Canal. We will serve you fine cuisine and provide one of the best dance bands in the Ottawa area. We will be awarding the team with the most points their prizes and dancing the night away. A cash bar will be available.

Tuesday, August 16 • Mardi le 16 août

08:00-16:00 **Registration/Inscription**

COAT CHECK/VESTIAIRE

08:15-08:30 **Announcements/Annonces**

CONFEDERATION BALLROOM I/ SALLE DE LA CONFÉDÉRATION I

08:30-09:30 **Plenary Session/Séance plénière**

CONFEDERATION BALLROOM I/ SALLE DE LA CONFÉDÉRATION I

Integrating a Pharmacist into Family Practice: Qualitative Results from the IMPACT Study

Barbara Farrell, PharmD, FCSHP
Sisters of Charity of Ottawa Health Services
Ottawa, ON

Kevin Pottie, MD, MClSc, CCFP
Sisters of Charity of Ottawa Health Services
Ottawa, ON

09:30-10:15 **Concurrent Sessions/ Sessions concomitantes**

PROVINCES BALLROOM I/SALLE DES PROVINCES I

1. Aboriginal Health Care Issues

Kurt Schroeder, BScPhm
Queensway Carleton Hospital
Ottawa, ON

PROVINCES BALLROOM II/SALLE DES PROVINCES II

2. New Antifungals – What's up with that?

Alfred Gin, PharmD
Health Sciences Centre, Winnipeg
Winnipeg, MB

10:15-10:45 **Break/Pause**

FOYER

10:45-12:45 **Workshops/Ateliers**

PROVINCES BALLROOM I/SALLE DES PROVINCES I

1. Addressing the Hospital Pharmacy Management Crisis: Development of Strategies and Solutions (A Workshop)

Neil MacKinnon, PhD, RPh
Dalhousie University
Halifax, NS

QUEBEC/QUÉBEC

2. Complete Care of Patients with Diabetes

Derek Jorgenson, PharmD
Saskatoon Health Region
Saskatoon, SK

LES SAISONS

3. The 10-minute Neurological Exam for Pharmacists of All Ages

Rakesh Patel, MSc, PharmD, MD
The Ottawa Hospital
Ottawa, ON

4. PSN Session – ID/ Session RSP – Infectiologie

PROVINCES BALLROOM II/SALLE DES PROVINCES II

The Role of the Microbiology Lab in Infectious Disease

Baldwin Toye, MD, FRCPC
The Ottawa Hospital
Ottawa, ON

Pharmacoeconomics of Infectious Diseases Pharmacotherapy: From Assessment to Decision

Erwin Friesen, PharmD, FCSHP
Capital Health
Edmonton, AB

12:45-14:15 **Lunch Break/Pause déjeuner**

14:15-15:00 **Plenary Session/Séance plénière**

CONFEDERATION BALLROOM I/ SALLE DE LA CONFÉDÉRATION I

Short and Snappies/En un clin d'oeil

Insulin Glargine

Maryann Hopkins, BSP, CDE
The Ottawa Hospital
Ottawa, ON

Bortezomib

Darcy McLurg, BScPhm, ACPR
The Ottawa Hospital
Ottawa, ON

Memantine – A Review of its Role in Alzheimer's Disease

Alexander Kuo, BScPhm, ACPR
The Ottawa Hospital
Ottawa, ON

15:00-16:00 **Plenary Session/Séance plénière**

CONFEDERATION BALLROOM I/ SALLE DE LA CONFÉDÉRATION I

The Cardiovascular Safety of COX-2 Inhibitors: What Should We Do Now?

Steven Shalansky, PharmD, FCSHP
St. Paul's Hospital
Vancouver, BC

16:00 **Close of the CSHP Educational Sessions/ Clôture de la 58e Assemblée générale annuelle**

Sunday, August 14 • Dimanche le 14 août

Pharmacists' Role in Peacekeeping

L. Col. Régis Vaillancourt, Canadian Forces Health Services, Ottawa, ON

The term "peacekeeping" has only been in our vernacular since 1956 when Lester B. Pearson proposed the deployment of an international peace force under the auspices of the United Nations (UN). Since then, Canadians have been involved in over 50 UN peacekeeping missions. As the face of peacekeeping has evolved, so too has the role of the pharmacist during these missions. A pharmacist deployed with a peacekeeping operation has a wide scope of duties and responsibilities.

During peacekeeping missions, the pharmacist plays an important role as an integral member of the multidisciplinary health care team. During a mission, pharmacists perform the duties of a hospital pharmacist, a drug information pharmacist, and community pharmacist all at the same time. In addition to the pharmacy specific tasks, pharmacists are responsible for medical supply encompassing procurement and management of everything from medications to major hospital equipment. Pharmacists are responsible for vaccine, blood and blood product management and storage. Pharmacists also liaise with allied military and civilian medical services in order to coordinate the practical provision of care for both the peacekeeping force and local personnel.

As with the role of pharmacists everywhere the pharmacists role during peacekeeping is ever changing and evolving to meet the requirements to provide optimal patient care in sometimes unique and challenging situations. The result is a very challenging but ultimately rewarding experience in playing a positive role on the global stage.

The Evolution of Electronic Health Record-Based Drug Information Systems in Canada

Kurtis Bishop, Canada Health Infoway, Toronto, ON

Canada Health Infoway was launched in late 2000 as a result of an accord among Canada's First Ministers agree "to work together to strengthen a Canada-wide health infostructure." Infoway is an independent, not-for-profit corporation equally accountable to 14 Federal, Provincial and Territorial governments. Infoway has received $1.2 billion in capitalization since inception.

One of Infoway's key programs is Drug Information Systems. The objective of this program is to create the drug information content for Electronic Health Records in each jurisdiction. This presentation will describe Infoway's EHR and Drug Information Systems (DIS) strategy. The objectives and expected benefits of DIS implementations will be outlined. The state of drug system planning and development will be described for each jurisdiction in Canada. Some of the challenges and obstacles will also be explored. There will be particular focus in the presentation on the opportunities that DIS development presents for hospital pharmacists.

Goals and Objectives

1. Explain Canada's approach to Electronic Health Record development and to describe Infoway's role.
2. Describe the blueprint for the EHR in Canada and the role of Drug Information Systems (DIS)
3. Outline the objectives, strategy and expected benefits from DIS development in Canada
4. Provide the audience with an understanding of the potential timeframe and implications of DIS development in each jurisdiction across Canada

Self-Assessment Questions

1. What are the main elements of an Electronic Health Record according to Canada Health Infoway?
2. What are some of the key benefits of Drug Information Systems – for patients, physicians and pharmacists?
3. What are the main implementation challenges associated with DIS implementation?

TNT: Blasting LDL to Lower Targets

Lynn Yang, BScPhm, ACPR, University of Ottawa Heart Institute, Ottawa, ON

Several large, randomized, controlled trials have demonstrated that HMG-CoA reductase inhibitors (statins) reduce the risk of death or cardiovascular events over a wide range of cholesterol levels. A previous trial has shown that lowering low density lipoprotein (LDL) below currently recommended levels benefits those with acute coronary syndrome. This presentation will focus on evidence for lowering LDL below current targets in patients with stable coronary heart disease (CHD).

Goals and Objectives

1. To demonstrate that achieving LDL levels lower than target may yield more benefits than just reaching target levels of LDL in stable CHD patients.
2. To make pharmacists aware of new target LDL levels in hyperlipidemia guidelines.

Self-Assessment Questions

1. What are the target values for LDL?
2. What benefits are achieved by lowering LDL to target levels or lower?
3. Should all patients with CHD be started on a statin regardless of LDL level?

Drotrecogin alfa (activated) for the Treatment of Severe Sepsis: Piecing Together the ENHANCE Study

Sal Kanji, BScPharm, PharmD, The Ottawa Hospital and Ottawa Health Research Institute, Ottawa, ON

Severe sepsis occurs when the body's normal protective response to infection is overwhelmed resulting in a systemic inflammatory and pro-coagulant state leading to multi-organ failure. It is common among adults admitted to the ICU and has a mortality rate of 30-60%.

In 2001 the PROWESS trial described the first novel anti-sepsis therapy, drotrecogin alfa (activated), to significantly reduce the mortality associated with severe sepsis.
\A subgroup analysis of this study suggested that the mortality benefit may be limited to more severely ill patients (i.e., APACHE II score $\geq$ 25). In December of 2002 Canadian guidelines were published suggesting that its use be limited to more severely ill patients and in March of 2003 drotrecogin alfa (activated) was made available in Canada.

Since the PROWESS trial was published, two more phase III-IV studies have been completed but not published. The ADDRESS trial (mandated by the FDA) was designed to evaluate mortality benefit with drotrecogin alfa (activated) in less severely ill patients with severe sepsis. The ENHANCE study was a large worldwide open label study that was conducted to further evaluate the mortality benefit and safety of drotrecogin alfa (activated). While neither of these trials have been published in full, a significant amount of data is available from partial publications, published abstracts, poster presentations, and company released data. This data will be compiled and reviewed in the context of how it relates to patient selection, timing of administration and safety.

Goals and Objectives

1. To compile and review the available data from the unpublished ENHANCE trial and identify issues related to patient selection, drug administration and safety that warrant review.
2. To emphasise the importance of post-marketing surveillance of new drugs.

Self-Assessment Questions

1. Should patients diagnosed with severe sepsis and single organ failure receive drotrecogin alfa (activated)?
2. What is the time window after diagnosis of severe sepsis after which drotrecogin alfa (activated) should not be administered?

Pharmacy Technician Delegation: Opportunities and Challenges

Anne-Marie Dugal, The Ottawa Hospital; Mike Tierney, Canadian Coordinating Office for Health Technology Assessment, Ottawa, ON

The goal of this session is to describe the use of pharmacy technicians to manage a clinical drug trial service in a hospital and to discuss the opportunities and challenges for the delegation of responsibilities that have traditionally been held by pharmacists, to pharmacy technicians.

The Pharmacy Department of the Ottawa Hospital actively supports approximately 60-70 clinical drug trials at any time and the clinical drug trial service of the department is largely delegated to pharmacy technicians. Responsibilities include protocol review, randomization, blinding, drug preparation, inventory control and drug accountability, meeting with study monitors, on-call support and billing. These activities are recognized in the job description and the classification of these positions. Support is provided by the department's drug information service and responsibility is assumed by pharmacy management.

This service provides an example of how hospital pharmacy can extend the role of the pharmacy technician to improve the efficiency and effectiveness of departmental operations. However, there is much variation in the degree of delegation amongst practice sites and across provincial jurisdictions. Regulatory, institutional and practice initiatives will be presented to illustrate the opportunities and challenges in moving forward with delegation to pharmacy technicians.

Goals and Objectives

1. To describe a pharmacy technician-managed clinical drug trial service.
2. To describe the challenges of delegation of responsibilities traditionally held by pharmacists, to pharmacy technicians.
3. To update CSHP members of the activities of the Task Force on Delegation of Functions to Pharmacy Technicians.

Self-Assessment Questions

1. What are the opportunities for delegating additional functions to pharmacy technicians in your institution?
2. What steps and processes need to be in place to safely delegate additional functions to pharmacy technicians?

Use of Old Drugs for Neuropathic Pain in Palliation – Methadone, Ketamine, Lidocaine

Sallyanne Tierney, BScPhm, SCO Health Service, Ottawa ON

Pain in palliative patients is challenging to treat and a threat to a patient's quality of life. Traditional mu opioids such as morphine, hydromorphone used to alleviate neuropathic pain are often ineffective and can result in opioid toxicity. Drugs such as: methadone, ketamine and lidocaine are finding new indications in difficult to treat neuropathic pain syndromes.

The basis of the neurobiology of pain and especially the phenomenon of neuropathic pain are important in understanding the new indications for these old drugs. Neuropathic pain represents a diverse group of conditions, and one single mechanism cannot explain the underlying pathology of these syndromes. The NDMA pathway is a major excitatory CNS system involved in the neurobiology of pain. Methadone is a combination of an opioid receptor agonist and NDMA receptor antagonist. Ketamine, a NDMA receptor antagonist combined in subanesthetic doses with mu opioids can help to manage difficult pain, reduces overall opioid dose and reverses opioid toxicity. Nerve conduction is mediated in part by changes in ion concentration across membranes. Lidocaine is a sodium channel blocker agent and thus interrupts the nerve conduction channels. It is beneficial in treating both neuropathic pain and mixed (neuropathic and nociceptive) pain syndromes.

Goals and Objectives

1. To provide pharmacists with an understanding of the basic neurobiology of pain, nerve conduction, pain receptors as it relates to pharmacologic treatment.
2. To appreciate the diversity of neuropathic pain syndromes and the multi-modal approach to its treatment.
3. To identify the effects, precautions, and drug interactions of drugs such as methadone, ketamine and lidocaine in treating neuropathic pain.

Self-Assessment Questions

1. What is the rational for using NDMA receptor antagonists or Sodium channel blocking agents in treating pain?
2. What should patients taking methadone for pain treatment be told regarding food and drug interactions?

Challenges of the Special Access Programme (SAP) – A Regulator and a Hospital Pharmacist's Perspectives

Joanne Garrah, BSc, MSc, Health Canada, Special Access Programme, Ottawa ON, Darcy L. Nicksy, BScPhm, RPh, Hospital for Sick Children, Toronto, ON

Health Canada's Special Access Programme is an emergency mechanism to provide limited access to products that are not available to practitioners treating patients with serious or life-threatening conditions, when alternatives have failed or are not available.

In recent years, the SAP has experienced tremendous pressure from manufacturers, health care professionals and patients to provide unimpeded access to products at many different stages of product development including: approved drugs that were never marketed; drugs that are in shortage or were discontinued and; approved drugs that were withdrawn from the market because of safety issues. In many cases, this has resulted in intentional and unintentional misuse of the programme and has challenged the programme from a regulatory, policy and operational perspective.

At the front-line hospital level the challenges include: confirmation of authorization (or not); delays in shipments for acutely ill patients; future use versus "borrowing" drug on hand; paper work and tracking of all patients for high use items, especially those previously marketed and either on backorder or discontinued by the manufacturer; after hours access to authorization and drug supply; knowing what drugs are on the SAP list for consideration; delays in getting a brand new drug on the list and subsequently to the patient; pharmaceutical compounding from chemicals not acquired in Canada; excessive delays for controlled drugs or narcotics.

The goal of this session is to provide a regulatory overview of the SAP and to discuss the challenges that pharmacists face on the front line in accessing products on an emergency basis through the SAP. A panel discussion will allow participants to ask questions.

Goals and Objectives

1. To provide pharmacists with an understanding of some of the challenges faced by both regulators and front line pharmacists in the operation and administration of the Special Access Programme (SAP)
2. To present pharmacists with solutions as to how to overcome some of these challenges.

Self-Assessment Questions

1. What is the mandate of the SAP?
2. List 5 challenges faced by hospital pharmacists in dealing with the SAP.

Giving And Receiving Constructive Feedback

Helen Roberts, B. Commerce, Masters Adult Education, Delta, B.C.

Pharmacists in a hospital setting often find themselves in situations where they are required to provide constructive feedback to students and residents. While this is an expectation of the pharmacists' role most individuals feel some anxiety in these situations. One of two results often occur due to this discomfort. Either the feedback is shared in a way that the student/resident cannot hear the message or key information is withheld. In either case this is a loss for the resident/student, it may also negatively impact the peers and patients of the resident/student.

What prevents most pharmacists from giving feedback is the lack of tools and training in this area. Once people feel confident that they are taking a fair and balanced approach; when they sense they are choosing words with will not cause and explosive reaction; and, when they have developed a clear idea of how to respond if people react negatively, their willingness to provide feedback and the effectiveness of their efforts increases dramatically.

An additional issue which will be addressed is the participants personal reaction to feedback. If an individual can become more open to feedback, no matter how poorly it is provided, it opens a wide range of possibilities for personal development. How one responds to "criticism" also impacts ones willingness to give it. A persons' reluctance give feedback will diminish as their ability to hear it increases.

Goals and Objectives

1. To help participants find ways of giving and receiving difficult feedback
2. To prepare for a negative (and positive) reaction
3. To help those who do not hear the message, "get it"

Self-Assesment Questions

1. Am I aware of the behaviours I have that might get in the way of providing effective feedback?
2. What are the key actions for giving and receiving constructive feedback?

Drugs Are Technologies Too: An Overview of Health Technology Assessment at the Canadian Coordinating Office for Health Technology Assessment (CCOHTA)

Donald R. Husereau, BScPharm, MSc, CCOHTA, Ottawa, ON

The goal of this session is to provide pharmacists with an understanding of what health technology assessment is, how it is currently conducted nationally and internationally and how it can be useful to them in their practice.

A health technology can be defined as any intervention inteneded to promote health; prevent, diagnose or treat disease; or aid in rehabilitation or long term care. In addition to drugs, health technolgies include vaccines, devices, equipment, materials, medical and surgical procedures, and health systems.

Health technology assessment is a multidisciplinary field of policy analysis that studies the medical, social, ethical, legal, economic and organisational implications of the development, diffusion, and use of health technologies. Its goal is to provide input into decision making in policy and practice.

The Canadian Coordinating Office for Health Technology Assessment (CCOHTA) was established in 1989. It is an independent, not-for-profit corporation funded by Federal, Provincial and Territorial (F/P/T) health ministries. As such, CCOHTA is a primary source of objective, evidence-based information on drugs, medical devices & health systems.

This session will provide in more detail the methods used to produce high quality health technology assessments, the issues that need to be considered when conducting assessments and differences in approaches of HTA nationally and internationally. It will also provide information about other HTA organizations and HTA-related initiatives that are occurring now and in the future.

Goals and Objectives

1. To provide pharmacists with an understanding of the field of health technology assessment and how it is practiced
2. To give pharmacists an understanding of what methods are required for rigorous health technology assessment

Self-Assesment Questions

1. What is health technology assessment and who benefits from it?
2. What should I consider when conducting HTA?
3. When is HTA information useful to me and where can I find it?

Metabolic Disturbances Associated with the Use of the Atypical Antipsychotics

Barbara Thomas, PhC, Clinical Pharmacist, Waterford Site, Health Care Corporation of St. John's, NL

Antipsychotic medication is an integral component of treatment for those with psychotic disorders. The introduction of the atypical antipsychotics over the past decade has led to significant advantages in the care of these individuals as the atypical agents have clearly shown less potential to cause extrapyramidal side effects (EPS) and tardive dyskinesia (TD).

However, use of these newer agents has been associated with metabolic disturbances including weight gain, diabetes and dyslipidemias. Because of the close associations between these metabolic disturbances and cardiovascular disease, there is heightened interest in the relationship between the atypical antipsychotics and the development of these major cardiovascular disease risk factors.

As the use of these agents continues to grow and expand into new indications such as bipolar affective disorder, it is crucial that we define and utilize monitoring parameters and treatment strategies to minimize risks for cardiovascular disease in this vulnerable patient population.

Goals and Objectives

1. Review data on the prevalence, patterns, and etiology of the various metabolic disturbances associated with the atypical antipsychotics including weight gain, diabetes and dyslipidemias
2. Discuss contributing factors that may affect the occurrence of these metabolic disturbances as well as their management
3. Identify monitoring parameters that should be employed with atypical use to appropriately assess for the occurrence of these metabolic adverse effects
4. Review treatment strategies that may be helpful in the prevention and treatment of these disturbances

So You Want to Be an Infectious Diseases Pharmacist

Margaret Gray, BSP, Capital Health, Edmonton AB, Rosemary Zvonar, BScPhm, The Ottawa Hospital, Ottawa, ON

Studies have consistently shown that antibiotic utilization is suboptimal 50% of the time. In addition, antimicrobials consistently rank as one of the top expenditures in a hospital or health region's drug budget. These factors, combined with the challenges of treating resistant organisms that result from inappropriate antibiotic use, make the area of infectious diseases an ever-increasing focus of hospital drug – and staff – budgets.

The goal of this session is to reinforce the importance of appropriate antimicrobial use as a public health issue (within the hospital environment) and to highlight the important role pharmacists can play in improving antimicrobial use within their institution. The desired outcomes include a reduction in the proliferation of multi-drug resistant organisms and a decrease in antimicrobial expenditures, without compromising patient care.

The workshop facilitators will outline key issues to support the establishment of an Infectious Diseases or Antimicrobial Utilization position in your institution. Practical strategies and approaches to optimize antimicrobial use in the hospital setting will be provided. The second part of the workshop will focus on pharmacist skills and resources needed to work in an environment where infectious disease remains a significant contributor to patient morbidity and mortality.

Goals and Objectives

1. To provide justification for the implementation of clinical Infectious Disease pharmacy services or an Antimicrobial Utilization program in the hospital setting.
2. To provide pharmacists with tools and resources to feel comfortable in providing care to patients with infectious complications.

Self-Assesment Questions

1. Describe three targeted areas or programs related to infectious diseases in which individual pharmacists can have an impact within their institution
2. Discuss the pharmacists' role in a multidisciplinary team to enhance antimicrobial utilization.

Complete Care of Patients with Diabetes

Derek Jorgenson, BSP, PharmD, Saskatoon Health Region, Saskatoon, SK

Realistically speaking, diabetes is not so much a disease as it is a risk factor for a multitude of other diseases. Luckily, the development of many of these other diseases can be delayed or even prevented using a variety of risk reduction strategies. Unfortunately, many of these strategies continue to be underutilized, despite the aging nature of the evidence that supports their use.

The value of including a pharmacist within the immediate circle of care of patients with diabetes is now well recognized by those within the medical world, as well as by members of the public. In addition to being a patient educator, pharmacists must be prepared to take the primary responsibility for managing these patients' very complex drug regimens.

This workshop will attempt to improve the participants' comfort level in providing pharmaceutical care for patients with diabetes. A generalist pharmacist, not an expert in diabetes care, will facilitate this case based workshop. Participants will use their existing knowledge base, in addition to the many "diabetes care tools" available, to demonstrate how a generalist pharmacist can identify and solve complex drug related problems in patients with diabetes, without being "experts". This session will require the interaction of the participants to be of value. Please arrive prepared to share your thoughts with the group.

Goals and Objectives

1. To improve the participants' comfort level in providing pharmaceutical care for patients with diabetes
2. To make participants aware of the many resources available to assist in the provision of pharmaceutical care for patients with diabetes

Self-Assessment Questions

1. List three resources (print or electronic) that can be used to assist in the provision of pharmaceutical care to patients with diabetes?
2. Should all diabetics be taking a statin regardless of their cholesterol level?
3. Which diabetics should be taking ASA for vascular protection?

The 10-minute Neurological Exam for Pharmacists of all Ages

Rakesh V. Patel, MD, PharmD, MSc, Staff Intensivist, University of Ottawa, Ottawa, ON

The Neurologic examination is steeped in tradition and can be quite mystifying and magical to all except the seasoned Neurologist. It is an exam that requires strict concentration by the patient and examiner. It has many components. The components utilized depend on the clinical situation and the ability of the patient to co-operate.

The effects of drugs on the Neurologic exam can vary from subtle to obvious. It all depends on the drug and amount taken.

There is no way that I can teach you, nor will you learn, the entire exam in this one session. That should not be the point. The point is to de-mystify the exam so that you can interpret the clinical findings documented in the patient's chart or observed by you during the course of your interaction with the patient, in order to help you identify, solve and prevent drug-related problems.

The knowledge may also come in handy to help you identify the effects of too many adult beverages, consumed during this conference, on your senses. Cheers!

Goals and Objectives

1. To provide pharmacists with a practical understanding of the basic screening Neurologic exam.
2. To enable pharmacists to recognize some of the effects drugs may have on the Central and Peripheral Nervous systems in order to identify, solve and prevent drug-related problems.

Medication Reconciliation: A New Patient Safety Goal

Ann Nickerson, BSc(Pharm), South-East Regional Health Authority, Moncton, NB

The driving force behind the concept of medication reconciliation is preventing adverse drug events. Studies have revealed that over half of all hospital medication errors occur at the interface of care including admission, and/or transfer to another setting, service provider or level of care within or outside the hospital setting. An accurate medication history on admission is an integral step in preventing adverse events. The most common error is omitting a medication that is taken at home. This omission may lead to further drug-related problems such as interruption of drug therapy or overlooking the root cause of the admission. At discharge, appropriate medication reconciliation and communication of any medication changes may prevent adverse drug events once the patient returns home. It has been reported that through a series of interventions using the medication reconciliation process, the rate of medication errors was reduced by 70% and adverse drug events by over 15%.

CCHSA expects that each accredited organization will have implemented or be working on implementation of the new patient safety goal of medication reconciliation by January 2006.

Medication reconciliation has been defined by the CCHSA as the process which ensures the collection and communication of accurate client/patient medication with the ultimate goal of facilitating continuity of pharmaceutical care for patients/clients at admission/beginning of service and/or at discharge/transition/end of service (e.g. from hospital to home or another level of care/service).

Goals and Objectives

1. To provide pharmacists with an understanding of CCHSA new patient safety goals and practices as they apply to medication reconciliation
2. To enable pharmacists to have tools and an understanding of the key points in the collection and communication of accurate client/patient medication information both at admission and at discharge.

Self-Assesment Questions

1. What are the 3 critical steps in the process of medication reconciliation?
2. What key transition areas in my hospital are problem-prone points in our medication management system?

Solid Organ Transplant 101 for Pharmacists

Nilu Partovi, PharmD, Vancouver General Hospital, University of British Columbia, Vancouver, BC

Over the last decade, the introduction of the new immunosuppressive agents has facilitated the short-term goal of reducing the incidence of acute rejection in Solid Organ Transplantation (SOT) recipients. However, as transplant recipients remain on these agents the impact of long-term use of anti-rejection medications remains unknown. The long-term success of SOT lies in the appropriate use of immunosuppressive medications. The goal of immunosuppression is to provide the transplant recipient with safe and effective treatment after transplant while minimizing the toxicities associated with the long-term use of immunosuppressive agents.

This presentation will provide an overview of the current immunosuppressants used in Solid Organ Transplantation, the advantages and disadvantages of different protocols, and controversies associated with monitoring of these agents.

Goals and Objectives

At the conclusion of this presentation, participants should be able to:

1. Describe the basis immune response to allografts.
2. Define the basic principles of immunosuppressive medications.
3. Recognize the advantages and disadvantages of common immunosuppressive medications used in solid organ transplant recipients.
4. Be familiar with importance of therapeutic drug monitoring for transplant immunosuppressants.
5. Describe strategies to improve long-term graft survival.

Tuesday, August 16 • Mardi le 16 août

Integrating a Pharmacist into Family Practice: Qualitative Results from the IMPACT Study

Barbara Farrell, BScPhm, PharmD, FCSHP – SCO Health Service and Elisabeth Bruyere Research Institute, Ottawa, ON, Kevin Pottie, MD, MCISc, CCFP – Elizabeth Bruyere Research Institute and University of Ottawa, Ottawa, ON (On behalf of IMPACT investigators)

The IMPACT study (Integrating family Medicine and Pharmacy to Advance primary Care Therapeutics) is an Ontario Primary Health Care Transition Fund project funded from March 2004 - March 2006. Seven pharmacists were integrated into physician-led group family practices for one year. Pharmacists provided patient medication assessments, drug information, academic detailing and developed office system innovations.

We examined the pharmacists' experiences as they integrated and adapted to meet the drug-related needs of family practice settings. We delineated factors that facilitated and hindered integration. A qualitative design was used involving pharmacist narrative reports, field notes, focus group and N-VIVO software. Researchers used immersion and crystallization to identify codes and iterative grounded theory to determine themes.

The integration process was challenging and rewarding for pharmacists. They characterized the integration process as an emotional "rollercoaster," complete with successes (feeling valued, contributing concretely to patient care), frustrations (feeling underutilized) and fears (being a nuisance, working too slowly). Pharmacists relied on adaptive strategies and practical demonstration of potential value to physicians to facilitate integration. They identified mentors, allied health professionals and accommodating doctors as key supports. System supports included office space promoting accessibility to physicians, communication tools, and participation in practice meetings or education sessions.

Goals and Objectives

1. To describe the experience of pharmacists as they integrated and adapted to meet the drug-related needs of family practice settings.
2. To describe factors that facilitated and hindered their integration.

Self-Assessment Questions

1. What evaluation approach and methods were used to examine pharmacist integration into family practice in the IMPACT study?
2. How can these evaluation results be utilized in planning for future integration of pharmacists into family practice settings?

Aboriginal Health Care Issues

Kurt B. Schroeder, BScPharm, Queensway-Carleton Hospital, Ottawa, ON

The goal of this session is to provide pharmacists with a broader understanding of the current and historical health care issues faced by Canadian Aboriginal populations.

From the point of first contact between Europeans and Native populations of North America, infectious and non-infectious diseases have dramatically altered the course of the health and culture of Canada's founding people. Small pox, influenza, tuberculosis, and current issues such as diabetes, environmental contamination, and mental health issues have all had significant impacts. The health status of First Nations continues to be shaped by socioeconomic factors such as high unemployment rates, substandard housing, and inadequate access to clean drinking water. Acute health care services are delivered to populations living on remote reserves in a different manner from provincial health programs thereby becoming an issue of concern. Genetic links between disease and First Nations people have yet to be fully elucidated although recent research has contributed to a better understanding of diabetes. A traditional reserve-based model may be ineffective in meeting the changing needs of Aboriginal populations as the demographics shift to an urban population. The role of the pharmacist has been under utilized in helping to address Aboriginal health issues and there is a great potential for an expanded role for clinical pharmacy services.

Goals and Objectives

1. To provide pharmacists with an understanding of the impact that diseases have had on Canadian Aboriginal populations.
2. To provide a better understanding of health service delivery on first nation reserves.
3. To review the contemporary health issues affecting Aboriginal patient populations.

Self-Assessment Questions

1. What epidemiologic factors predispose aboriginal populations to diabetes?
2. How are acute health care services provided differently for patients living on reserve from patients living elsewhere in Canada?

New Antifungals – What's up with that?

Alfred Gin, BScPharm, PharmD, Health Sciences Centre, Winnipeg, MB

The management of invasive fungal infections (IFI) is challenging. Depending on risk factors and neutropenia status, IFI related mortality is extremely high despite treatment with traditional antifungals such as amphotericin B. Amphotericin B (AMB) has been considered the gold standard but is associated with renal and infusion-related adverse effects. Lipid formulations of AMB have decreased these events but not completely. Within the last 2 years, antifungals such as caspofungin and voriconazole have become available. Caspofungin is the first of the novel class of echinocandin antifungals, which inhibit the synthesis of the fungal cell wall polysaccharide beta-1-3-glucan. Voriconazole is a newer triazole antifungal which like all other azoles inhibit fungal lanosterol 14-alpha-demethylase thus inhibiting ergosterol formation. These agents exhibit broad activity against many Candida spp. and Aspergillus spp.. Depending on the yeast/mould, these agents may exhibit fungicidal activity. Clinical studies support the use of these agents in the specific management of IFIs. Other investigational antifungals include micafungin (echinocandin), posaconazole and ravuconazole. Pharmacists should be aware of the potential for adverse effects, drug interactions and cost implications with these new agents. This presentation will review the pharmacology, efficacy, adverse effects, role and implications with the new antifungals.

Goals and Objectives

1. To provide an overview of new antifungals
2. To identify potential patient care cost issues with the new antifungals.

Self-Assessment Questions

1. What patient populations are most likely to receive these new agents?
2. List the cytochrome P450 systems that metabolize voriconazole?

Addressing The Hospital Pharmacy Management Crisis: Development of Strategies & Solutions (A Workshop)

Note: Funding for this workshop has been provided by the Canadian Institutes of Health Research (CIHR), Institute of Health Services and Policy Research (IHSPR)

Neil J. MacKinnon, PhD, RPH, Dalhousie University College of Pharmacy, Halifax, NS

The goal of this session is to provide an interactive forum (a workshop) where hospital pharmacy directors and managers can discuss issues related to

retention, recruitment, and leadership and where possible solutions to these challenges can be generated.

In recent years, papers have documented the severe shortage of hospital pharmacy directors and the related problems of recruitment and retention, and gaps in the managerial competencies of current directors. A survey of 254 Canadian pharmacy directors identified which managerial competencies are deemed to be important by these individuals, the self-assessed skill level of these competencies by these individuals, and gaps between the perceived importance and skill level. A qualitative analysis identified several themes:

1. many managers in rural hospitals feel overwhelmed and unable to sufficiently utilize their managerial skills,
2. the work environment has had a negative impact on morale,
3. difficulty in recruitment and retention has had a negative impact on departments of pharmacy, and
4. directors perceive a need for more management training.

With pharmaceuticals being the second largest and fasting rising category of healthcare expenditures, and the demand for a safe and effective medication use system, the ramifications of a leadership crisis in hospital pharmacy departments are widespread.

Goals and Objectives

1. To discuss the best approaches to improving the recruitment and retention of hospital pharmacy directors
2. To explore the training/experiential methods that are most effective at nurturing the next generation of leaders in hospital pharmacy practice in Canada
3. To consider how changing demographics influence the work experiences and expectations of hospital pharmacy directors

Self-Assesment Questions

1. What is the current state of hospital pharmacy management in Canada?
2. Are there effective strategies that could be used to attract pharmacy students to hospital pharmacy management?
3. How can the training of hospital pharmacy directors, both current and future, be optimized?

The Role of the Microbiology Lab in Infectious Diseases

Baldwin Toye, MD, FRCPC, The Ottawa Hospital, Ottawa, ON

This session will provide an overview of the microbiology laboratory and its role in the management of patients with infectious diseases. Pharmacists must be familiar with the basic interpretation and limitations of microbiology results in order to aid in clinical decision making with respect to selection and dosing of antimicrobials. The laboratory is involved in the diagnosis and treatment of infectious diseases through the isolation, identification, and susceptibility testing of microorganisms, as well as the interpretation and reporting of such results. The effectiveness of the laboratory is highly dependent on a properly collected and transported specimen, appropriate for the type of suspected infection. For certain specimens, a Gram's stain may provide preliminary information that may be useful for empiric therapy of a patient prior to the availability of culture results. A positive culture does not necessarily indicate infection or clinical significance but must be interpreted in the context of the clinical picture. This is particularly important when interpreting positive sputum cultures or blood and wound cultures growing common skin organisms. In vitro susceptibility testing of bacterial pathogens is routinely performed to provide therapeutic guidance but there are limitations in the methodology and interpretive criteria available for some pathogens. Bacteria with certain resistance mechanisms will test "susceptible" to an antibiotic but are associated with clinical failures if treated with that agent. In addition to providing patient specific results, the microbiology laboratory can also indirectly impact treatment decisions and antibiotic stewardship programs by providing hospital or ward-specific antibiograms, selective and clinically relevant susceptibility reporting, and other clinical programs.

Goals and Objectives

1. To provide pharmacists with an understanding of the methods used in a diagnostic microbiology laboratory and the limitations of such methods, particularly those associated with susceptibility testing.
2. To illustrate how to interpret Gram's stains, culture, and susceptibility results for various clinical specimens.

Self-Assessment Questions

1. Give an example of suboptimal clinical response to an antibiotic despite "susceptible" in vitro results and the explanation for it.
2. Give two examples of specific programs where the microbiology laboratory can significantly influence the clinical outcomes of patients.
3. Under which situations might a cultured organism(s) be considered "contamination" or "colonization"?

Pharmacoeconomics of Infectious Diseases Pharmacotherapy: From Assessment to Decision

Erwin Friesen, BSc(Pharm), PharmD, Capital Health, Edmonton, AB

Using pharmacoeconomic information in making sound policy decisions is where "the rubber hits the road". This workshop will examine two "infectious disease" cases and review how pharmacoeconomics information was used in the drug review process for Capital Health Drug Formulary and how it informed the recommendation/decision making process.

The workshop leader will relate the experience of Capital Health drug evaluation process and Drugs and Therapeutics Committee (DTC). The DTC was established in 1995 for the regional health authority. The Capital Health DTC currently manages drug policy and formulary decisions for 14 active treatment sites in the region. The review process is predicated on the principles of evidence-based decision making and consideration of the scientific, therapeutic, clinical and pharmacoeconomic merits of drug products. The DTC provides advice and recommendations on funding of drug products and program policy to the Regional Medical Advisory Council.

The underlying question that needs to be addressed in the deliberations is whether the drug product under review is 'good value for money'. In formulating the recommendations, Capital Health attempts to incorporate pharmacoeconomic information whenever possible; however, a number of challenges and barriers to consistently being able to do so exist.

Goals and Objectives

1. Provide an overview of how pharmacoeconomics information is used in Capital Health in the antimicrobial drug review process
2. Illustrate how pharmacoeconomic information has been used in the recommendation/decision making process with two examples
3. Discuss the challenges, barriers, pros and cons of incorporating Pharmacoeconomics information into the review process

Self-Assesment Questions

1. What are two clinical data limitations when evaluating pharmacoeconomic information?
2. Which data is more useful in pharmacoeconomic analysis, efficacy or effectiveness data?

Bortezomib

Darcy McLurg, BSc(Pharm), The Ottawa Hospital, Ottawa, ON

Multiple myeloma remains a challenge to treat. Depending on the stage of the disease, therapy ranges from watch and wait to stem cell transplantation. The disease eventually relapses in nearly all patients. Bortezomib is a novel proteosome inhibitor with antimyeloma activity. It has been shown to improve response in patients who have failed at least two lines of therapy.

Bortezomib is given on a 3-week cycle as an IV bolus injection. The patient is given 1.3mg/m2 IV on days 1,4,8 and 11 followed by a 10-day rest. Each dose must be separated by at least 72 hours.

Adverse effects requiring dosage adjustment include peripheral neuropathy and thrombocytopenia. The most commonly reported adverse effects include fever, diarrhea, vomiting, dehydration, and nausea.

No drug interaction studies have been completed to date.

There are no randomized, controlled studies to date which have looked at overall survival benefits but phase 2 studies have shown a promising response rate (CR + PR) at a median of 38 days. Bortezomib is also being studied in combination with other agents such as liposomal doxorubin and dexamethasone.

Goals and Objectives

- To briefly review mechanism of action, dosing, adverse effects and interactions of bortezomib
- To discuss place in therapy in view of cost implications

Self-Assesment Questions

- What is the dose of bortezomib?
- What are the two most common adverse effects of bortezomib?
- Which patients should receive bortezomib?

Memantine – A Review of its Role in Alzheimer's Disease

Alexander Kuo, BScPharm, ACPR, The Ottawa Hospital, Ottawa, ON

The number of people affected by Alzheimer's disease (AD) is increasing considerably as our population ages. Previously, the majority of pharmacologic treatment focused on the deficiency of acetylcholine associated in AD by using cholinesterase inhibitors.

More recently, it is thought that overstimulation of the N-methyl-D-aspartate (NMDA) receptors by glutamate results in neuronal damage and has alternatively been implicated in the pathogenesis of AD. Therapy to prevent this progression logically

utilizes antagonists of such receptors. Memantine is an NMDA antagonist that is indicated in the symptomatic treatment of patients with moderate-to-severe dementia of the Alzheimer's type. In a randomized, double-blinded, controlled trial, memantine was compared to placebo in the treatment of moderate-to-severe AD. It was concluded that there was significantly less clinical deterioration and better cognitive and functional outcomes in the treatment group compared with placebo. Furthermore, in another randomized, double-blinded, controlled trial, memantine was compared with placebo in patients with moderate-to-severe AD already receiving stable treatment with donepezil. Patients in the memantine+donepezil group demonstrated significantly better outcomes than placebo+donepezil on measures of cognition, activities of daily living, global outcome, and behaviour. In both of these trials, adverse events were not significantly different from placebo indicating that memantine is well tolerated.

Goals and Objectives

1. To discuss the pharmacology of memantine.
2. To review the efficacy and safety of memantine in patients with moderate-to-severe AD based on clinical trial data.

Self-Assessment Questions

1. How effective and safe is memantine?
2. What is memantine's place in therapy: is it beneficial to add therapy in patients with moderate-to-severe AD already receiving stable treatment with donepezil or other cholinesterase inhibitors?

The Cardiovascular Safety of COX-2 Inhibitors: What Should We Do Now?

Stephen Shalansky, PharmD, FCSHP, Research Coordinator, Pharmacy Dept, St. Paul's Hospital, Clinical Professor, Faculty of Pharmaceutical Sciences, UBC, Vancouver, BC

The recent worldwide withdrawal of rofecoxib and valdecoxib has raised questions about the safety of other available coxibs and NSAIDs. The comparative pharmacodynamics, clinical trial evidence, and Health Canada warnings on this topic can be used to formulate advice for patients requiring analgesic and anti-inflammatory medications.

COX-2 specificity appears to predict the potential for cardiovascular toxicity amongst the coxibs, and this has been reflected in most clinical and epidemiological trials published to date. Although clinical trials have not evaluated cardiovascular endpoints as the primary outcome, the trials do provide a large amount of cardiovascular safety data in a range of populations. There is less direct evidence available to assess the cardiovascular safety of non-selective NSAIDs. The FDA hearings on the cardiovascular safety of coxibs in February 2005 assembled a wealth of information and expertise on this topic. This information, and the resultant statements issued by the FDA and Health Canada are useful tools for formulating recommendations for all patients, including those with cardiovascular disease.

While celecoxib appears to pose less risk for cardiovascular toxicity than rofecoxib or valdecoxib, it should not be used in patients with heart disease and should be used cautiously in patients with cardiovascular risk factors. There is little evidence to evaluate the cardiovascular safety of melocoxam, but its pharmacology suggests a risk similar to celecoxib. Alternatives to coxibs include prescription NSAIDs, over-the-counter ibuprofen, acetaminophen or higher dose aspirin; however, patients should be made aware of cautions associated with each option including potential cardiovascular toxicity of all NSAIDs. A patient information sheet on this topic will be available as an example.

Goals and Objectives

1. To briefly review the pharmacodynamics of coxibs and NSAIDS for the purpose of understanding differences in cardiovascular risk potential amongst these agents.
2. To review the clinical trial evidence evaluating the cardiovascular toxicity of coxibs and NSAIDS.
3. To review Health Canada and FDA recommendations regarding the cardiovascular safety of coxibs and NSAIDs.
4. To present alternatives to coxibs, and review relevant safety information.
5. To provide pharmacists with an understanding of the above topics for purpose of counseling patients with and without cardiovascular disease who require medication for mild to moderate pain and inflammation.

Self-Assessment Questions

1. Health Canada recommends that caution should be used for patients taking celecoxib who have significant risk factors for heart attack or stoke. What risk factors should be considered?
2. Patients may choose over-the-counter ibuprofen as an alternative to coxibs, however ibuprofen may interfere with the antiplatelet effects of low dose aspirin. How can this interaction be avoided?

Sunday, August 14 • Dimanche le 14 août

Viewing: 10:00-10:30
Presentation: 12:00-14:00

1. National Survey of Hospital Policies on Patients' Own Medications
2. Systematic Literature Review of Patients' Own Medication use in Hospitals
3. Impact of Drug Policy Tools and Techniques on Economic, Clinical and Humanistic Outcomes in Canada: A Systematic Review
4. Patient & Health Professional Perceptions of Medication Errors: Identifying Contributing Factors and Solutions
5. Implementing and Assessing the Benefits and Feasibility of the "Safe Sampling" Pilot Project in the Community
6. Implementation of Telepharmacy Care in a Northern Ontario Hospital
7. Post-Pertussis Exposure Prophylaxis with Erythromycin: Follow-up for Possible Infection and Infantile Hypertrophic Pyloric Stenosis
8. Use of Learning Needs Assessment to Develop Continuing Education Programs for Pharmacy Technicians in the Winnipeg Regional Health Authority
9. Formulary Management in an Environment of Cost-Containment in Capital Health
10. Cost-Effectiveness of Patients Self-Managed vs. Physician-Managed Oral Anticoagulation: A Bayesian Approach

NATIONAL SURVEY OF HOSPITAL POLICIES ON PATIENTS' OWN MEDICATIONS

Heather Lummis[1], Ingrid Sketris[2], Mary Ellen Gurnham[1], Sander Van Zanten[1,2]

[1] Capital Health, Halifax, NS and
[2] Dalhousie University, Halifax, NS

Rationale: Patients' own medications (POM) may be used in hospitals under certain circumstances but there may be legal and safety issues. There is very little known about the use of POMs in Canadian hospitals, although POM programs are common in other countries.

Objectives: To collect information on POM policies and current practices.

Methods: Surveys were emailed to 166 pharmacy directors of hospitals with ≥ 50 acute care beds. Addresses were obtained from the Lilly Hospital Pharmacy Survey.

Results: The response rate was 52%. POM use was allowed only when necessary (89%), actively encouraged (8%), or not allowed (2%). The most common types of POMs allowed were nonformulary/non-stocked, prepacked, investigational, and multidose medications.

Most hospitals have a POM policy (72%), pharmacy usually verifies the medication (64%), and most require a physician's order to use POMs (70%). In hospitals that are part of a region or authority, only 49% have an approved policy. Several hospitals indicated legal issues were a challenge in developing their policy (18%).

Main advantages to the use of POMs were cost savings (67%), decreased inventory (57%), and continuity of care (19%). The main disadvantages were the potential for medication errors (51%), time consuming (32%) and loss of POMs (32%).

Conclusions: Allowing the use of POMs was very common in Canadian hospitals, although respondents had concerns about hospital liability and potential errors. It is recommended that policies be in place that describe identification, storage, and documentation procedures to address these issues.

SYSTEMATIC LITERATURE REVIEW OF PATIENTS OWN MEDICATION USE IN HOSPITALS

Heather Lummis[1], Ingrid Sketris[2], Sander Van Zanten[1,2], Mary Ellen Gurnham[1]

[1] Capital Health, Halifax, NS and
[2] Dalhousie University, Halifax, NS

Rationale: Using patients' own medications (POM) in institutions may save drug costs. Policymakers may be concerned about hospital liability, medication error, and other implications to patients and staff.

Objectives: To synthesize the literature to identify benefits and risks to the patient and the hospital.

Methods: Four health databases were systematically searched. Published and unpublished primary studies, letters, reports, reviews, guidelines and policies were included but not abstracts. References were reviewed and selected pharmaceutical journals and the internet were searched. Information was assessed for relevance and categorized as a primary study, review, guideline or anecdotal report.

Results: Nineteen primary studies of quasi-experimental design were identified; 15 were from the United Kingdom (UK). National pharmacy standards and practical issues such as how to identify POMs and the need for staff training were found.

Patient benefits included: more accurate medication histories, streamlined therapy by reviewing medications at admission and discharge, prevent loss and wastage of POMs, and continuity of treatment. A small number of medication errors have been reported.

Hospital benefits were cost savings although a wide variation was found. Several studies documented the workload associated with the use of POMs. Risks can be minimized when policies are developed based on best practices and with multidisciplinary input.

Conclusions: The quality of POM studies was poor and they may not apply to the Canadian health care system. Nevertheless, the literature contains many examples of benefits to the patient and hospital, as well as assistance with practical issues.

IMPACT OF DRUG POLICY TOOLS AND TECHNIQUES ON ECONOMIC, CLINICAL AND HUMANISTIC OUTCOMES IN CANADA: A SYSTEMATIC REVIEW

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Rationale for Review of Topic: Several evaluations of drug policy tools such as formularies have been conducted in Canada, yet, there has not been a comprehensive review of these evaluations.

Objectives of Review: The objective was to determine the impact of drug policy tools in Canada on economic, clinical and humanistic outcomes.

Methods Used: The inclusion criteria consisted of all Canadian studies that had been published in peer-reviewed journals whose primary objective was to evaluate the impact of a drug policy tool. Nine databases were searched, including PubMed, Embase, and Cochrane Library. The reference lists of eligible studies were reviewed for relevant citations. The authors of studies meeting eligibility criteria were contacted. Two reviewers independently abstracted data (study design, study sample, outcome measures, drugs studied, and clinical, economic and humanistic outcomes) from eligible studies.

Results of Review: Twenty-two studies met the inclusion criteria. In 86.4% of studies, the intended effect of the tool on drug costs/utilization was achieved. In 68.3% of studies, the impact of the tool on medical care was not measured and in 22.7% no impact on medical care was found. 86.4% of studies did not measure the impact of the tool on clinical outcomes and 100% did not measure humanistic outcomes.

Conclusion of Review and Implication to Practice: While drug policy tools seem to be effective at achieving drug cost savings, their impact on other outcomes remains unexplored in the vast majority of the studies. Healthcare organizations should make the evaluation of these tools a priority.

PATIENT & HEALTH PROFESSIONAL PERCEPTIONS OF MEDICATION ERRORS: IDENTIFYING CONTRIBUTING FACTORS AND SOLUTIONS

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Reason for Initiative: The reason was to determine the contributing factors and solutions to medication errors as perceived by health professionals and patients, and to compare and contrast these perceptions.

Description of Initiative: Medication errors documented at South Shore Health (SSH) hospitals from February 2002 - June 2004 were compiled and analyzed for trends. The trends and four examples of medication errors were presented to two focus groups: one of nine health professionals from SSH and one of eight patients recently discharged from a SSH hospital. Nominal group technique was used to answer the question "What are the contributing factors to medication errors at SSH?"

Evaluation of Initiative: From 227 medication reports, the most common error types were incorrect drug given (32%), omissions (19%) and incorrect dose (18%). Seventy three percent of errors occurred during administration, and 86% were classified as minor.

Health professionals considered the top four contributing factors to medication errors to be multi-tasking, handwriting, transcription errors, and failure to follow the "5 R's" (right drug, dose, person, route, and time). Patients considered the top four contributing factors to medication errors to be human error, patients who are unwilling/unable to provide pertinent information, overworked doctors and nurses, and inadequate patient identification.

Importance and Usefulness of Initiative for Pharmacists: Valuable insight was gained, from both the perspective of health professionals and patients, into how the medication use system can be improved at SSH. The next step is to discuss with senior administration how to implement these findings.

IMPLEMENTING AND ASSESSING THE BENEFITS AND FEASIBILITY OF THE "SAFE SAMPLING" PILOT PROJECT IN THE COMMUNITY

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Rationale: "Traditional" medication sampling occurs when pharmaceutical companies promote products by providing free samples to physicians, who then pass these on to patients. Limitations to the current practice include the following: lack of documentation on patients' medication profiles, no pharmacist involvement, and limited inventory control in physician offices.

Description: We present an improved method called "Safe Sampling," to mitigate limitations of "traditional" medication sampling.

Objective: To implement a "Safe Sampling" pilot project, and to assess benefits and feasibility from the patients', pharmacists', and pharmaceutical company's perspectives.

Steps for implementation: When patients required rabeprazole samples, participating physicians provided rabeprazole vouchers in lieu of samples. Patients redeemed vouchers at the participating pharmacy for a complimentary 7-day supply. The pharmacist processed the voucher like a prescription; if applicable, they documented all reasons for not filling vouchers. Patients, pharmacists and pharmaceutical company employees were surveyed for feedback.

Results: Seven physicians issued 59 vouchers to 43 patients (September 2004-January 2005). The pharmacy filled all vouchers. The majority of patients (64-95%) agreed with various benefits of "Safe Sampling." All pharmacists (n=5) and pharmaceutical company employees (n=2) agreed "Safe Sampling" was feasible to implement. Recommendations to enhance "Safe Sampling" included the following: involve >1 pharmacy, dispense rabeprazole from existing pharmacy stock, and utilize on-line billing.

Importance: Our surveys indicate that "Safe Sampling" is beneficial and feasible to implement in community practice. This project provides groundwork for the implementation of a safer method of medication sampling. The next step is to incorporate the recommendations to enhance "Safe Sampling."

IMPLEMENTATION OF TELEPHARMACY CARE IN A NORTHERN ONTARIO HOSPITAL

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With the longstanding shortage of pharmacists across Canada, hospitals in remote areas have difficulty attracting pharmacists to their community to work. Many of these hospitals have vacant pharmacist positions, and consequently patient care suffers and the risk of medical errors increases.

A telepharmacy model of care was designed and implemented at a small hospital. Telepharmacy is defined as the use of electronic technologies to provide pharmaceutical services from a distant location. After early visits to implement the necessary changes, the pharmacist worked from his home office environment in a different city. Written medication orders at the hospital are scanned into portable document format (.pdf) on the hospital network. The pharmacist accesses the hospital network using the Internet, views the medication orders, resolves potential problems with them, verifies them with the electronic patient profile, and enters them into the pharmacy computer system. The labels are printed out in the hospital's pharmacy where a technician-check-technician system is used to dispense the medication. The pharmacist also participates in multidisciplinary patient care rounds, education in-services, committee meetings, and patient counseling utilizing e-mail, videoconferencing, and teleconferencing technologies.

Telepharmacy can be used to link many hospitals in remote areas of Canada with pharmacists to provide pharmaceutical care. Pharmacists may be attracted to this work since they can live in their own communities and work in their own home-office environment while helping hospital staff and patients in need. Much of the technology is already in place and the potential to share a pharmacist between hospitals exists.

POST-PERTUSSIS EXPOSURE PROPHYLAXIS WITH ERYTHROMYCIN: FOLLOW-UP FOR POSSIBLE INFECTION AND INFANTILE HYPERTROPHIC PYLORIC STENOSIS

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Rationale: Neonatal pertussis infection is associated with significant morbidity and mortality. Treatment with erythromycin has been recommended for post exposure pertussis prophylaxis to decrease the risk of infection; however its use has been linked to an increased risk of infantile hypertrophic pyloric stenosis (IHPS).

Description: Twenty-one neonates in the Level 2 Neonatal Intensive Care Unit (NICU), Mount Sinai Hospital (MSH), were exposed to pertussis in September 2004. The exposed neonates were given erythromycin prophylaxis. MSH NICU dosing guidelines were used due to lack of specific guidelines for preterm neonates exposed to pertussis. Parents of the neonates and exposed staff were also given prophylaxis. A follow-up was completed to determine if any of the neonates developed a clinical illness consistent with pertussis or adverse effects from erythromycin with a focus on IHPS.

Analysis: None of the neonates developed pertussis infection. Two neonates developed symptoms of projectile vomiting. One neonate had the prophylaxis discontinued on day 12 of treatment with resolution of symptoms. The other neonate developed projectile vomiting about 4 weeks following erythromycin therapy. The neonate was investigated for IHPS with an abdominal ultrasound, which was negative.

Importance of case to pharmacy practitioners: The dosage regimen used for erythromycin administration in preterm neonates at MSH was effective in preventing pertussis infection. In our small series the use of erythromycin was not associated with the occurrence of IHPS.

USE OF LEARNING NEEDS ASSESSMENT TO DEVELOP CONTINUING EDUCATION PROGRAMS FOR PHARMACY TECHNICIANS IN THE WINNIPEG REGIONAL HEALTH AUTHORITY

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Rationale: Most pharmacy technicians (Techs) train at technical schools before entering hospital practice. Continuing education (CE) is important for patient safety and staff retention but Tech CE programs are scarce. Limited resources and a large geographically separated workforce pose challenges to design and deliver Tech CE.

Steps Taken: To inform planning for Tech CE programs, we performed a learning needs assessment (LNA) of Techs and Tech Supervisors (Tech-SPVR). A mail-in survey with demographic, learning capabilities, felt needs and learning preference domains was developed and field-tested, then sent to Techs at long-term/ambulatory (LTC-A), tertiary (AC-T) and community (AC-C) facilities. A survey with demographic, ascribed needs and resource domains was developed, field-tested and sent to Tech-SPVR. Responses were coded electronically, analyzed using descriptive and inferential statistics then applied to a CE planning model.

Results: Response rates were 59.5% (N=164) for Techs and 62.1% (N=29) for Tech-SPVR, and were representative of Tech and Tech-SPVR workforces at LTC-A, AC-C and AC-T facilities. Techs uniformly expressed strong desire for a wide range of CE programs, preferably 1 hour or half-day duration during scheduled shifts. Medication and disease state information, plus IV admixture, medication order entry, and computer skills upgrading were strongly preferred. Tech-SPVR ascribed computer, interpersonal and aseptic skill upgrading as high priority Tech learning needs. Not all Tech-SPVR had resources for Tech CE at their site. Capability for use of distance electronic media was limited. This poster will demonstrate how LNA findings and program planning models were used to develop Tech CE Programs in the Winnipeg Region.

FORMULARY MANAGEMENT IN AN ENVIRONMENT OF COST-CONTAINMENT IN CAPITAL HEALTH

Margaret Gray, Erwin Friesen, Chuck Wilgosh, Ken Gardener, Gail Hufty, Capital Health Region, Edmonton Alberta

Drug expenditures are the fastest rising component of health care. In an attempt to control the rising expenditures in drugs, Capital Health instituted new formulary management processes which ensure both the clinical value and economic affordability of medications reviewed for formulary are assessed prior to their addition to formulary.

New procedures for the formulary process, or non-formulary use of high cost drugs have been adopted in Capital Health since 2003. In addition to the assessment of clinical and economic factors, and broad stakeholder input, the New High Cost Drug Approval Process (NDAP) incorporates early notification of Capital Health's Regional Executive Medication Committee (REMC) of the potential addition of high cost drugs to the regional formulary. A drug can not be approved for formulary in Capital Health until both the Drugs & Therapeutics Committee (DTC) and REMC approvals have been acquired.

The Emerging Drug Approval Process (EDAP) is designed to review patient-specific requests for high cost drugs which have not yet been reviewed by DTC, or were reviewed by DTC but did not have sufficient evidence to support the addition of the agent to the regional formulary (e.g. Level C evidence). For each request, the clinical and economic factors are considered, including approval from the Vice President of Medical Affairs, before the drug is dispensed. Funds must be made available through existing program resources, unless a source of external funding is identified. If use of the drug is approved, the prescriber is required to submit written follow-up on the patient outcomes, which form the basis for future use of the agent.

Capital Health has used these new formulary management processes to ensure that affordability of new drugs is considered in the DTC decision, and that the programs receive funding to support new therapies.

COST-EFFECTIVENESS OF PATIENT SELF-MANAGED VS. PHYSICIAN-MANAGED ORAL ANTICOAGULATION: A BAYESIAN APPROACH

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Rationale: Self-management (SM) of warfarin by patients is attractive but cost is a major barrier. Canadian cost-effectiveness analyses to aid decision making for reimbursement programs are lacking.

Objective: To evaluate the incremental cost-effectiveness of patient SM vs. physician-managed (PM) anticoagulation from the British Columbia Ministry of Health perspective.

Methods: We developed a Bayesian discrete-state discrete-time Markov model to compare the costs and quality adjusted life years (QALYs) accrued to patients receiving SM vs. PM over five years. Five distinct health states were defined: no events; minor or major hemorrhagic events; thromboembolic events; and death. Transition to health states depended on time spent below, in, and above therapeutic range (TTR). Data used to inform TTR were derived from a randomized trial conducted at Vancouver General Hospital directly comparing SM to PM. Clinical event rates were modeled from two published cohort studies. Canadian 2003 costs were modeled and utility estimates were obtained from various sources. A Dirichlet prior distribution was specified for the multinomial data and probabilistic sensitivity analysis characterized uncertainty. The model was estimated using the Bayesian specialist software WinBUGS.

Results: Model results indicate that per 100 patients over a 5-year period SM is expected to result in 3 fewer thrombotic events, 1 fewer major hemorrhagic event, and 0.12 fewer deaths. The expected average discounted incremental cost of SM over PM is $616 (95% CI, $502-$723) and the average QALYs gained is 0.060 (95%CI 0.048-0.072). The discounted incremental cost per QALY gained is $10,266. If decision makers are willing to pay $14,000 per QALY, there is a 95% probability that SM is cost-effective.

Conclusion: SM appears to be an economically appealing strategy.

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Monday, August 15 • Lundi le 15 août

Viewing: 10:00-10:30
Presentation: 12:00-14:30

1. Mandatory Reporting of Adverse Drug Reactions
2. Pharmacist-Managed, Physician-Directed Management of Allergic Rhinitis in the Canadian Forces – A Trial
3. Computerized Discharge Prescriptions: A Retrospective Survey
4. Assessment of Risks Associated with Short-Term use of Mefloquine in Canadian Forces Members
5. Evaluation of Health Products used by the Canadian Forces Health and Lifestyle Information Survey Respondents
6. Stability of Zoledronic Acid in 5% Dextrose or 0.9% Sodium Chloride Solutions at 4C and Room Temperature (24C)
7. Stability of Pantoprazole in 0.9% Sodium Chloride Injection (NS) at 4C and Room Temperature (24C)
8. Y-Site Compatibility Study of Moxifloxacin with Other Drugs and Infusion Solutions
9. Development of the Family Medicine Medication use Processes Matrix
10. Torsades de Pointes Associated with Cesium Chloride
11. Pharmacokinetics of Ciprofloxacin in Asians with Different CYP2C19 and CYP3A5 Genotypes

MANDATORY REPORTING OF ADVERSE DRUG REACTIONS

Régis Vaillancourt, Directorate of Medical Policy, Pharmacy Policy and Standards, Canadian Forces Health Services, Ottawa, ON Alan Gervais, Directorate of Medical Policy, Pharmacy Policy and Standards, Canadian Forces Health Services, Ottawa, ON Claire Gauthier RPT Directorate of Medical Policy, Pharmacy Policy and Standards, Canadian Forces Health Services, Ottawa, ON

Rationale: The benefits of reporting adverse drug reactions (ADR) became evident in two studies completed by the Canadian Forces (CF). The results of these studies influenced the implementation of the present procedure. A health professional must report an ADR to a drug on the CF drug benefit list to the Canadian Forces Drug Exception Centre (CFDEC) if the patient subsequently requires a drug not listed on the CF drug benefit list.

Description: The program was implemented in November 2003. Between November 2003 and August 31st 2004, the CFDEC has received 79 requests for drugs that are not on the CF drug benefit list as a result of an ADR to a benefit drug. An ADR form has been completed for each of these cases and a copy forwarded to the Canadian Adverse Drug Reaction Monitoring Program where these case reports are reviewed and entered into a database that is constantly monitored for signals. Since the knowledge of drug risk evolves over the lifetime of the drug, the CF contributes to the risk assessment that must continue beyond the pre-market evaluation phase. Although not all ADRs are captured, it is an improvement over the underreporting documented in the literature

Conclusions: As the results of the previous two studies assisted in managing the formulary to promote positive patient health outcomes and to minimize adverse reactions, the forthcoming documented adverse reactions will continue to assist in assessing the risk of drugs on the CF drug benefit list in the CF population.

PHARMACIST-MANAGED, PHYSICIAN-DIRECTED MANAGEMENT OF ALLERGIC RHINITIS IN THE CANADIAN FORCES – A TRIAL

Régis Vaillancourt, Directorate of Medical Policy, Pharmacy Policy and Standards, Canadian Forces Health Services, Ottawa, ON. Mark Kearney, Directorate of Medical Policy, Pharmacy Policy and Standards, Canadian Forces Health Services, Ottawa, ON. Jeff Taylor, College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK.

Background: According to the 2000 Canadian Forces Health and Lifestyle Information Survey, 21% of male and 32% of female Canadian Forces (CF) members suffered from allergic rhinitis (AR).

Objective: To evaluate the impact of pharmacist-managed care on the quality of life of AR patients in the CF.

Study Design: CF members with a confirmed diagnosis of AR who presented to sick parade, physician appointments or a base pharmacy at 4 CF bases between September 2003 and December 2004 were included in the study. Patients at the 2 control bases received standard care from pharmacists. Patients at the 2 treatment bases received enhanced care from pharmacists including monthly follow-up consultations to assess the patient, provide detailed counselling and modify medication therapy via a collaborative prescribing protocol. As the primary outcome, study participants completed the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ(S)) at 4 week intervals, these were then mailed submitted to the study coordinator. Patients were followed for 12 weeks.

Results: Eighty two patients have been recruited to date. Results suggest a trend whereby CF members receiving enhanced care from pharmacists report an improvement in allergy symptoms and related RQLQ(S) scores at week 12, while CF members receiving usual care report worsening allergy symptoms and related RQLQ(S) scores.

Conclusion: Regular interaction with a pharmacist over a 12-week period, where counselling can be provided and pharmacotherapy adjusted, appears to positively impact AR symptoms and quality of life.

COMPUTERIZED DISCHARGE PRESCRIPTIONS: A RETROSPECTIVE SURVEY

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Objective: To determine the acceptability of a computerized hospital discharge prescription program.

Method: A retrospective survey to evaluate satisfaction on a numerical scale from 0 to 10 the computerized discharge prescription (CDP) pilot project survey was distributed internally to physicians, ward clerks and nurses and externally to community pharmacists. Community pharmacies within 6 km of the hospital and selected pharmacies in Orleans were visited and surveyed.

Results: Internal: 34.8 % of the physicians (15/43), 67 % (8/12) of the clerks 0% of nurses responded to the survey. The overall satisfaction of physicians was of 95 ± 13.2 %. Physicians evaluated the estimated time required to complete the process at 4 ± 3.22 minutes and the time gained at 5 ± 5.11 minutes. Physicians did not find any mistakes on the CDP. The clerks' overall satisfaction was of 92 ± 6.41 %. The time required to print the CDP was of 3 ± 1.16 minutes.

External: Fifty-nine community pharmacies were visited with a response rate of 78%(n=46).

Of the respondents, 39.1 % had already received CDP from the hospital and reported an overall satisfaction of 83.3 ± 9.73 %, with 61% indicating that CDP reduced the number of calls needed for clarification and 67% reporting no mistakes on these prescriptions.

Of the respondents, 60.9% had not yet received a CDP but reported an overall satisfaction of 87.7 ± 17.4 %, with 68% indicating that CDP would reduce the number of calls needed for clarification.

ASSESSMENT OF RISKS ASSOCIATED WITH SHORT-TERM USE OF MEFLOQUINE IN CANADIAN FORCES MEMBERS

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Objective: To investigate the short-term health effects associated with the use of Mefloquine in Canadian Armed Forces personnel.

Design: All Regular Force personnel who served in Somalia between 1992-1993 were eligible for inclusion in this descriptive, cross-sectional study. Individuals not prescribed Mefloquine for antimalarial prophylaxis were excluded.

Methods: Data was extracted from CF medical documents, all events, including injuries, symptoms and signs reported during Mefloquine treatment were identified and classified according to the Canadian Enhancement to the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10-CA). For each event, severity either minor/major as well as causal relationship to Mefloquine was noted.

Results: The study involved 1413 individuals, 554 (39.2%) of whom reported one or more adverse events (AE) related to Mefloquine for a total of 2030-recorded AE. The most frequently reported AE were: non-infective gastroenteritis and colitis (N=343,24.3%); non-specific signs involving the digestive system and abdomen (N=272,19.2%); abdominal and pelvic pain (N=204,14.4%); nausea and vomiting (N=203,14.4%); sleep disorders (N=152,10.8%); malaise and fatigue (N=147,10.4%); headache (N=135,9.6%), symptoms and signs concerning food and fluid intake (N=122,8.6%); fever of unknown origin (N=106,7.5%) and rash or non-specific skin eruption (N=102,7.2%). Of the total AE, 13 were major, with 12 cases of dizziness and 1 case of cardiac arrest. The reported AE related to Mefloquine per individual were distributed as follows: 1AE (N=114,20.6%), 2AE (N=101,18.2%), 3AE (N=82,14.8%), 4AE (N=82,14.8%), ≥5 AE (178,32.1%).

Conclusion: This study shows that the majority of the adverse events were mild with a low rate of major events.

EVALUATION OF HEALTH PRODUCTS USED BY THE CANADIAN FORCES HEALTH AND LIFESTYLE INFORMATION SURVEY RESPONDENTS

Régis Vaillancourt, Directorate of Medical Policy, Pharmacy Policy and Standards, Canadian Forces Health Services, Ottawa, ON. Myrella Roy, Canadian Society of Hospital Pharmacists, Ottawa, ON. John Sampalis, JSS Medical Research, Montreal, QC. Susan Groves, Directorate of Medical Policy, Pharmacy Policy and Standards, Canadian Forces Health Services, Ottawa, ON

Objectives: To identify the patterns of natural health product (NHP) use among Canadian Forces (CF) members. The secondary objective was to compare NHP use with first language (English/French), gender, age, marital status, education, rank, duration of service, Non NHP medication use, chronic conditions, weight (Body Mass Index BMI), and self reported health status.

Methods: A cross-sectional survey of CF members was performed and all 6,841 respondents to version B of the CF 2000 Health and Lifestyle Information Survey (HLIS) were included in the study. Descriptive statistics, using SPSS software, were determined for the demographics of the study sample and the frequencies of health products use. Odds ratios and 95% confidence intervals were determined for the association between the independent and dependent variables. A logistic regression analysis was done for independent characteristics associated with health products use.

Results: Data from the 6,841 respondents was analyzed: mean age was 37.2 years (7.52) with the majority of respondents rating their health status (41.3%) as very good. Of the respondents, 44.1% used health products on a regular basis and 2134 (31.2%) used a NHP in the previous two days.

Conclusions: CF members, in common with the general population, utilize the full range of NHP. All CF health care providers need to be knowledgeable about NHP and be able to provide accurate information to their patients. Further follow up studies should be conducted to determine where CF members obtain their NHP and from whom they obtain information on NHP.

STABILITY OF ZOLEDRONIC ACID IN 5% DEXTROSE OR 0.9% SODIUM CHLORIDE SOLUTIONS AT 4C AND ROOM TEMPERATURE (24C).

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Rationale: The Zometa® product monograph recommends that the total time between reconstitution and/or dilution, storage under refrigeration, and end of administration must not exceed 24 hours.

Objective: The objective of this study was to evaluate the stability of 0.04 mg/mL of zoledronic acid (4mg/100mL) diluted in 5% dextrose in water (D5W) or 0.9% sodium chloride (NS) stored at 24C or 4C for 14 days.

Methods: Vials of zoledronic acid were reconstituted and then further diluted in PVC bags containing D5W or NS to prepare 0.04 mg/mL solutions. These solutions were stored at 4C or 24C. Concentration and physical inspection were completed on each solution on study days 0, 1, 2, 3, 6, 7, and 14. Zoledronic acid concentrations were determined by a validated stability-indicating, liquid chromatographic method.

Results: Over the 14-day study period, deviation from the initial concentration averaged less than 5%. There was no significant difference in zoledronic acid degradation rate between solutions (NS vs. D5W) or temperature (4C vs. 24C). During the study period
the average absolute deviation from the known concentration for standards and QC samples was 0.83% and 0.72% respectively. Analytical reproducibility within a day (CV) averaged less than 1% for standards and QC samples. All solutions remained clear and colorless with no visible changes observed for the study duration.

Conclusions: We conclude that 0.04 mg/mL zoledronic acid solutions are physically and chemically stable for up to 14 days at 4C or 24C in PVC bags containing 5% dextrose in water or 0.9% sodium chloride.

STABILITY OF PANTOPRAZOLE IN 0.9% SODIUM CHLORIDE INJECTION (NS) AT 4°C AND ROOM TEMPERATURE (24°C).

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Rationale: The Canadian Panto IV® product monograph recommends that the reconstituted product and diluted admixtures be used within 6 hours of preparation.

Objective: The objective of this study was to evaluate the stability of pantoprazole (0.16 and 0.8mg/mL) diluted in NS stored at 24C or 4C for 14 days.

Methods: 40 mg pantoprazole sodium injection vials were reconstituted with 10 mL of NS and then further diluted with NS to prepare 6 – 50 mL PVC bags of 0.16 and 0.8 mg/mL of pantoprazole. An additional 6 - 50 mL bags containing 0.8 mg/mL pantoprazole and 1 mg of EDTA were also prepared (US formulation contains EDTA). Half of the bags of each concentration were stored at 4C and the remaining at 24C. Concentration and physical inspection were completed on each solution on study days 0, 2, 5, 7, 9 12 and 14. Pantoprazole concentrations were determined by a validated, stability-indicating, liquid chromatographic method.

Results: The initial observed concentration averaged 0.16 and 0.79 mg/mL. All solutions remained clear and colorless. Solutions stored at 4C lost less than 0.2% of the initial concentration per day and had more than 97% of the initial concentration remaining on day 14. 0.8 mg/mL solutions stored at 24C lost approximately 1.4% of the initial concentration per day while 0.16 mg/mL solutions lost approximately 3.4% per day. During the study period the average absolute deviation from the known concentration for standards and QC samples averaged 1.63% and analytical reproducibility within a day (CV) averaged less than 1.5%.

Conclusions: We conclude that pantoprazole solutions are physically and chemically stable for up to 14 days at 4C in PVC bags containing NS. Concentration-dependent stability indicates that solutions stored at 24C retain more than 90% of the initial concentration for at least 48 hours. This data predicts that admixtures of pantoprazole containing 40 or 80 mg/100 mL stored for 7 days at 4C and followed by an additional 24 hours at 24C will retain more than 95% of the initial concentration.

Y-SITE COMPATIBILITY STUDY OF MOXIFLOXACIN WITH OTHER DRUGS AND INFUSION SOLUTIONS.

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Background & Objective: Patients receiving moxifloxacin often require concomitant IV drugs and solutions. The objective of this study was to evaluate the Y-site physical compatibility of moxifloxacin (Avelox® IV, Bayer Inc.) with 33 drugs at room temperature over a 24-hour period.

Methods: Thirty three drugs (aminophylline, calcium chloride, calcium gluconate, cefazolin, ceftriaxone, clindamycin, dimenhydrinate, dobutamine, dopamine, epinephrine, esmolol, fentanyl, furosemide, gentamicin, hydromorphone, insulin, labetolol, magnesium sulphate, meperidine, methylprednisolone, metronidazole, midazolam, morphine, multivitamins, nitroglycerine, norepinephrine, octreotide, pantoprazole, piperacillin, potassium chloride, potassium phosphate, sodium bicarbonate, vasopressin) diluted in D5W to each of three different concentrations, in addition to 0.3% sodium chloride and 3.3% dextrose, were selected for compatibility testing with a 1.6 mg/mL solution of moxifloxacin diluted in 0.8% sodium chloride. A total of 9-moxifloxacin-second-drug concentration combinations were prepared and inspected visually for particulate matter or colour change immediately and at 0.25, 1, 4 and 24 hours after mixing during storage at 24∞C. When a precipitate or colour change was observed additional mixtures were prepared to determine the range of compatible/incompatible concentrations.

Results: A colour change was observed when moxifloxacin was mixed with methprednisolone, sodium bicarbonate, or aminophylline. When pantoprazole is mixed with moxifloxacin a coloured precipitate develops within 24 hours. A precipitate develops immediately when moxifloxacin is mixed with furosemide.

Conclusions: Moxifloxacin 1.6 mg/mL in 0.8% sodium chloride is physically compatible with a large number of compounds over a 24-hour period. A precipitate or colour change on mixing indicates that moxifloxacin (1.6 mg/mL) is incompatible with aminophylline, furosemide, pantoprazole, methylprednisolone and sodium bicarbonate.

DEVELOPMENT OF THE FAMILY MEDICINE MEDICATION USE PROCESSES MATRIX

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Rationale: Successful integration of pharmacists into family practice requires the development of a shared understanding of team members' expertise and roles yet there is no tool to measure this.

Description of tool: A matrix was developed and validated to measure perceptions of contribution of various primary health care professionals to family practice medication related processes.

Steps taken: Project investigators generated a list of medication-related processes commonly occurring in primary care and contributing team members. Clinical appropriateness was assessed using a sensibility questionnaire (for clarity, face validity, content validity, ease of use, and comprehensiveness) with 7-point Likert-type scales. Second and third revised versions were pilot-tested with practising pharmacists and physicians. A principle components factor analysis (to group the medication-related tasks in order to simplify scoring and interpretation) was performed.

Results: Eight research team members completed the matrix and sensibility questionnaire, agreeing the matrix was feasible to complete in 10-20 minutes. Several main changes included: scale descriptors changed to reflect 'contribution' rather than 'responsibility', items reworded for clarity and missing items added. Seven pharmacists and physicians assessed the second version and 4 assessed the third. Minor changes were made. Mean sensibility ratings improved to >5 for each component. Factor analysis did not present significant grouping patterns of variables (small sample size), however, 5 theoretical groupings (diagnosis/prescribing, monitoring, administrative/documentation, education, medication review) are presented.

Importance for practice: Explicit description of medication-related processes in primary care can delineate the pharmacist's and other's contribution to the processes and encourage discussion about improvements.

TORSADES DE POINTES ASSOCIATED WITH CESIUM CHLORIDE

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Cesium chloride has been claimed to cure cancer due to its alkalinic nature. We present a case of torsades de pointes associated with cesium chloride infusion.

A 58-year-old female with a history of inoperable breast cancer was admitted to hospital for syncope. The patient had no history of cardiovascular disease or sudden death. She was undergoing a series of cesium chloride infusions when she

started experiencing syncopal episodes at the end of the infusions. On the day of admission, she had another episode with documented bursts of ventricular tachycardia and multiple ventricular premature beats. While in the emergency room, she had a recurrent episode of syncope with torsades de pointes. On admission, her QTc was 690, potassium level was 2.9, magnesium level 0.89 and calcium level 2.24. Treatment in hospital consisted of magnesium and potassium replenishment, and intermittent lidocaine infusion. Since cesium cannot be dialyzed, prussian blue was used to prevent its re-absorption into the circulation. The QTc normalized and the patient stabilized. After 6 months of follow-up, the patient has not had any further episode of syncope.

A Naranjo Causality score suggested that cesium chloride was a probable cause of the torsades de pointes. Hypokalemia may have played a part but QT interval remained prolonged after normalization of the serum potassium level.

This is the first report of the use of prussian blue for nonradioactive cesium toxicity. This case also illustrates the importance for pharmacists to be aware of the clinical caution in alternative therapies.

PHARMACOKINETICS OF CIPROFLOXACIN IN ASIANS WITH DIFFERENT CYP2C19 AND CYP3A5 GENOTYPES

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Ciprofloxacin is subjected to first-pass metabolism in the liver. It is known that P450 is involved in the free radical formation during the metabolism of ciprofloxacin. However, little is known about the impact of P450 polymorphisms on the metabolism of ciprofloxacin. Our study was designed to investigate the effect of genetic polymorphisms of P450 on the pharmacokinetics of ciprofloxacin in CYP2C19 and CYP3A5 genotyped Asian subjects. We recruited 24 volunteers to determine the genotypes of CYP2C19 and CYP3A5 by PCR-RFLP. The plasma concentrations of ciprofloxacin after a single oral 500mg dose of ciprofloxacin in the subjects were determined by HPLC. The results indicated that the pharmacokinetics of ciprofloxacin was independent of CYP3A5 expression. However, the polymorphism of CYP2C19 may play an important role in the metabolism of ciprofloxacin in Asians, as our results showed, ciprofloxacin CL was significantly higher in extensive metabolizers (EM) than in poor metabolizers (PM) (0.039 ± 0.012 L/h vs 0.029 ± 0.005 L/h, $p < 0.05$). The Vd in EM was also significantly higher than that in PM (0.27 ± 0.11 L vs 0.19 ± 0.03 L, $p < 0.05$). In this study, PM showed a 27% increase in ciprofloxacin AUC and a 26% increase in Cmax compared with EM.

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c. study design and methods,
d. results of study, including statistical analysis used
e. conclusion of study (which should be supported by results presented)

Case Reports:

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b. description of case and problem
c. analysis of problem
d. importance of case to pharmacy practitioners

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Erythropoietic therapies may increase the risk of cardiovascular events, including death. The higher risk of cardiovascular events may be associated with higher hemoglobin and/or higher rates of rise of hemoglobin. The hemoglobin level should be managed carefully, with a target not exceeding 120 g/L. **It is recommended that the dose of Aranesp® be decreased if the hemoglobin increase exceeds 10 g/L in any 2-week period, because of the association of excessive rate of rise of hemoglobin with these events (see Dose Adjustment).**

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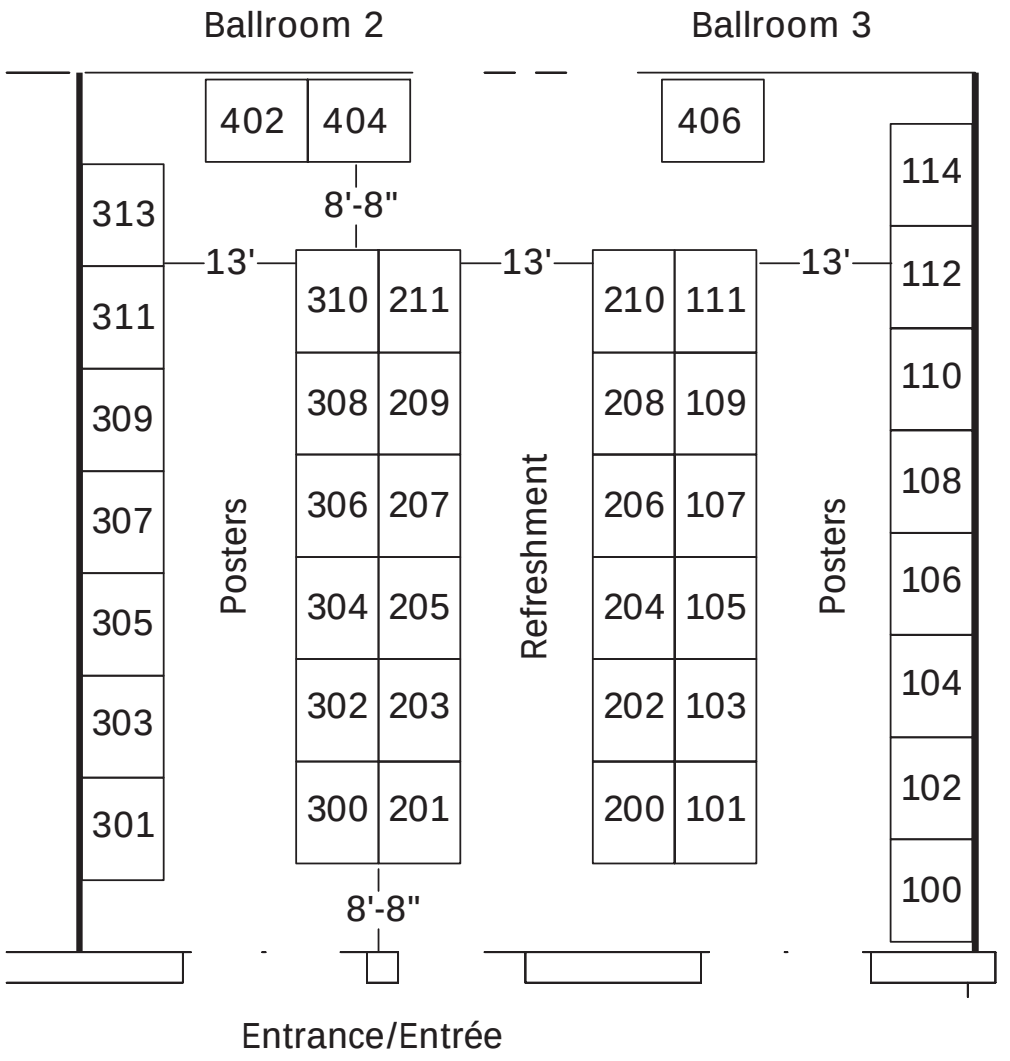

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Clinical Studies

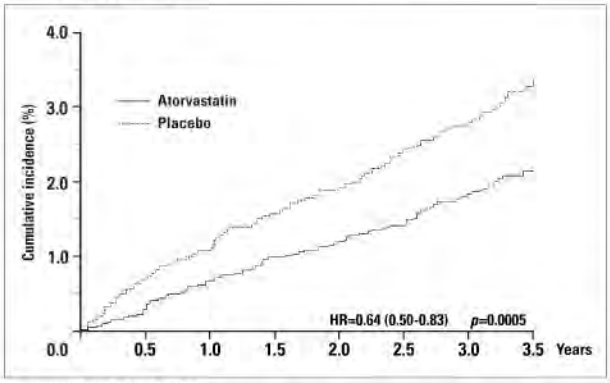
Prevention of Cardiovascular Disease

In the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), the effect of LIPITOR (atorvastatin calcium) on fatal and non-fatal coronary heart disease was assessed in 10,305 hypertensive patients 40-80 years of age (mean of 63 years), without a previous myocardial infarction and with TC levels ≤6.5 mmol/L. Additionally all patients had at least 3 of the following cardiovascular risk factors: male gender (81.1%), age >55 years (84.5%), smoking (33.2%), diabetes (24.3%), history of CHD in a first-degree relative (26%), TC:HDL >6 (14.3%), peripheral vascular disease (5.1%), left ventricular hypertrophy (14.4%), prior cerebrovascular event (9.8%), specific ECG abnormality (14.3%), proteinuria/albuminuria (62.4%). In this double-blind, placebo-controlled study, patients were treated with anti-hypertensive therapy (Goal BP <140/90 mm Hg for non-diabetic patients, <130/80 mm Hg for diabetic patients) and allocated to either LIPITOR 10 mg daily (n=5168) or placebo (n=5137), using a covariate adaptive method which took into account the distribution of nine baseline characteristics of patients already enrolled and minimized the imbalance of those characteristics across the groups. Patients were followed for a median duration of 3.3 years.

The effect of 10 mg/day of LIPITOR on lipid levels was similar to that seen in previous clinical trials.

LIPITOR significantly reduced the rate of coronary events (either fatal coronary heart disease (46 events in the placebo group vs 40 events in the LIPITOR group) or nonfatal MI (108 events in the placebo group vs 60 events in the LIPITOR group)) with an absolute risk reduction of 1.1% and a relative risk reduction of 36% (based on incidences of 1.9% for LIPITOR vs 3.0% for placebo), p=0.0005 (see figure 1). This risk reduction yields a Number Needed to Treat of 311 patients per year. The risk reduction was consistent regardless of age, smoking status, obesity or presence of renal dysfunction. The effect of LIPITOR was seen regardless of baseline LDL levels. Due to the small number of events, results for women were inconclusive.

Figure 1: Effect of LIPITOR 10 mg/day on Cumulative Incidence of Nonfatal Myocardial Infarction or Coronary Heart Disease Death (in ASCOT-LLA)



INDICATIONS AND CLINICAL USE

Hypercholesterolemia

LIPITOR (atorvastatin calcium) is indicated as an adjunct to lifestyle changes, including diet, (at least equivalent to the Adult Treatment Panel III (ATP III) TLC diet), for the reduction of elevated total cholesterol, (total-C), LDL-C, TG and apolipoprotein B (apo B) in hyperlipidemic and dyslipidemic conditions, when response to diet and other nonpharmacological measures alone has been inadequate, including:

- Primary hypercholesterolemia (Type IIa);
- Combined (mixed) hyperlipidemia (Type IIb), including familial combined hyperlipidemia, regardless of whether cholesterol or triglycerides are the lipid abnormality of concern;
- Dysbetalipoproteinemia (Type III);
- Hypertriglyceridemia (Type IV);
- Familial hypercholesterolemia (homozygous and heterozygous). For homozygous familial hypercholesterolemia, LIPITOR should be used as an adjunct to treatments such as LDL apheresis, or as monotherapy if such treatments are not available.

LIPITOR also raises HDL-cholesterol and therefore lowers the LDL-C/HDL-C and total-C/HDL-C ratios in patients with primary hypercholesterolemia and combined (mixed) hyperlipidemia (Fredrickson Type IIa and IIb dyslipidemia). In pooled data from 24 controlled clinical trials, LIPITOR raised HDL-C levels 5%-7% in primary hypercholesterolemic (type IIa) patients and 10%-15% in mixed (type IIb) dyslipidemic patients.

In clinical trials, LIPITOR (10 to 80 mg/day) significantly improved lipid profiles in patients with a wide variety of hyperlipidemic and dyslipidemic conditions. In 2 dose-response studies in mildly to moderately hyperlipidemic patients (Fredrickson Types IIa and IIb), LIPITOR reduced the levels of total cholesterol (29-45%), LDL-C (39-60%), apo B (32-50%), TG (19-37%), and increased high density lipoprotein cholesterol (HDL-C) levels (5-9%). Comparable responses were achieved in patients with heterozygous familial hypercholesterolemia, non-familial forms of hypercholesterolemia, combined hyperlipidemia, including familial combined hyperlipidemia and patients with non-insulin dependent diabetes mellitus. In patients with hypertriglyceridemia (Type IV), LIPITOR (10 to 80 mg daily) reduced TG (25 - 56%) and LDL-C levels (23 - 40%). LIPITOR has not been studied in conditions where the major abnormality is elevation of chylomicrons (TG levels > 11 mmol/L), i.e., types I and V.

In an open-label study in patients with dysbetalipoproteinemia (Type III), LIPITOR (10 to 80 mg daily) reduced total-C (40-57%), TG (40-56%) and IDL-C + VLDL-C levels (34-58%).

In an open label study in patients with homozygous familial hypercholesterolemia (FH) LIPITOR (10 to 80 mg daily) reduced mean LDL-C levels (22%). In a pilot study, LIPITOR 80 mg/day showed a mean LDL-C lowering of 30% for patients not on plasmapheresis and of 31% for patients who continued plasmapheresis. A mean LDL-C lowering of 35% was observed in receptor defective patients and of 19% in receptor negative patients (see PHARMACOLOGY, Clinical Studies).

Prior to initiating therapy with LIPITOR, secondary causes should be excluded for elevations in plasma lipid levels (e.g. poorly controlled diabetes mellitus, hypothyroidism, nephrotic syndrome, dysproteinemias, obstructive liver disease, and alcoholism), and a lipid profile performed to measure total cholesterol, LDL-C, HDL-C, and TG. For patients with TG <4.52 mmol/L (<400 mg/dL), LDL-C can be estimated using the following equation:

$$\text{LDL-C (mmol/L)} = \text{total-C} - [(0.37 \times \text{(TG)}) + \text{HDL-C)}]$$

$$\text{LDL-C (mg/dL)} = \text{total-C} - [(0.2 \times \text{(TG)}) + \text{HDL-C)}]$$

For patients with TG levels >4.52 mmol/L (>400 mg/dL), this equation is less accurate and LDL-C concentrations should be measured directly or by ultracentrifugation.

Patients with high or very high triglyceride levels, i.e. > 2.2 mmol/L (200 mg/dL) or > 5.6 mmol/L (500 mg/dL), respectively, may require triglyceride-lowering therapy (fenofibrate, bezafibrate or nicotinic acid) alone or in combination with LIPITOR.

In general, combination therapy with fibrates must be undertaken cautiously and only after risk-benefit analysis (see WARNINGS, Muscle Effects, PRECAUTIONS, Pharmacokinetic Interaction Studies and Potential Drug Interactions).

Elevated serum triglycerides are most often observed in patients with the metabolic syndrome (abdominal obesity, atherogenic dyslipidemia (elevated triglycerides, small dense LDL particles and low HDL-cholesterol), insulin resistance with or without glucose intolerance, raised blood pressure and prothrombotic and proinflammatory states).

(For the treatment of specific dyslipidemias refer to the Report of the Canadian Working Group on Hypercholesterolemia and Other Dyslipidemias or to the US NCEP Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [Adult Treatment Panel III]).

When drugs are prescribed attention to therapeutic lifestyle changes (reduced intake of saturated fats and cholesterol, weight reduction, increased physical activity, ingestion of soluble fibers) should always be maintained and reinforced.

Prevention of Cardiovascular Disease

LIPITOR is indicated to reduce the risk of myocardial infarction in adult hypertensive patients without clinically evident coronary heart disease, but with at least three additional risk factors for coronary heart disease such as age ≥55 years, male sex, smoking, type 2 diabetes, left ventricular hypertrophy, other specified abnormalities on ECG, microalbuminuria or proteinuria, ratio of plasma total-cholesterol to HDL-cholesterol ≥6, or premature family history of coronary heart disease.

The Atorvastatin Versus Revascularization Treatments (AVERT) study examined the effect of intensive lipid-lowering in patients with stable coronary artery disease and LDL-C at least 3.0 mmol/L. In patients referred for percutaneous transluminal coronary angioplasty (PTCA). Patients were randomised for 18 months to LIPITOR 80 mg daily or to PTCA with usual medical care which could include lipid metabolism regulators. The results of the AVERT study should be considered as exploratory since several limitations may affect its design and conduct. In the medical-treated group with LIPITOR there was a trend for a reduced incidence of ischemic events and a delayed time to first ischemic event. The results also suggest that intensive treatment to target LDL-C levels with LIPITOR is **additive and complementary** to angioplasty and would benefit patients referred for this procedure.

CONTRAINDICATIONS

Hypersensitivity to any component of this medication.

Active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal (see WARNINGS).

Pregnancy and lactation (see PRECAUTIONS).

WARNINGS

Pharmacokinetic Interactions

The use of HMG-CoA reductase inhibitors has been associated with severe myopathy, including rhabdomyolysis, which may be more frequent when they are co-administered with drugs that inhibit the cytochrome P-450 enzyme system. Atorvastatin is metabolized by cytochrome P-450 isoform 3A4 and as such may interact with agents that inhibit this enzyme. (See WARNINGS, Muscle effects and PRECAUTIONS, Drug Interactions and Cytochrome P-450-mediated Interactions).

Hepatic Effects

In clinical trials, persistent increases in serum transaminases greater than three times the upper limit of normal occurred in <1% of patients who received LIPITOR. When the dosage of LIPITOR was reduced, or when drug treatment was interrupted or discontinued, serum transaminase levels returned to pretreatment levels. The increases were generally not associated with jaundice or other clinical signs or symptoms. Most patients continued treatment with a reduced dose of LIPITOR without clinical sequelae.

Liver function tests should be performed before the initiation of treatment, and periodically thereafter. Special attention should be paid to patients who develop elevated serum transaminase levels, and in these patients measurements should be repeated promptly and then performed more frequently.

If increases in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) show evidence of progression, particularly if they rise to greater than 3 times the upper limit of normal and are persistent, the dosage should be reduced or the drug discontinued.

LIPITOR should be used with caution in patients who consume substantial quantities of alcohol and/or have a past history of liver disease. Active liver disease or unexplained transaminase elevations are contraindications to the use of LIPITOR; if such a condition should develop during therapy, the drug should be discontinued.

Muscle Effects

Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatinine phosphokinase (CPK) values to greater than ten times the upper limit of normal, should be considered in any patient with diffuse myalgia, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. LIPITOR therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. The risk of myopathy and rhabdomyolysis during treatment with HMG-CoA reductase inhibitors is increased with concurrent administration of cyclosporin, fibric acid derivatives, erythromycin, clarithromycin, niacin (nicotinic acid), azole antifungals or nefazodone. As there is no experience to date with the use of LIPITOR given concurrently with these drugs, with the exception of pharmacokinetic studies conducted in healthy subjects with erythromycin and clarithromycin, the benefits and risks of such combined therapy should be carefully considered (see PRECAUTIONS, Pharmacokinetic Interaction Studies and Potential Drug Interactions).

Rhabdomyolysis has been reported in very rare cases with LIPITOR (see PRECAUTIONS, Drug Interactions).

Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has also been reported with HMG-CoA reductase inhibitors. LIPITOR therapy should be temporarily withheld or discontinued in any patient with an acute serious condition suggestive of a myopathy or having a risk factor predisposing to the development of renal failure secondary to rhabdomyolysis (such as severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures).

PRECAUTIONS

General

Before instituting therapy with LIPITOR (atorvastatin calcium), an attempt should be made to control elevated serum lipoprotein levels with appropriate diet, exercise, and weight reduction in overweight patients, and to treat other underlying medical problems (see INDICATIONS AND CLINICAL USE). Patients should be advised to inform subsequent physicians of the prior use of LIPITOR or any other lipid-lowering agents.

Effect on the Lens

Current long-term data from clinical trials do not indicate an adverse effect of atorvastatin on the human lens.

Effect on Ubiquinone (CoQ_{10}) Levels

Significant decreases in circulating ubiquinone levels in patients treated with atorvastatin and other statins have been observed. The clinical significance of a potential long-term statin-induced deficiency of ubiquinone has not been established. It has been reported that a decrease in myocardial ubiquinone levels could lead to impaired cardiac function in patients with borderline congestive heart failure.

Effect on Lipoprotein (a)

In some patients, the beneficial effect of lowered total cholesterol and LDL-C levels may be partly blunted by a concomitant increase in Lp(a) lipoprotein concentrations. Present knowledge suggests the importance of high Lp(a) levels as an emerging risk factor for coronary heart disease. It is thus desirable to maintain and reinforce lifestyle changes in high risk patients placed on atorvastatin therapy.

Hypersensitivity

An apparent hypersensitivity syndrome has been reported with other HMG-CoA reductase inhibitors which has included 1 or more of the following features: anaphylaxis, angioedema, lupus erythematous-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, eosinophilia, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome. Although to date hypersensitivity syndrome has not been described as such, LIPITOR should be discontinued if hypersensitivity is suspected.

Use in Pregnancy

LIPITOR is contraindicated during pregnancy (see CONTRAINDICATIONS).

Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since

1. Friedewald WT, *et al. Clin Chem* 1972;18(6):489-502.

HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause harm to the fetus when administered to pregnant women.

There are no data on the use of LIPITOR during pregnancy. LIPITOR should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the patient becomes pregnant while taking LIPITOR, the drug should be discontinued and the patient apprised of the potential risk to the fetus.

Nursing Mothers

In rats, milk concentrations of atorvastatin are similar to those in plasma. It is not known whether this drug is excreted in human milk. Because of the potential for adverse reactions in nursing infants, women taking LIPITOR should not breast-feed (see CONTRAINDICATIONS).

Pediatric Use

Treatment experience in a pediatric population is limited to doses of LIPITOR up to 80 mg/day for 1 year in 8 patients with homozygous familial hypercholesterolemia. No clinical or biochemical abnormalities were reported in these patients.

Geriatric Use

Treatment experience in adults 70 years or older (N=221) with doses of LIPITOR up to 80 mg/day has demonstrated that the safety and effectiveness of atorvastatin in this population was similar to that of patients <70 years of age. Pharmacokinetic evaluation of atorvastatin in subjects over the age of 65 years indicates an increased AUC. As a precautionary measure, the lowest dose should be administered initially.

Renal Insufficiency

Plasma concentrations and LDL-C lowering efficacy of LIPITOR was shown to be similar in patients with moderate renal insufficiency compared with patients with normal renal function. However, since several cases of rhabdomyolysis have been reported in patients with a history of renal insufficiency of unknown severity, as a precautionary measure and pending further experience in renal disease, the lowest dose (10 mg/day) of LIPITOR should be used in these patients. Similar precautions apply in patients with severe renal insufficiency [creatinine clearance <30 mL/min (<0.5 mL/sec)]; the lowest dosage should be used and implemented cautiously (see WARNINGS, Muscle Effects; PRECAUTIONS, Drug Interactions).

Refer also to DOSAGE AND ADMINISTRATION.

Endocrine Function

HMG-CoA reductase inhibitors interfere with cholesterol synthesis and as such might theoretically blunt adrenal and/or gonadal steroid production. Clinical studies with atorvastatin and other HMG-CoA reductase inhibitors have suggested that these agents do not reduce plasma cortisol concentration or impair adrenal reserve and do not reduce basal plasma testosterone concentration. However, the effects of HMG-CoA reductase inhibitors on male fertility have not been studied in adequate numbers of patients. The effects, if any, on the pituitary-gonadal axis in premenopausal women are unknown.

Patients treated with atorvastatin who develop clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients receiving other drugs (e.g. ketoconazole, spironolactone or cimetidine) that may decrease the levels of endogenous steroid hormones.

Pharmacokinetic Interaction Studies and Potential Drug Interactions

Pharmacokinetic interaction studies conducted with drugs in healthy subjects may not detect the possibility of a potential drug interaction in some patients due to differences in underlying diseases and use of concomitant medications (see also Geriatric Use; Renal Insufficiency; Patients with Severe Hypercholesterolemia).

Concomitant Therapy with Other Lipid Metabolism Regulators: Combined drug therapy should be approached with caution as information from controlled studies is limited.

Bile Acid Sequestrants:

Patients with mild to moderate hypercholesterolemia: LDL-C reduction was greater when LIPITOR 10 mg and colestipol 20 g were coadministered (-45%) than when either drug was administered alone (-35% for LIPITOR and -22% for colestipol).

Patients with severe hypercholesterolemia: LDL-C reduction was similar (-33%) when LIPITOR 40 mg and colestipol 20 g were coadministered when compared to that with LIPITOR 80 mg alone. Plasma concentration of atorvastatin was lower (approximately 26%) when LIPITOR 40 mg plus colestipol 20 g were coadministered compared with LIPITOR 40 mg alone.

However, the combination drug therapy was less effective in lowering the triglycerides than LIPITOR monotherapy in both types of hypercholesterolemic patients.

When LIPITOR is used concurrently with colestipol or any other resin, an interval of at least 2 hours should be maintained between the two drugs, since the absorption of LIPITOR may be impaired by the resin.

Fibric Acid Derivatives (Gemfibrozil, Fenofibrate, Bezafibrate) and Niacin (Nicotinic Acid): Although there is limited experience with the use of LIPITOR given concurrently with fibric acid derivatives and niacin, the benefits and risks of such combined therapy should be carefully considered. The risk of myopathy during treatment with other drugs in this class, including atorvastatin, is increased with concurrent administration (see WARNINGS, Muscle Effects).

Coumarin Anticoagulants: LIPITOR had no clinically significant effect on prothrombin time when administered to patients receiving chronic warfarin therapy.

Digoxin: In healthy subjects, digoxin pharmacokinetics at steady-state were not significantly altered by coadministration of digoxin 0.25 mg and LIPITOR 10 mg daily. However, digoxin steady-state concentrations increased approximately 20% following coadministration of digoxin 0.25 mg and LIPITOR 80 mg daily. Patients taking digoxin should be monitored appropriately.

Antihypertensive agents (amlodipine): In clinical studies, LIPITOR was used concomitantly with antihypertensive agents without evidence to date of clinically significant adverse interactions. In healthy subjects, atorvastatin pharmacokinetics were not altered by the coadministration of LIPITOR 80 mg and amlodipine 10 mg at steady state.

(quinapril): In a randomized, open-label study in healthy subjects, steady-state quinapril dosing (80 mg QD) did not significantly affect the pharmacokinetic profile of atorvastatin tablets (10 mg QD).

Oral Contraceptives and Hormone Replacement Therapy: Coadministration of LIPITOR with an oral contraceptive, containing 1 mg norethindrone and 35 µg ethinyl estradiol, increased plasma concentrations (AUC levels) of norethindrone and ethinyl estradiol by approximately 30% and 20%, respectively. These increases should be considered when selecting an oral contraceptive. In clinical studies, LIPITOR was used concomitantly with estrogen replacement therapy without evidence to date of clinically significant adverse interactions.

Antacids: Administration of aluminum and magnesium based antacids, such as Maalox® TC Suspension, with LIPITOR decreased plasma concentrations of LIPITOR by approximately 35%. LDL-C reduction was not altered but the triglyceride-lowering effect of LIPITOR may be affected.

Cimetidine: Administration of cimetidine with LIPITOR did not alter plasma concentrations or LDL-C lowering efficacy of LIPITOR, however, the triglyceride-lowering effect of LIPITOR was reduced from 34% to 26%.

Cytochrome P-450-mediated Interactions: Atorvastatin is metabolized by the cytochrome P-450 isoenzyme, CYP 3A4. Erythromycin, a CYP 3A4 inhibitor, increased atorvastatin plasma levels by 40%. Coadministration of CYP 3A4 inhibitors, such as grapefruit juice, some macrolide antibiotics (i.e. erythromycin, clarithromycin), immunosuppressants (cyclosporine), azole antifungal agents (i.e. itraconazole, ketoconazole), protease inhibitors, or the antidepressant, nefazodone, may have the potential to increase plasma concentrations of HMG-CoA reductase inhibitors, including LIPITOR. Caution should thus be exercised with concomitant use of these agents (see WARNINGS, Pharmacokinetic Interactions; Muscle Effects; PRECAUTIONS, Renal Insufficiency and Endocrine Function; DOSAGE AND ADMINISTRATION).

In healthy subjects, coadministration of maximum doses of both atorvastatin (80 mg) and terfenadine (120 mg), a CYP 3A4 substrate, was shown to produce a modest increase in terfenadine AUC. The QTc interval remained unchanged. However, since an interaction between these two drugs cannot be excluded in patients with predisposing factors for arrhythmia, (e.g. preexisting prolonged QT interval, severe coronary artery disease, hypokalemia), caution should be exercised when these agents are coadministered (see WARNINGS, Pharmacokinetic Interactions; DOSAGE AND ADMINISTRATION).

Antipyrine: Antipyrine was used as a non-specific model for drugs metabolized by the microsomal hepatic enzyme system (cytochrome P-450 system). LIPITOR had no effect on the pharmacokinetics of antipyrine, thus interactions with other drugs metabolized via the same cytochrome isozymes are not expected.

Macrolide Antibiotics (azithromycin, clarithromycin, erythromycin): In healthy adults, coadministration of LIPITOR (10 mg QD) and azithromycin (500 mg QD) did not significantly alter the plasma concentrations of atorvastatin. However, coadministration of atorvastatin (10 mg QD) with erythromycin (500 mg QID) or clarithromycin (500 mg BID), which are both CYP 3A4 inhibitors, increased plasma concentrations of atorvastatin approximately 40% and 80%, respectively (see WARNINGS, Muscle Effects).

Protease Inhibitors (nelfinavir mesylate): In healthy adults, coadministration of nelfinavir mesylate (1250 mg BID), a known CYP 3A4 inhibitor, and atorvastatin (10 mg QD) resulted in increased plasma concentrations of atorvastatin. AUC and C_{max} of atorvastatin were increased by 74% and 122% respectively.

Patients with Severe Hypercholesterolemia: Higher drug dosages (80 mg/day) required for some patients with severe hypercholesterolemia (including familial hypercholesterolemia) are associated with increased plasma levels of atorvastatin. **Caution should be exercised in such patients who are also severely renally impaired, elderly, or are concomitantly being administered digoxin or CYP 3A4 inhibitors (see WARNINGS, Pharmacokinetic Interactions, Muscle Effects; PRECAUTIONS, Drug Interactions; DOSAGE AND ADMINISTRATION).**

Drug/Laboratory Test Interactions

LIPITOR may elevate serum transaminase and creatinine phosphokinase levels (from skeletal muscle). In the differential diagnosis of chest pain in a patient on therapy with LIPITOR, cardiac and noncardiac fractions of these enzymes should be determined.

ADVERSE REACTIONS

LIPITOR is generally well-tolerated. Adverse reactions have usually been mild and transient. In controlled clinical studies (placebo-controlled and active-controlled comparative studies with other lipid-lowering agents) involving 2502 patients, <2% of patients were discontinued due to adverse experiences attributable to LIPITOR. Of these 2502 patients, 1721 were treated for at least 6 months and 1253 for 1 year or more.

Adverse experiences occurring at an incidence ≥1% in patients participating in placebo-controlled clinical studies of LIPITOR and reported to be possibly, probably or definitely drug related are shown in Table 1 below:

TABLE 1. Associated Adverse Events Reported in ≥1% of Patients in Placebo-Controlled Clinical Trials

	Placebo % (n=270)	LIPITOR % (n=1122)
GASTROINTESTINAL		
Constipation	1	1
Diarrhea	1	1
Dyspepsia	2	1
Flatulence	2	1
Nausea	0	1
NERVOUS SYSTEM		
Headache	2	1
MISCELLANEOUS		
Pain	<1	1
Myalgia	1	1
Asthenia	<1	1

The following additional adverse events were reported in clinical trials; not all events listed below have been associated with a causal relationship to LIPITOR therapy: Muscle cramps, myositis, myopathy, paresthesia, peripheral neuropathy, pancreatitis, hepatitis, cholestatic jaundice, anorexia, vomiting, alopecia, pruritus, rash, impotence, hyperglycemia, and hypoglycemia.

Post-marketing experience: Very rare reports: severe myopathy with or without rhabdomyolysis (see WARNINGS, Muscle Effects; PRECAUTIONS, Renal Insufficiency and Drug Interactions). Isolated reports: thrombocytopenia, arthralgia and allergic reactions including urticaria, angioneurotic edema, anaphylaxis and bullous rashes (including erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis)[. These may have no causal relationship to atorvastatin.

Ophthalmologic observations: see PRECAUTIONS.

Laboratory Tests: Increases in serum transaminase levels have been noted in clinical trials (see WARNINGS).

DOSAGE AND ADMINISTRATION

Patients should be placed on a standard cholesterol-lowering diet [at least equivalent to the Adult Treatment Panel III (ATP III) TLC diet] before receiving LIPITOR, and should continue on this diet during treatment with LIPITOR. If appropriate, a program of weight control and physical exercise should be implemented.

Primary Hypercholesterolemia and Combined (Mixed) Dyslipidemia, Including Familial Combined Hyperlipidemia

The recommended starting dose of LIPITOR is 10 or 20 mg once daily. Patients who require a large reduction in LDL-C (more than 45%) may be started at 40 mg once daily. The dosage range of LIPITOR is 10 to 80 mg once daily. Doses can be given at any time of the day, with or without food, and should preferably be given in the evening. Doses should be individualized according to the level of risk, the baseline LDL-C and/or TG levels; the desired LDL-C and/or TG target; and/or TC/HDL-C target (see the Detection and Management of Hypercholesterolemia, Working Group on Hypercholesterolemia and other Dyslipidemias [Canada] and/or the US National Cholesterol Education Program [NCEP Adult Treatment Panel III]); the goal of therapy and the patient's response. A significant therapeutic response is evident within 2 weeks, and the maximum response is usually achieved within 2-4 weeks. The response is maintained during chronic therapy. Adjustments of dosage, if necessary, should be made at intervals of 2-4 weeks. The maximum dose is 80 mg/day.

Lipid levels should be monitored periodically and, if necessary, the dose of LIPITOR adjusted based on target lipid levels recommended by guidelines.

The following reductions in total cholesterol and LDL-C levels have been observed in 2 dose-response studies, and may serve as a guide to treatment of patients with mild to moderate hypercholesterolemia:

TABLE 2. Dose-Response in Patients With Mild to Moderate Hypercholesterolemia
(Mean Percent Change from Baseline)

Lipid Parameter	LIPITOR Dose (mg/day)			
	10 (N=22)	20 (N=20)	40 (N=21)	80 (N=23)
Total-C: 7.1 mmol/L* (273 mg/dL)	-29	-33	-37	-45
LDL-C: 4.9 mmol/L* (190 mg/dL)	-39	-43	-50	-60

* Results are pooled from 2 dose-response studies.
† Mean baseline values.

Severe Dyslipidemias

In patients with severe dyslipidemias, including homozygous and heterozygous familial hypercholesterolemia and dysbetalipoproteinemia (Type III), higher dosages (up to 80 mg/day) may be required (see WARNINGS, Pharmacokinetic Interactions; Muscle Effects; PRECAUTIONS, Drug Interactions).

Concomitant Therapy

See PRECAUTIONS, Drug Interactions.

Dosage in Patients With Renal Insufficiency

See PRECAUTIONS.

AVAILABILITY OF DOSAGE FORMS

LIPITOR (atorvastatin calcium) is available in dosage strengths of 10 mg, 20 mg, 40 mg and 80 mg atorvastatin per tablet.

10 mg: White, elliptical, film-coated tablet, coded "10" on one side and "PD 155" on the other. Available in bottles of 90 tablets.

20 mg: White, elliptical, film-coated tablet, coded "20" on one side and "PD 156" on the other. Available in bottles of 90 tablets.

40 mg: White, elliptical, film-coated tablet, coded "40" on one side and "PD 157" on the other. Available in bottles of 90 tablets.

80 mg: White, elliptical, film-coated tablet, coded "80" on one side and "PD 158" on the other. Available in blisters of 30 tablets (3 strips X 10).

References:

1. LIPITOR (atorvastatin calcium) Product Monograph, Pfizer Canada Inc., September 2004. **2.** IMS Health, IMS MIDAS™ (Standard Units: Year 1997 through to March 2004). **3.** Data on file, Pfizer Canada Inc. **4.** Simon Day Dictionary for Clinical Trials, 1999, John Wiley & Sons Ltd. 137-39.

For a copy of the Product Monograph or full Prescribing Information, please contact:

This product has been approved under the Notice of Compliance with Conditions (NOC/c) policy for one or all of its indicated uses.

What is a Notice of Compliance with Conditions (NOC/c)?

An NOC/c is a form of market approval granted to a product on the basis of **promising** evidence of clinical effectiveness following review of the submission by Health Canada.

Products approved under Health Canada's NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed-upon time frame.

What will be different about this Product Monograph?

The following Product Monograph will contain boxed text at the beginning of each major section clearly stating the nature of the market authorization. Sections for which NOC/c status holds particular significance will be identified in the left margin by the symbol **NOC/c**. These sections may include, but are not limited to, the following:

- Indications and Clinical Use;
- Action and Clinical Pharmacology;
- Warnings and Precautions;
- Adverse Reactions;
- Dosage and Administration; and
- Clinical Trials.

Adverse Drug Reaction Reporting and Re-Issuance of the Product Monograph

Healthcare providers are encouraged to report Adverse Drug Reactions associated with normal use of these and all drug products to Health Canada's Health Product Safety Information Division at 1-866-234-2345. The Product Monograph will be re-issued in the event of serious safety concerns previously unidentified or at such time as the sponsor provides the additional data in support of the product's clinical benefit. Once the latter has occurred, and in accordance with the NOC/c policy, the conditions associated with market authorization will be removed.

VELCADE®

bortezomib mannitol boronic ester for injection

3.5 mg/vial bortezomib
Antineoplastic Agent

HEALTH PROFESSIONAL INFORMATION

VELCADE, indicated for the treatment of multiple myeloma patients who have relapsed following front-line therapy and are refractory to their most recent therapy, has been issued marketing authorization with conditions, pending the results of studies to verify its clinical benefit. Patients should be advised of the nature of the authorization.

Treatment must be initiated and administered under the supervision of a healthcare professional qualified and experienced in the use of antineoplastic agents.

SUMMARY PRODUCT INFORMATION

Route of Administration	Pharmaceutical Form/Strength	Clinically Relevant Nonmedicinal Ingredients
intravenous	sterile lyophilized powder for injection/3.5 mg	None

VELCADE (bortezomib mannitol boronic ester) for injection will be referenced throughout the Product Monograph as VELCADE (bortezomib) for injection.

NOC/c INDICATIONS AND CLINICAL USE

VELCADE (bortezomib) for injection is indicated for the treatment of multiple myeloma patients who have relapsed following front-line therapy and are refractory to their most recent therapy.

The effectiveness of VELCADE is based on response rates (see ***Product Monograph*** **PART II, CLINICAL TRIALS**). There are no controlled trials demonstrating a clinical benefit such as an improvement in survival.

VELCADE should be administered under the supervision of a qualified healthcare professional who is experienced in the use of antineoplastic therapy.

Geriatrics (> 65 years of age):

Of the 202 patients enrolled, 35% were 65 years of age or older. Nineteen percent (19%) of patients aged 65 years or older experienced responses versus 32% in patients under the age of 65. (See **ADVERSE REACTIONS, ACTION AND CLINICAL PHARMACOLOGY**, and ***Product Monograph*** **PART II, CLINICAL TRIALS**.)

Pediatrics and adolescents (<18 years of age):

The safety and effectiveness of VELCADE in children and adolescents have not been established.

NOC/c CONTRAINDICATIONS

VELCADE (bortezomib) for injection is contraindicated in patients with hypersensitivity to bortezomib, boron or to any of the excipients.

NOC/c WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

VELCADE should be administered under the supervision of a qualified healthcare professional who is experienced in the use of antineoplastic therapy. (See **INDICATIONS AND CLINICAL USE**.)

General

Tumor Lysis Syndrome:

Because VELCADE (bortezomib) for injection is a cytotoxic agent and can rapidly kill malignant plasma cells, the complications of tumor lysis syndrome may occur. The patients at risk of tumor lysis syndrome are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

Carcinogenesis and Mutagenesis

Carcinogenicity studies have not been conducted. Bortezomib was clastogenic in mammalian cells in the *in vitro* chromosomal aberration assay. Bortezomib was not mutagenic in bacteria (Ames assay) and in the *in vivo* micronucleus assay in mice. (See ***Product Monograph*** **PART II, TOXICOLOGY**).

Cardiovascular

VELCADE treatment is commonly associated with orthostatic/postural hypotension which is not an acute reaction and is observed throughout treatment (see **ADVERSE REACTIONS**). There was no prior history of orthostatic hypotension in these patients but half had pre-existing hypertension, one-third had evidence of peripheral neuropathy and it was associated with syncope in some patients. The mechanism is unknown although may be due to bortezomib-induced autonomic neuropathy. Most cases required pharmacological treatment, including hydration and/or adjustment of antihypertensive medications. Administration of mineralocorticoids was infrequently required. Caution should be used when treating patients with a history of syncope, patients receiving medications known to be associated with hypotension, and patients who are dehydrated. Patients should be instructed to seek medical advice if they experience symptoms of dizziness, light-headedness or fainting spells.

Acute development or exacerbation of congestive heart failure has been seen in patients with risk factors for, or existing, heart disease. Such patients should be monitored closely.

Gastrointestinal

Gastrointestinal events, including nausea, diarrhea, constipation, and vomiting occur frequently during VELCADE treatment (see **ADVERSE REACTIONS**). Cases of ileus have been reported and patients who experience constipation should be closely monitored. Events usually occur earlier in treatment (Cycles 1 and 2), may persist for several cycles, sometimes requiring administration of antiemetics and antidiarrheals. Fluid and electrolyte replacement should be administered if the patient becomes dehydrated.

Hematologic

Although VELCADE treatment may be associated with hematological toxicities, significant myelosuppression is uncommon (see **ADVERSE REACTIONS**). The most common hematological toxicity is thrombocytopenia which is characterized by a dose-related decrease in platelet count during the VELCADE dosing period (Days 1 to 11), generally with a return to baseline in platelet count during the rest period (Days 12 to 21) in each treatment cycle. Onset is common in Cycles 1 and 2 but can continue throughout therapy. On average, the pattern of platelet count decrease and recovery remained consistent over the 8-cycle study period and there was no evidence of cumulative thrombocytopenia. The mean platelet count nadir measured was approximately 40% of baseline. The severity of thrombocytopenia related to pre-treatment platelet count is shown in Table 1. Platelet count should be monitored prior to each dose of VELCADE. VELCADE therapy should be held when the platelet count is < 25,000/μL and re-initiated at a reduced dose. There have been reports of gastrointestinal and intracerebral hemorrhage in association with VELCADE induced thrombocytopenia (see **DOSAGE AND ADMINISTRATION** and **ADVERSE REACTIONS**). Platelet transfusions, red blood cell transfusions and administration of growth factors may be utilized in the management of hematological toxicities.

Table 1:

The Severity of Thrombocytopenia Related to Pre-Treatment Platelet Count

Pre-treatment Platelet Count	Number of Patients (N=228)	Number of Patients with Platelet Count <10,000/μL
≥ 75,000/μL	186	1 (1%)
≥ 50,000/μL - < 75,000/μL	15	2 (13%)
≥ 10,000/μL - < 50,000/μL	27	8 (30%)

Hepatic/Biliary/Pancreatic

Bortezomib is metabolized by liver enzymes and bortezomib's clearance may decrease in patients with hepatic impairment. No formal studies evaluating the effect of liver dysfunction on the pharmacokinetics or pharmacodynamics of VELCADE have been completed. These patients should be treated with extreme caution and monitored for toxicity and a dose reduction should be considered (see **DOSAGE AND ADMINISTRATION**).

Neurologic

Treatment with VELCADE is commonly associated with peripheral neuropathy that is predominantly sensory, although cases of mixed sensorimotor neuropathy have also been reported (see **ADVERSE REACTIONS**). Worsening of existing neuropathy is dose-related and cumulative. Of the patients who experienced treatment-emergent neuropathy, 70% had previously been treated with neurotoxic agents and 80% had signs or symptoms of peripheral neuropathy at baseline. The mechanism underlying VELCADE induced peripheral neuropathy is not known and the complete time-course of this toxicity has not been fully characterized. Full reversibility has not been demonstrated in preclinical studies (see ***Product Monograph*** **PART II, TOXICOLOGY**). Full reversibility has been documented in 14% of patients with severe symptoms with limited follow-up data available. Patients

with pre-existing symptoms (numbness, pain or a burning feeling in the feet or hands) and/or signs of peripheral neuropathy (hyperesthesia, hypoesthesia, paresthesia, or neuropathic pain) may experience worsening during treatment with VELCADE and it is recommended that all patients should be monitored for symptoms of neuropathy. Patients experiencing new or worsening peripheral neuropathy may require a change in the dose and schedule or cessation of VELCADE (see **DOSAGE AND ADMINISTRATION**).

Autonomic neuropathy may contribute to some adverse reactions, such as postural hypotension, diarrhea, constipation with ileus and pyrexia, but information on this is limited.

Seizures are uncommonly reported in patients without previous history of seizures. Caution should be exercised when treating patients with any risk factors.

Renal

No clinical information is available on the use of VELCADE in patients on hemodialysis. Six patients with creatinine clearances of less than 30 mL/minute received VELCADE at a dose of 1.3 mg/m² in the Phase II studies. Patients with creatinine clearance of less than 30 mL/minute should be closely monitored for toxicities when treated with VELCADE (see **ACTION AND CLINICAL PHARMACOLOGY, Special Populations and Conditions**).

Sexual Function/Reproduction

Fertility studies with bortezomib have not been performed. Degenerative effects in ovary and testes in the general toxicity studies suggest a potential effect on either male or female fertility (see ***Product Monograph*** **PART II, TOXICOLOGY**).

Special Populations

Pregnant Women:

Women of child-bearing potential should avoid becoming pregnant while being treated with VELCADE. Males and females of child-bearing capacity should use effective contraceptive measures during treatment and for 3 months following treatment.

Bortezomib was not teratogenic in rats and rabbits at highest dose tested (0.45 and 0.55 mg/m², respectively) but caused post-implantation loss in rabbits (see ***Product Monograph*** **PART II, TOXICOLOGY**).

No placental transfer studies have been conducted with bortezomib. There are no adequate and well-controlled studies in pregnant women. If VELCADE is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus.

Nursing Women:

It is not known whether bortezomib is excreted in milk. Because many drugs are excreted in milk and because of the potential for serious adverse reactions from VELCADE in nursing infants, women should be advised against breast-feeding while being treated with VELCADE.

Pediatrics and Adolescents (< 18 years of age):

The safety and effectiveness of VELCADE in children and adolescents have not been established.

Monitoring and Laboratory Tests

Complete blood counts including platelet counts should be frequently monitored throughout treatment with VELCADE.

NOC/c ADVERSE REACTIONS

Adverse Drug Reaction Overview

Two Phase II studies (see ***Product Monograph*** **PART II, CLINICAL TRIALS**) evaluated 228 patients with multiple myeloma receiving VELCADE (bortezomib) for injection 1.3 mg/m²/dose twice weekly for 2 weeks followed by a 10-day rest period (21-day treatment cycle length) for a maximum of 8 treatment cycles.

The most commonly reported adverse events were asthenia (including fatigue, malaise, weakness, fatigue aggravated and lethargy) (65%), nausea (64%), diarrhea (including loose stools) (55%), appetite decreased (including anorexia) (43%), constipation (43%), thrombocytopenia (43%), peripheral neuropathy (including peripheral sensory neuropathy and peripheral neuropathy aggravated) (37%), pyrexia (36%), vomiting (36%), and anemia (32%). Fourteen percent (14%) of patients experienced at least one episode of Grade 4 toxicity, with the most common toxicity being thrombocytopenia (3%) and neutropenia (3%).

During the studies, a total of 113 (50%) of the 228 patients experienced serious adverse events (SAEs), defined as any event, regardless of causality, that: results in death, is life-threatening, requires hospitalization or prolongs a current hospitalization, results in a significant disability or is deemed to be an important medical event. The most commonly reported SAEs included pyrexia (7%), pneumonia (7%), diarrhea (6%), vomiting (5%), dehydration (5%), and nausea (4%).

Adverse events thought by the investigator to be drug-related and leading to discontinuation occurred in 18% of patients. The reasons for discontinuation included peripheral neuropathy (5%), thrombocytopenia (4%), diarrhea (2%), and fatigue (2%).

Two deaths were reported and considered by the investigator to be possibly related to study drug: one case of cardiopulmonary arrest and one case of respiratory failure.

Clinical Trial Adverse Drug Reactions

The most common treatment-emergent adverse drug reactions occurring at ≥10% are presented in Table 2 by System Organ Class.

Table 2:
Most Commonly Reported (≥10% overall) Adverse Events Reported from 2 Phase II Clinical Trials by Multiple Myeloma Patients (N=228)

System Organ Class	VELCADE Treated Patients at 1.3 mg/m²/dose (N=228) All Events n (%)	Grade 3 Events n (%)	Grade 4 Events n (%)
Blood and lymphatic system disorders			
Thrombocytopenia	97 (43)	61 (27)	7 (3)
Anemia NOS or anemia NOS aggravated, hemoglobin decreased, red blood cell count decreased[1]	74 (32)	21 (9)	0
Neutropenia or neutropenia aggravated	54 (24)	29 (13)	6 (3)
Eye disorders			
Vision blurred	25 (11)	1 (<1)	0
Gastrointestinal disorders			
Nausea or nausea aggravated	145 (64)	15 (7)	0
Diarrhea NOS or loose stools	125 (55)	16 (7)	2 (1)
Constipation or constipation aggravated	99 (43)	5 (2)	0
Vomiting NOS	82 (36)	16 (7)	1 (<1)
Abdominal pain NOS, abdominal pain upper or abdominal discomfort	46 (20)	5 (2)	0
Dyspepsia	30 (13)	0	0
General disorders and administration site conditions			
Asthenia (fatigue, weakness, malaise, fatigue aggravated, lethargy)	149 (65)	42 (18)	1 (<1)
Pyrexia	82 (36)	9 (4)	0
Edema peripheral, edema lower limb, peripheral swelling[4]	48 (21)	2 (1)	0
Rigors	27 (12)	1 (<1)	0
Pain NOS	22 (10)	3 (1)	0
Infections and infestations			
Upper respiratory tract infection NOS	41 (18)	0	0
Herpes zoster	26 (11)	2 (1)	0
Pneumonia NOS	23 (10)	12 (5)	0
Metabolism and nutrition disorders			
Anorexia, appetite decreased NOS	99 (43)	6 (3)	0
Dehydration	42 (18)	15 (7)	0
Weight decreased, failure to thrive[5]	26 (11)	2 (1)	0
Musculoskeletal and connective tissue disorders			
Arthralgia, joint stiffness	63 (28)	11 (5)	0
Pain in the limb	59 (26)	16 (7)	0
Muscle cramps, muscle spasms, muscle stiffness, myalgia	60 (26)	8 (4)	0
Bone pain, bone pain aggravated	39 (17)	11 (5)	0
Back pain	31 (14)	9 (4)	0
Nervous system disorders			
Peripheral neuropathy NOS, peripheral neuropathy aggravated, peripheral sensory neuropathy	84 (37)	31 (14)	0
Headache NOS	63 (28)	8 (4)	0
Dizziness (excl. vertigo)	48 (21)	3 (1)	0
Paresthesia, burning sensation NOS	32 (14)	5 (2)	0
Dysgeusia	29 (13)	1 (<1)	0
Hypoesthesia	26 (11)	1 (<1)	0
Psychiatric disorders			
Insomnia	62 (27)	3 (1)	0
Anxiety NEC	32 (14)	0	0

System Organ Class	VELCADE Treated Patients at 1.3 mg/m²/dose (N=228) All Events n (%)	Grade 3 Events n (%)	Grade 4 Events n (%)
Respiratory, thoracic and mediastinal disorders			
Dyspnea NOS, dyspnea exertional, dyspnea exacerbated	66 (29)	8 (4)	1 (<1)
Cough	39 (17)	1 (<1)	0
Epistaxis	23 (10)	1 (<1)	0
Skin and subcutaneous tissue disorders			
Rash NOS, rash pruritic, rash erythematous, rash generalized, rash macular, rash papular erythema, urticaria NOS	63 (28)	1 (<1)	0
Pruritus NOS, pruritus generalized	28 (12)	0	0
Vascular disorders			
Orthostatic hypotension, hypotension NOS, postural hypotension	27 (12)	8 (4)	0

[1] Preferred terms mapped to Blood and Lymphatic System Disorders System Organ Class (SOC) or Investigations SOC
Preferred terms mapped to General Disorders and Administration Site Conditions SOC or Musculoskeletal and Connective Tissue Disorders SOC
Preferred terms mapped to Investigations SOC or Metabolism and Nutrition Disorders SOC

Serious Adverse Events from Other Clinical Studies (hematological malignancy and solid tumors)
In approximately 580 patients, the following serious adverse events (not described above) were reported, considered at least possibly related to study medication, in at least one patient treated with VELCADE administered as monotherapy or in combination with other chemotherapeutics. These studies were conducted in patients with hematological malignancies and in solid tumors.

Blood and lymphatic system disorders: Disseminated intravascular coagulation

Cardiac disorders: Atrial fibrillation aggravated, atrial flutter, cardiac amyloidosis, cardiac arrest, congestive heart failure, myocardial ischemia, myocardial infarction, peripheral effusion, pulmonary edema, ventricular tachycardia

One case of torsades de pointes (not described above) has been reported in a patient receiving VELCADE; causality has not been established.

Gastrointestinal disorders: Ascites, dysphagia, fecal impaction, gastritis hemorrhagic, gastrointestinal hemorrhage, hematemesis, ileus paralytic, large intestinal obstruction, paralytic intestinal obstruction, small intestinal obstruction, large intestinal perforation, stomatitis, melena, pancreatitis acute

Hepatobiliary: Hyperbilirubinemia, portal vein thrombosis

Immune system disorders: Anaphylactic reaction, drug hypersensitivity, immune complex mediated hypersensitivity, acute renal failure (proliferative glomerulonephropathy), diffuse polyarthritis and rash

Infections and infestations: Bacteremia

Injury, poisoning and procedural complications: Skeletal fracture, subdural hematoma

Metabolism and nutrition disorders: Hypocalcemia, hyperuricemia, hypokalemia, hypernatremia, hyponatremia, tumor lysis syndrome

Nervous system: Ataxia, coma, dizziness, dysarthria, dysautonomia, cranial palsy, grand mal convulsion, hemorrhagic stroke, motor dysfunction, spinal cord compression, transient ischemic attack

Psychiatric: Agitation, confusion, psychotic disorder, suicidal ideation

Renal and urinary: Calculus renal, bilateral hydronephrosis, bladder spasm, hematuria urinary incontinence, urinary retention, renal failure - acute and chronic, glomerular nephritis proliferative

Respiratory, thoracic and mediastinal: Acute respiratory distress syndrome, atelectasis, chronic obstructive airways disease exacerbated, dysphagia, dyspnea, dyspnea exertional, epistaxis, hemoptysis, hypoxia, lung infiltration, pleural effusion, pneumonitis, respiratory distress, respiratory failure

Vascular: Cerebrovascular accident, deep venous thrombosis, peripheral embolism, pulmonary embolism

Abnormal Hematologic and Clinical Chemistry Findings
Hematological abnormalities are expected in patients with advanced multiple myeloma. With bortezomib, cyclical thrombocytopenia was seen, with a general progressive decrease in platelet count during the bortezomib dosing period (Days 1 to 11) and a return to baseline in platelet count during the rest period (Days 12 to 21) in each treatment cycle. A trend towards an increase in hemoglobin and absolute neutrophil count across treatment cycles was noted especially with an improvement in the underlying disease. A trend towards a decrease in the absolute lymphocyte count was noted across the 8 treatment cycles; however, no trend was noted by cycle. Effects on electrolytes and calcium (hyper- and hypokalemia, hyper- and hyponatremia, hyper- and hypocalcemia) and hypophosphatemia, hypochloremia and hypomagnesemia were noted.

Post-Market Adverse Drug Reactions
The following adverse events have been reported from post-marketing experience:

- central neurotoxicity/psychiatric events including seizures, mental status changes, encephalopathy, acute psychosis, bilateral hearing loss, dysautonomia
- cardiovascular and pulmonary events, tachycardia, heart failure, cardiac tamponade, pericarditis, pulmonary hypertension, cardiac and cardiopulmonary arrest, complete heart block, pneumonitis, respiratory failure, pulmonary alveolar hemorrhage, pleural effusion, acute pulmonary edema, cardiogenic shock
- serious bleeding events, subarachnoid hemorrhage, intracerebral hemorrhage, disseminated intravascular coagulation, ischemic stroke
- hypersensitivity events including immune complex type diseases
- tumor lysis syndrome
- amyloidosis
- hepatic abnormalities including increased transaminases, alkaline phosphatase, gamma-glutamyl transferase, hepatocellular damage, hepatitis, pancreatitis
- renal abnormalities including acute renal failure, nephrotic syndrome, renal tubular acidosis
- sepsis and septic shock
- gastrointestinal events including ischemic colitis and paralytic ileus
- hyper- and hypocalcemia, hyper- and hypokalemia, severe hyponatremia, inappropriate ADH secretion

DRUG INTERACTIONS

Drug-Drug Interactions
No formal drug interaction studies have been conducted with bortezomib.

Bortezomib is a substrate for cytochrome P450 (CYP) 3A4, 2D6, 2C19, 2C9, and 1A2 in human liver microsomes and a weak inhibitor of CYP isozymes 1A2, 2C9, 2D6 and 3A4 (IC_{20} ≥30 µM or 11.5 µg/mL) and CYP2C19 (IC_{20} ≥18 µM or 6.9 µg/mL).

The effect of concomitant medicinal products that are potent CYP inhibitors and inducers on the pharmacokinetics of bortezomib is unknown at this time. With bortezomib's extensive metabolism, caution must be used in the co-administration with agents that are known to be potent inducers and inhibitors of the CYP3A4 and 2C19 isoforms.

During clinical trials, hypoglycemia and hyperglycemia were reported in diabetic patients receiving oral hypoglycemics. Patients on oral antidiabetic agents receiving VELCADE treatment may require close monitoring of their blood glucose levels and adjustment of the dose of their antidiabetic medication.

Drug-Food Interactions
Interactions with food have not been established.

Drug-Herb Interactions
Interactions with herbal products have not been established.

Drug-Laboratory Interactions
Interactions with results of laboratory tests have not been established.

Drug-Lifestyle Interactions
VELCADE may be associated with fatigue, dizziness, syncope, orthostatic/postural hypotension or blurred vision. Therefore, patients are advised to be cautious when operating machinery, or when driving.

NOC/c DOSAGE AND ADMINISTRATION

Dosing Considerations
Treatment must be initiated and administered under the supervision of a healthcare professional qualified and experienced in the use of antineoplastic agents.

VELCADE (bortezomib) for Injection has not been formally studied in patients with impaired renal function. Patients with compromised renal function should be monitored carefully, especially if creatinine clearance is ≤30 mL/minute. (See **WARNINGS AND PRECAUTIONS** and **ADVERSE REACTIONS**.)

VELCADE has not been studied in patients with impaired hepatic function. Patients with impaired liver function should be treated with extreme caution and a dose reduction should be considered. (See **WARNINGS AND PRECAUTIONS**.)

There is no evidence to suggest that dose adjustments are necessary in the elderly patients. (See **ADVERSE REACTIONS**.)

The safety and effectiveness of VELCADE in children and adolescents have not been established.

Recommended Dose and Dosage Adjustment
The recommended starting dose of bortezomib is 1.3 mg/m² body surface area administered as a bolus intravenous injection twice weekly for two weeks (Days 1, 4, 8, and 11) followed by a 10-day rest period (Days 12-21). This 3-week period is considered a treatment cycle. At least 72 hours should elapse between consecutive doses of VELCADE.

For tolerability reasons, dose reduction to 1.0 mg/m² has been found effective. VELCADE therapy should be withheld at the onset of any Grade 3 non-hematological or any Grade 4 hematological toxicities, excluding neuropathy as discussed below (see **WARNINGS AND PRECAUTIONS**). Once the symptoms of the toxicity have resolved, VELCADE treatment may be re-initiated at a 25% reduced dose (1.3 mg/m² reduced to 1.0 mg/m²; 1.0 mg/m² reduced to 0.7 mg/m²). If toxicity is not resolved or if it recurs at the lowest dose, discontinuation of VELCADE must be considered unless the benefit of treatment clearly outweighs the risk.

In a supportive study in which the majority of patients were not refractory and had received less than 2 prior lines of therapy, a dose of 1.0 mg/m² was investigated (see ***Product Monograph*** **PART II, CLINICAL TRIALS**).

It is recommended that patients with a confirmed complete response receive 2 additional cycles of VELCADE beyond a confirmation. It is also recommended that responding patients who do not achieve a complete remission receive a total of 8 cycles of VELCADE therapy

Currently there are limited data concerning retreatment with VELCADE.

Patients who experience VELCADE related neuropathic pain and/or peripheral sensory neuropathy are to be managed as presented in Table 3. Patients with pre-existing severe neuropathy may be treated with VELCADE only after careful risk/benefit assessment.

Table 3:
Recommended Dose Modification for VELCADE Related Neuropathic Pain and/or Peripheral Sensory Neuropathy based on Experience from Phase II Clinical Trials in Multiple Myeloma Patients

Severity of Peripheral Neuropathy Signs and Symptoms	Modification of Dose and Regimen
Grade 1 (paresthesia and/or loss of reflexes) without pain or loss of function	No action
Grade 1 with pain or Grade 2 (interfering with function but not with activities of daily living)	Reduce VELCADE to 1.0 mg/m²
Grade 2 with pain or Grade 3 (interfering with activities of daily living)	Withhold VELCADE treatment until symptoms of toxicity resolved. When toxicity resolves, re-initiate VELCADE treatment and reduce dose to 0.7 mg/m² and change treatment schedule to once per week.
Grade 4 (permanent sensory loss that interferes with function)	Discontinue VELCADE

NCI Common Toxicity Criteria

Missed Dose

A minimum of 72 hours is required between doses. In a day 1, 4, 8 and 11 dose schedule, if day 4, 8 or 11 dose is missed, that dose is not made up.

Administration

The reconstituted solution is administered as a 3-5 second bolus intravenous injection through a peripheral or central intravenous catheter followed by a flush with 0.9% Sodium Chloride Injection, USP.

VELCADE is a cytotoxic agent. Caution should be used during handling and preparation. Proper aseptic technique should be used since no preservative is present. Use of gloves and other protective clothing to prevent skin contact is recommended. In clinical trials, local skin irritation was reported in 6% of patients, but extravasation of VELCADE was not associated with tissue damage.

Reconstitution:

Prior to use, the contents of each vial must be reconstituted with 3.5 mL of 0.9% Sodium Chloride Injection, USP. The reconstituted product should be a clear and colourless solution.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit. If any discolouration or particulate matter is observed, the reconstituted product should not be used.

Vial Size	Volume of Diluent to be Added to Vial	Approximate Available Volume	Nominal Concentration per mL
10 mL	3.5 mL 0.9% Sodium Chloride Injection, USP	3.5 mL	1 mg/mL

Stability:

VELCADE contains no antimicrobial preservative. When reconstituted as directed, VELCADE may be stored at 25°C. Reconstituted VELCADE should be administered within eight hours of preparation. The reconstituted material may be stored in the original vial and/or the syringe prior to administration. The product may be stored for up to three hours in a syringe; however, total storage time for the reconstituted material must not exceed eight hours when exposed to normal indoor lighting.

OVERDOSAGE

Cardiovascular safety pharmacology studies in monkeys show that a single IV dose of ≥3 mg/m² is lethal in monkeys and is associated with altered temperature control, decreases in blood pressure, increases in heart rate and ultimately terminal hypotension. (See ***Product Monograph*** **PART II, DETAILED PHARMACOLOGY**.)

No cases of overdosage with VELCADE (bortezomib) for Injection were reported during clinical trials. Single doses of up to 2.0 mg/m² per week have been administered in adults. In the event of overdosage, patient's vital signs should be monitored and appropriate supportive care given to maintain body temperature and blood pressure. (See **WARNINGS AND PRECAUTIONS** and **DOSAGE AND ADMINISTRATION**.)

There is no known specific antidote for VELCADE overdosage.

NOC/c ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Bortezomib is a reversible inhibitor of the chymotrypsin-like activity of the 26S proteasome in mammalian cells. The 26S proteasome is a large protein complex that degrades ubiquitinated proteins. The ubiquitin-proteasome pathway plays an essential role in regulating the intracellular concentration of specific proteins, thereby maintaining homeostasis within cells. Inhibition of the 26S proteasome prevents this targeted proteolysis which can affect multiple signaling cascades within the cell. This disruption of normal homeostatic mechanisms can lead to cell death.

Pharmacodynamics

Bortezomib is a selective, reversible proteasome inhibitor and experiments have demonstrated that bortezomib is cytotoxic to a variety of cancer cell types. Bortezomib causes a reduction of tumor growth *In vivo* in many preclinical tumor models, including multiple myeloma.

Pharmacokinetics

The kinetic profile of bortezomib has not been extensively characterized. After a single IV dose of 1.45 to 2.0 mg/m², bortezomib is rapidly and extensively distributed with an estimated distribution half-life of less than 30 minutes followed by a longer elimination phase with a half-life ranging from 9 to 15 hours. There is a wide inter-individual variability in plasma concentration with a median C_{max} of 509 ng/mL (range 109-1300 ng/mL) in seven patients following a 1.3 mg/m² single dose. Following multiple doses of bortezomib, there was doubling of AUC associated with a decrease in clearance, approximately 50% between dose 1 and 3 of the first cycle, and an increased terminal elimination half-life from 9 to 17 hours. These results were obtained in patients with solid tumors as combination therapy in a small study (n=22, 5 at 1.3 mg/m²), nevertheless, similar findings have been observed in preclinical studies after multiple dosing. (See ***Product Monograph*** **PART II, DETAILED PHARMACOLOGY, Non-Clinical Pharmacokinetics**)

Distribution:

The distribution volume of bortezomib as a single agent was not assessed at the recommended dose in patients with multiple myeloma. *In vitro* bortezomib binding to human plasma protein averaged 83% over a concentration range of 10 to 1000 ng/mL.

Metabolism:

Bortezomib is primarily metabolized via cytochrome P450-mediated deboronation to metabolites that subsequently are hydroxylated. *In vitro* studies indicate that CYP3A4 and 2C19 are quantitatively the major isoforms with CYP1A2, 2C9 and 2D6 having a minor contribution to the overall metabolism of bortezomib. Evaluated deboronated-bortezomib metabolites are inactive as 26S proteasome inhibitors. Pooled plasma data from 8 patients at 10 min and 30 min after dosing indicate that the plasma levels of metabolites are low compared to the parent drug.

Elimination:

The pathway of elimination of bortezomib has not been characterized in humans. The predominant route of elimination is biliary excretion in the rat whereas in the monkey, renal elimination is higher than biliary/fecal elimination.

Special Populations and Conditions

Gender and Race, Pediatrics, Geriatrics, Hepatic Insufficiency and Renal Insufficiency: There are no data on effects of bortezomib on the pharmacokinetics in these special populations and conditions.

STORAGE AND STABILITY

Unopened vials may be stored between 15 and 30° C. Retain in original package to protect from light.

Single-use vials. Discard unused portion.

The product may be stored for up to three hours in a syringe, however, total storage time for the reconstituted material must not exceed eight hours when exposed to normal indoor lighting.

SPECIAL HANDLING INSTRUCTIONS

VELCADE (bortezomib) for Injection is a cytotoxic agent. Caution should be used during handling and preparation. Proper aseptic technique should be used since no preservative is present. Use of gloves and other protective clothing to prevent skin contact is recommended.

DOSAGE FORMS, COMPOSITION AND PACKAGING

VELCADE (bortezomib) for Injection is supplied in individually cartoned 10 mL vials containing 3.5 mg of bortezomib as a mannitol boronic ester, as a white to off-white cake or powder.

Product Monograph available upon request.

ORTHO BIOTECH
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Plavix®
clopidogrel 75mg

PRESCRIBING INFORMATION

℞PLAVIX

clopidogrel bisulfate tablets

(equivalent to clopidogrel 75 mg)

THERAPEUTIC CLASSIFICATION

Platelet Aggregation Inhibitor

CLINICAL PHARMACOLOGY

CURE:

The CURE study included 12,562 patients with an acute coronary syndrome, defined as unstable angina or non Q-wave myocardial infarction without significant ST-segment elevation and presenting within 24 hours of onset of the most recent episode of chest pain or symptoms consistent with ischemia.

Patients were required to have either ECG changes compatible with new ischemia (without significant ST-segment elevation) or elevated cardiac enzymes or Troponin I or T to at least twice the upper limit of normal. Patients with contraindication to antithrombotic or antiplatelet therapy, at high risk for bleeding, severe heart failure, on oral anticoagulants, and those with recent revascularization or those having received IV glycoprotein IIb/IIIa inhibitors in the previous 3 days were excluded. During the trial, patients were allowed to receive other standard cardiovascular therapies such as heparin, glycoprotein IIb/IIIa inhibitors, lipid-lowering drugs, calcium channel blockers, nitrates, beta blockers, ACE-inhibitors, percutaneous coronary intervention (with or without stent) or CABG, as needed.

Patients were randomized to PLAVIX (300 mg loading dose followed by 75 mg/day) or placebo, in addition to ASA (75–325 mg once daily; median 150 mg, mean 160 mg). Patients were treated for 3 to 12 months (median 10.8 months; mean 9 months; 4,806 patients were followed for entire 12 months). The baseline characteristics, medical history, electrocardiographic changes, and drug therapy were similar for both treatment groups.

The number of patients experiencing the primary outcome, a composite of cardiovascular (CV) death, non-fatal myocardial infarction (MI) and stroke was 582 (9.30%) in the PLAVIX-treated group and 719 (11.41%) in the placebo-treated group; an absolute risk reduction of 2.11%, and a relative risk reduction of 20% (p= 0.00009) for the PLAVIX-treated group (see Table 1).

The number of patients experiencing the co-primary outcome (CV death, non-fatal MI, stroke or refractory ischemia) was 1,035 (16.54%) in the PLAVIX-treated group and 1,187 (18.83%) in the placebo-treated group; an absolute risk reduction of 2.29% and a relative risk reduction of 14% (p=0.0005) for the PLAVIX-treated group.

Events for each component of the composite outcome (CV death, non-fatal myocardial infarction, stroke, refractory ischemia) occurred less frequently with PLAVIX than in the placebo group but the differences did not reach statistical significance except for non-fatal MI. The results are summarized in Table 1.

Table 1: Incidence of the Main Study Outcomes in the CURE Study

Outcome	PLAVIX+ASA* (N=6259)	Placebo+ASA* (N=6303)	Absolute Risk Reduction %	Relative Risk (95% CI)
Primary outcome (Cardiovascular death, non-fatal MI, Stroke)	582 (9.30%)	719 (11.41%)	2.11%	0.80 (0.72, 0.90) p=0.00009
Co-primary outcome (Cardiovascular death, non-fatal MI, Stroke, Refractory Ischemia)	1035 (16.54%)	1187 (18.83%)	2.29%	0.86 (0.79, 0.94) p=0.00052
All Individual Outcome Events:†				
CV death	318 (5.08%)	345 (5.47%)	0.39%	0.93 (0.79, 1.08)
Non-fatal MI**	324 (5.18%)	419 (6.65%)	1.47%	0.77 (0.67, 0.89)
Q-wave	116 (1.9%)	193 (3.1%)	1.20%	0.60 (0.48, 0.76)
Non-Q-wave	216 (3.5%)	242 (3.8%)	0.30%	0.89 (0.74, 1.07)
Stroke	75 (1.20%)	87 (1.38%)	0.18%	0.86 (0.63, 1.18)
Refractory ischemia‡	544 (8.69%)	587 (9.31%)	0.62%	0.93 (0.82, 1.04)
During initial hospitalization	85 (1.4%)	126 (2.0%)	0.60%	0.68 (0.52, 0.90)
After discharge	459 (7.6%)	461 (7.6%)	0%	0.99 (0.87, 1.13)

*Other standard therapies were used as appropriate. All patients received acetylsalicylic acid (ASA) 75–325 mg daily (mean = 160 mg).

**Some patients had both a Q-wave and a non-Q-wave MI.

†The individual components do not represent a breakdown of the primary and co-primary outcomes, but rather the total number of subjects experiencing an event during the course of the study.

‡Only the first ischemic event was counted for each patient.

CV death: excludes clear non-CV deaths;

MI: two of three usual criteria (chest pain, ECG or enzyme/cardiac marker changes);

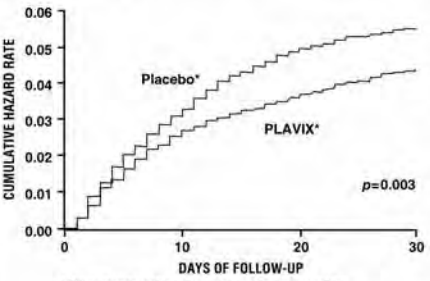
Stroke: neurological deficit ≥24 hours (CT/MRI encouraged).

Refractory ischemia (in-hospital): recurrent chest pain lasting more than 5 minutes with new ischemic ECG changes while patient on optimal medical therapy and leading to additional interventions ranging from thrombolytic therapy to coronary revascularization.

Refractory ischemia (after discharge): rehospitalization lasting at least 24 hours for unstable angina with ischemic ECG changes.

The event curves for CV death, non-fatal MI and stroke separated within the first 24 hours after initiation of therapy (Figure 1) and continued to diverge throughout the study follow-up (up to 12 months) (Figure 2). The rate of the first primary outcome was significantly lower in the clopidogrel group both within the first 30 days after randomization (relative risk, 0.79; 95 percent confidence interval, 0.67 to 0.92) and between 30 days and the end of the study (relative risk, 0.82; 95 percent confidence interval, 0.70 to 0.95).

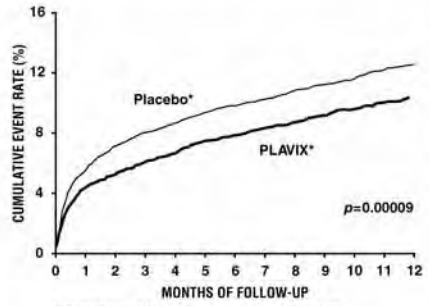
Figure 1: Cumulative Hazard Rates for First Primary Outcome (death from cardiovascular causes, non-fatal myocardial infarction or stroke) During the First 30 Days After Randomization in the CURE Study



*Other standard therapies were used as appropriate.
All patients received ASA 75–325 mg daily (mean 160 mg).

No. AT RISK				
Placebo	6303	6108	5998	5957
Clopidogrel	6259	6103	6035	5984

Figure 2: Cardiovascular Death, Myocardial Infarction or Stroke During 12 Months Follow-up in the CURE Study



*Other standard therapies were used as appropriate.
All patients received ASA 75–325 mg daily (mean 160 mg).

No. AT RISK					
Placebo	6303	5780	4664	3600	2388
Clopidogrel	6259	5866	4779	3644	2418

The risk reduction of the secondary prospectively chosen outcomes (in-hospital severe ischemia without urgent intervention, need for revascularization and heart failure) were lower in the PLAVIX group than in the placebo group and the differences observed were statistically significant.

Table 2: Secondary In-Hospital Outcomes in the CURE Study

	PLAVIX+ASA* (N=6259)	Placebo+ASA* (N=6303)	Absolute Risk Reduction %	Relative Risk (95% CI)
Severe ischemia	176 (2.81%)	237 (3.76%)	1.0%	0.74 (0.61, 0.90)
Revascularization procedure	1302 (20.8%)	1431 (22.7%)	1.9%	0.92 (0.69, 0.98)
Heart failure	229 (3.7%)	280 (4.4%)	0.7%	0.82 (0.69, 0.98)

Severe ischemia: chest pain lasting more than 5 minutes with new ischemic ECG changes while patient on optimal medical therapy and leading to additional interventions ranging from thrombolytic therapy to coronary revascularization but no urgent intervention performed.

* Other standard therapies were used as appropriate. All patients received ASA 75–325 mg daily (mean 160 mg; median 150 mg).

In general, the results obtained in populations with different characteristics, including patients with low to high risk and on other acute and long-term cardiovascular therapies, were consistent with the results of the primary analyses irrespective of other treatments or interventions.

INDICATIONS AND CLINICAL USE

MI, Stroke or Established Peripheral Arterial Disease

PLAVIX (clopidogrel bisulfate) is indicated for the secondary prevention of atherothrombotic events (myocardial infarction, stroke and vascular death) in patients with atherosclerosis documented by stroke, myocardial infarction, or established peripheral arterial disease.

Acute Coronary Syndrome

PLAVIX, in combination with ASA, is indicated for the early and long-term secondary prevention of atherothrombotic events (myocardial infarction, ischemic stroke, cardiovascular death and/or refractory ischemia) in patients with acute coronary syndromes without ST-segment elevation (i.e., unstable angina or non-Q-wave myocardial infarction). These benefits of PLAVIX have been shown only when these patients were concomitantly treated with ASA in addition to other standard therapies. These benefits were also seen in patients who were managed medically and those who were managed with percutaneous coronary intervention (with or without stent) or CABG (coronary artery bypass graft).

CONTRAINDICATIONS

- Hypersensitivity to the drug substance or any component of the product.
- Active bleeding such as peptic ulcer and intracranial hemorrhage.
- Significant liver impairment or cholestatic jaundice.

WARNINGS

Active GI Lesions: PLAVIX (clopidogrel bisulfate) prolongs bleeding time. Although PLAVIX has shown a lower incidence of gastrointestinal bleeding compared to ASA in a large controlled clinical trial (CAPRIE), PLAVIX should not be used in patients who have lesions with a propensity to bleed. In CURE, the incidence of major GI bleeding was 1.3% versus 0.7% (PLAVIX + ASA versus placebo + ASA, respectively). In patients taking PLAVIX, drugs that might induce GI lesions should be used with caution.

Anticoagulant Drugs: In view of the possible increased risk of bleeding, anticoagulant drugs should be used with caution as tolerance and safety of simultaneous administration with clopidogrel has not been established (See **PRECAUTIONS** – Drug interactions). Risk factors should be assessed for individual patients before using clopidogrel.

Because of the increased risk of bleeding, the concomitant administration of warfarin with clopidogrel should be undertaken with caution.

Thrombotic Thrombocytopenic Purpura (TTP): Thrombotic thrombocytopenic purpura (TTP) has been reported rarely following the use of PLAVIX, sometimes after a short exposure (<2 weeks). TTP is a serious condition requiring prompt treatment with plasmapheresis. It is characterized by thrombocytopenia, microangiopathic hemolytic anemia (schistocytes [fragmented RBCs] seen on peripheral smear), neurological findings, renal dysfunction, and fever. TTP was not seen during clinical trials which included over **17,500** clopidogrel-treated patients. The incidence of reported TTP in worldwide postmarketing experience has been about four reported cases per million patients exposed, which is about 11 cases per million patient-years. The background rate of TTP in the general population is thought to be about four cases per million person-years.

Pregnancy: There are no adequate and well-controlled studies in pregnant women. Reproduction studies have been performed in rats at doses up to 500 mg/kg per day and in rabbits at doses up to 300 mg/kg per day and have revealed no evidence of impaired fertility or harm to the fetus due to clopidogrel. Because animal reproduction studies are not always predictive of a human response, PLAVIX should be used during pregnancy only if the potential benefits outweigh the potential risks to the fetus.

Nursing Mothers: Studies in rats have shown that clopidogrel and/or its metabolites are excreted in milk. Therefore, clopidogrel should not be used by lactating women.

Pediatric Use: Safety and effectiveness in subjects below the age of 18 have not been established.

PRECAUTIONS

General: As with other antiplatelet agents, when considering prescribing PLAVIX (clopidogrel bisulfate), physicians should inquire whether the patient has a history of bleeding. Clopidogrel should be used with caution in patients who may be at risk of increased bleeding from recent trauma, surgery or other pathological condition(s). If a patient is to undergo elective surgery, consideration should be given to discontinue PLAVIX 5 to 7 days prior to surgery to allow for the reversal of the effect.

Platelet transfusion may be used to reverse the pharmacological effects of PLAVIX when quick reversal is required.

Use in Patients with Renal Impairment: Therapeutic experience with clopidogrel is limited in patients with severe and moderate renal impairment. Therefore PLAVIX should be used with caution in these patients.

Use in Patients with Hepatic Impairment: Experience is limited in patients with moderate hepatic impairment who may have bleeding diatheses. As with any patient exhibiting hepatic impairment, liver function should be carefully monitored and PLAVIX should be used with caution.

In the CAPRIE study, there were 344 hepatically impaired patients (Alkaline phosphatase >300 U/L, or ALT>120 U/L, or AST>75 U/L) and 168 received clopidogrel for a mean duration of 18 months. The adverse events were more common in this population, compared to the rest of the CAPRIE population, and more common in the clopidogrel (N=168) than in the ASA (N=176) group (any bleeding disorders, N=17 vs N=14; any rash, N=11 vs N=6; diarrhea, N=8 vs N=3, respectively).

Table 3: Drug Interactions

Agents	Observed Interactions
ASA	ASA (2 X 500 mg once) did not modify the clopidogrel-mediated inhibition of ADP-induced platelet aggregation, but clopidogrel potentiated the effect of ASA on collagen-induced platelet aggregation. PLAVIX 75 mg and ASA (75–325 mg) have been administered together for up to one year.

Table 3: Drug Interactions (cont'd)

Agents	Observed Interactions
NSAIDS	The short-term concomitant administration of PLAVIX and naproxen increased occult gastrointestinal blood loss, in a clinical study conducted in healthy volunteers. Consequently, there is a potential increased risk of gastrointestinal bleeding (See **WARNINGS**).
Heparin	Clopidogrel at steady state did not modify the effect of heparin on coagulation in a clinical study conducted in healthy volunteers. Coadministration of heparin had no effect on platelet aggregation inhibition induced by PLAVIX.
Warfarin	Because of the increased risk of bleeding the concomitant administration of warfarin with clopidogrel should be undertaken with caution (See **WARNINGS**).
Digoxin, Theophylline, Antacids	There was no modification of the pharmacokinetics of digoxin or theophylline with the coadministration of PLAVIX at steady state. Antacids did not modify the extent of PLAVIX absorption.
Other	No clinically significant pharmacodynamic interactions were observed when clopidogrel was coadministered in clinical studies to investigate drug interaction with atenolol, nifedipine, or both atenolol and nifedipine. The pharmacodynamic activity of PLAVIX was slightly enhanced by the coadministration of phenobarbital; however, this was not considered to be clinically significant. Pharmacodynamic activity of PLAVIX was not changed with the coadministration of cimetidine. Pharmacodynamic activity of PLAVIX was not significantly influenced by the coadministration of estrogen.

Clinically significant adverse interactions were not detected in the CAPRIE and/or CURE studies where patients received a variety of concomitant medications including ASA, diuretics, beta-blocking agents, angiotensin converting enzyme (ACE) inhibitors, calcium channel blockers, lipid-lowering agents, coronary vasodilators, antidiabetic agents (including insulin), antiepileptic agents, hormone replacement therapy, unfractionated and/or LMW heparin, and glycoprotein IIb/IIIa inhibitors. A review of the clinical trial data indicates that there is no evidence of an interaction between PLAVIX and atorvastatin. In CAPRIE, patients on HMG CoA reductase inhibitors and clopidogrel experienced a higher incidence of bleeding events (primarily epistaxis). Patients on HMG CoA reductase inhibitors and ASA experienced a higher incidence of intracranial hemorrhage. There is no known pathophysiological or pharmacological explanation for these observations.

At high concentrations *in vitro*, clopidogrel inhibits isoenzyme CYP 2C9 of the cytochrome P450 system. Accordingly, PLAVIX may interfere with the metabolism of drugs such as phenytoin, tamoxifen, tolbutamide, warfarin, torsemide, fluvastatin, and many non-steroidal anti-inflammatory agents. There are no data with which to predict the magnitude of these interactions. Caution should be used when any of these drugs is coadministered with PLAVIX.

Laboratory Test Interactions: None known.

ADVERSE REACTIONS

PLAVIX (clopidogrel bisulfate) has been evaluated for safety in more than 17,500 patients, including over 9,000 patients treated for 1 year or more.

CAPRIE:

PLAVIX was well tolerated compared to ASA in CAPRIE. With few exceptions, the overall tolerability of PLAVIX was similar regardless of age, sex and race. However, in women there was a slightly higher incidence of bleeding disorders in the clopidogrel group (11.36 % vs 9.88%).

Clinically Important Adverse Events The clinically important adverse events observed in CAPRIE were the following:

Neutropenia and thrombocytopenia: Although these events were observed, PLAVIX was not associated with an increase in the incidence of neutropenia or thrombocytopenia.

Granulocytopenia: Granulocytopenia (<1,200/mm³) occurred in 8 patients taking PLAVIX and 14 patients taking ASA. Among those, severe granulocytopenia (<450/mm³) was observed in 4 patients (0.04%) that received PLAVIX and 2 patients (0.02%) that received ASA. Two of the 9,599 patients who received PLAVIX had neutrophil counts of zero. None of the 9,586 patients who received ASA had neutrophil counts of zero. Although the risk of myelotoxicity with clopidogrel appears to be quite low, this possibility should be considered when a patient receiving clopidogrel demonstrates fever or other signs of infection.

One case of aplastic anemia occurred on clopidogrel treatment.

Bleeding and clotting disorders: One case of Henoch-Schonlein purpura (acute visceral symptoms: vomiting, diarrhea, abdominal distension, hematuria, renal colic) was reported in a patient taking PLAVIX. The patient recovered without sequelae within one month. Rare cases of platelet count ≤30,000/mm³ have been reported.

Skin disorders: There was no notable difference between treatment groups in the incidence of bullous eruptions (0.23% PLAVIX vs 0.16% ASA). One case of a severe bullous eruption was reported in a patient taking PLAVIX.

Hepatic and biliary disorders: The overall incidence of hepatic and biliary disorders was similar in patients treated with clopidogrel (3.5%) compared to ASA (3.4%). The most frequent events were increased liver enzymes and bilirubinemia.

Table 4: Patients Discontinued Because of Adverse Experiences in CAPRIE (Number and Percentage of Patients)

	Study drug permanently discontinued	
Adverse Experience	PLAVIX	ASA
Rash	86 (0.90%)	39 (0.41%)*
Diarrhea	40 (0.42%)	26 (0.27%)
Indigestion/nausea/vomiting	182 (1.90%)	231 (2.41%)*
Any bleeding disorder	115 (1.20%)	131 (1.37%)
Intracranial hemorrhage	20 (0.21%)	32 (0.33%)
Gastrointestinal hemorrhage	50 (0.52%)	89 (0.93%)*
Abnormal liver function	22 (0.23%)	28 (0.29%)

* Statistically significant, $p<0.05$

A summary of the clinically relevant adverse effects observed in CAPRIE are presented in the table below. In CAPRIE, patients with a known intolerance to ASA were excluded from the study.

Table 5: Summary of Adverse Events – CAPRIE Trial

Adverse Event	PLAVIX % Incidence (N=9599)	ASA % Incidence (N=9586)
Hemorrhages or bleeding disorders:		
– intracranial hemorrhage	0.4	0.5
– gastrointestinal bleeding	2.0	2.7*
– requiring hospitalization	0.7	1.1
– purpura (primarily bruising and ecchymosis)	5.3*	3.7
– epistaxis	2.9	2.5
– eye bleeding	0.8	0.5
– conjunctival†	0.3	0.2
– with sequelae†	0.1	0.1
Platelet disorders:		
– severe thrombocytopenia ($0 \le x < 80{,}000/mm^3$)	0.2	0.1
– thrombocytopenia ($0 \le x < 100{,}000/mm^3$)	0.1	0.2
Skin disorders:		
– rash	4.2*	3.5
– severe†	0.1	0.1
– leading to discontinuation†	0.5	0.2
– pruritus	3.3*	1.6
Gastrointestinal disorders:		
– peptic, gastric, duodenal ulcer	0.7	1.2
– diarrhea	4.5*	3.4
– severe†	0.2	0.1
– leading to discontinuation†	0.4	0.3
– dyspepsia	5.2	6.1*
– constipation	2.4	3.3*
– stomatitis	0.2	0.1
– nausea	3.4	3.8
– abdominal pain	5.6	7.1*
– gastritis	0.8	1.3*
Cardiovascular and rhythm disorders:		
– heart and rhythm disorder	4.3	5.0*
– pulmonary embolism	0.4	0.2
Other:		
– allergic reaction	0.9	1.0
– influenza-like symptoms	7.5	7.0
– fatigue	3.3	3.4
– pain	6.4	6.3
– headache	7.6	7.2
– coughing	3.1	2.7

* Statistically significant difference between treatments ($p \le 0.05$)
† Patients may be included in more than one category

CURE: The clinically important adverse events observed in CURE are discussed below:

In CURE, PLAVIX was given with ASA, and was not associated with a significant increase in life-threatening or fatal bleeds compared to placebo given with ASA; the incidences of non-life threatening major bleeding and minor bleeding were significantly larger in the PLAVIX + ASA group. The incidence of intracranial hemorrhage was 0.1% in both groups. There was an excess in major bleeds, primarily gastrointestinal and at puncture sites. In patients receiving both PLAVIX and ASA in CURE, the incidence of bleeding is described in Table 6 below:

Table 6: CURE Incidence of Bleeding Complications (% Patients)

Event	PLAVIX+ASA* (N=6256)	Placebo+ASA* (N=6303)	*p*-value
Life-threatening bleeding	2.2	1.8	0.13
Fatal	0.2	0.2	
5 g/dL hemoglobin drop	0.9	0.9	
Requiring surgical intervention	0.7	0.7	
Hemorrhagic strokes	0.1	0.1	
Requiring inotropes	0.5	0.5	
Requiring transfusion (≥4 units)	1.2	1.0	
Other major bleeding	1.6	1.0	0.005
Significantly disabling	0.4	0.3	
Intraocular bleeding with significant loss of vision	0.05	0.03	
Requiring 2 – 3 units of blood	1.3	0.9	
Major bleeding†	3.7‡	2.7§	0.001
Minor bleeding¶	5.1	2.4	< 0.001
Total with bleeding complications	8.5	5.0	< 0.001

* Other standard therapies were used as appropriate. All patients received ASA 75 – 325 mg daily (mean=160 mg)
† Life threatening and other major bleeding necessitating transfusion of ≥ 2 units of blood.
‡ Major bleeding event rate for PLAVIX + ASA was dose-dependent on ASA: <100 mg=2.6%; 100 – 200 mg=3.5%; >200 mg=4.9%
§ Major bleeding event rate for placebo + ASA was dose-dependent on ASA: <100 mg=2.0%; 100 – 200 mg=2.3%; >200 mg=4.0%
¶ Led to interruption of study medication.

The number of patients with bleeding that met the criteria for major bleeding established by the Thrombolysis in Myocardial Infarction (TIMI) trial was 68 (1.09%) in the clopidogrel group and 73 (1.16%) in the placebo group (relative risk, 0.94; $p=0.70$). The number with bleeding that met the criteria for life-threatening or severe bleeding established by the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) trial was 78 in the clopidogrel group and 70 in the placebo group (relative risk, 1.12; $p=0.48$). Some patients had more than one bleeding episode.

Ninety-two percent (92%) of the patients in the CURE study received unfractionated or low molecular weight heparin, and the rate of bleeding in these patients was similar to the overall results.

There was no excess in major bleeds within seven days after coronary bypass graft surgery in patients who stopped therapy more than five days prior to surgery (event rate 4.6% PLAVIX + ASA; 5.5% placebo + ASA). In patients who remained on therapy within five days of bypass graft surgery, the event rate was 8.9% for PLAVIX + ASA, and 6.2% for placebo + ASA, which was not significantly different.

Thrombocytopenia: In CURE, the number of patients with thrombocytopenia (19 PLAVIX + ASA versus 24 placebo + ASA) or neutropenia (3 versus 3) was similar.

Gastrointestinal: In the CURE trial, the incidence of gastrointestinal events (e.g., abdominal pain, dyspepsia, gastritis and constipation) for patients receiving PLAVIX + ASA was 11.7% compared to 12.5% for those receiving placebo + ASA. The incidence of peptic, gastric or duodenal ulcers was 0.4% for PLAVIX + ASA and 0.3% for placebo + ASA. The incidence of diarrhea for patients receiving PLAVIX + ASA was 2.1% compared to 2.2% for those receiving placebo + ASA. The incidence of patients withdrawing from treatment because of gastrointestinal adverse reactions was 0.9% for PLAVIX + ASA compared with 0.8% for placebo + ASA.

Rash and other skin disorders: In the CURE trial, the incidence of rash or other skin disorders in patients receiving PLAVIX + ASA was 4.0% compared to 3.5% for those receiving placebo + ASA. In the CURE trial, the incidence of patients withdrawing because of skin and appendage disorder adverse reactions was 0.7% for PLAVIX + ASA compared with 0.3% for placebo + ASA.

Post Marketing Experience: The following additional adverse reactions were reported in marketed use, however a causal relationship with clopidogrel has not been clearly established.

Skin disorders: Maculopapular or erythematous rash, urticaria, pruritus. Very rarely: angioedema, bullous eruption (erythema multiforme).

Musculo-skeletal disorders: Very rarely: arthralgia, arthritis.

Collagen disorders: Very rarely: vasculitis.

Neurological disorders: Very rarely: confusion, hallucinations, taste disorders.

Gastro-intestinal disorders: Very rarely: colitis (including ulcerative or lymphocytic colitis).

Liver and biliary disorders: Very rarely: abnormal liver function test, hepatitis.

Respiratory system disorders: Very rarely: bronchospasm.

Hematological disorders: Very rarely: serious cases of bleeding, mainly skin, musculo-skeletal, eye (conjuctival, ocular, retinal) and respiratory tract bleeding, epistaxis, hematuria and hemorrhage of operative wound, hematoma; cases of bleeding with fatal outcome (especially intracranial, gastrointestinal and retroperitoneal hemorrhage). Very rarely: agranulocytosis, aplastic anemia/pancytopenia, thrombotic thrombocytopenic purpura (TTP). TTP was not observed in clinical studies involving more than 11,300 patients receiving clopidogrel (including over 7,000 patients treated for one year or more).

Urinary system disorders: Very rarely: glomerulopathy, abnormal creatinine levels.

Allergic disorders: Very rarely: anaphylactoid reactions, fever.

DOSAGE AND ADMINISTRATION

MI, Stroke or Established Peripheral Arterial Disease: The recommended dose of PLAVIX is 75 mg once daily long term with or without food.

Acute Coronary Syndrome: PLAVIX should be initiated with a 300 mg loading dose and continued long term at 75 mg once a day with ASA (80 mg–325 mg daily).

No dosage adjustment is necessary for elderly patients or patients with renal impairment.

AVAILABILITY OF DOSAGE FORMS

PLAVIX (clopidogrel bisulfate) is available as pink, round, slightly biconvex, film-coated tablets engraved with "75" on one side and "1171" on the other side, available in cartons containing a blister of 28 tablets and bottles containing 500 tablets.

Product Monograph available upon request.

REFERENCES: 1. Harker LA, et al. Comparative safety and tolerability of clopidogrel and aspirin. *Drug Safety* 1999;21(4):325–35. **2.** Hankey GJ. Current oral antiplatelet agents to prevent atherothrombosis. *Cerebrovasc Dis* 2001;11(Suppl 2):11–17. **3.** CAPRIE Steering Committee. A randomised, blinded trial of clopidogrel versus aspirin in patients at risk of ischemic events (CAPRIE). *Lancet* 1996;348:1329–39. **4.** CURE Study Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001;345(7):494–502. **5.** PLAVIX Product Monograph. Sanofi-Synthelabo Canada Inc., April 27, 2004.

An agreement between Bristol-Myers Squibb and sanofi-aventis for the codevelopment and marketing of irbesartan and clopidogrel, two compounds from sanofi-aventis research.

CDN.CLO.05.02.02E BPX52101E

Aranesp®
(darbepoetin alfa)
Erythropoiesis regulating hormone

ACTION AND CLINICAL PHARMACOLOGY
The etiology of anemia in cancer patients is multifactorial. Erythropoietin deficiency and a blunted response of erythroid progenitor cells to endogenous erythropoietin contribute significantly towards anemia in these patients. Aranesp® has been shown to stimulate erythropoiesis, resulting in increased hemoglobin levels and a reduced need for red blood cell transfusions in cancer patients. Increased hemoglobin levels have been shown to result in improved quality of life.

PHARMACOKINETICS
Following SC administration of 2.25 mcg/kg to adult cancer patients (n = 26), a mean peak concentration of 10.6 ng/mL (range 1.23 to 25.2 ng/mL) was achieved at a mean time of 94.5 hours (range: 70.8 to 123 hours). The data were consistent with dose-linear pharmacokinetics over a wide dose range (0.5 to 8.0 mcg/kg weekly and 3.0 to 9.0 mcg/kg every 2 weeks). Upon multiple dosing over 12 weeks (dosing every week or every 2 weeks), the pharmacokinetic properties did not change. The expected moderate increases (< 2-fold) in Aranesp® serum concentrations upon multiple dosing were observed as steady state was approached. Accumulation was negligible across a wide range of doses at once weekly and once every 2 weeks dosing schedules. Although the accumulation potential of Aranesp® is unknown for longer-term (i.e. > 12 weeks) treatment in cancer patients, the extent (< 2-fold) accumulation observed at 12 weeks was the same as that observed at 4 weeks.

INDICATIONS AND CLINICAL USE
Treatment of Anemia in Chronic Renal Failure
Aranesp® (darbepoetin alfa) is indicated for the treatment of anemia associated with chronic renal failure (CRF), including patients on dialysis and patients not on dialysis. Aranesp® is not intended for patients who require immediate correction of severe anemia or emergency transfusions. Blood pressure should be adequately controlled prior to initiation of Aranesp® therapy and must be closely monitored and controlled during treatment. Aranesp® is not indicated for other causes of anemia such as iron or folate deficiencies, hemolysis, or gastrointestinal bleeding which should be managed appropriately.

Treatment of Anemia in Cancer
Aranesp® is indicated for the treatment of anemia in patients with nonmyeloid malignancies, where anemia is due to the effect of concomitantly administered chemotherapy.

CONTRAINDICATIONS
Aranesp® (darbepoetin alfa) is contraindicated in patients with:
- Uncontrolled hypertension
- Known hypersensitivity to the active substance or any of the excipients
- Sensitivity to mammalian cell-derived products
- Sensitivity to albumin (where applicable with the albumin formulation)†

WARNINGS
General
Cardiovascular Events, Hemoglobin, and Rate of Rise of Hemoglobin
Erythropoietic therapies may increase the risk of cardiovascular events, including death. The higher risk of cardiovascular events may be associated with higher hemoglobin and/or higher rates of rise of hemoglobin. The hemoglobin level should be managed carefully, with a target not exceeding 120 g/L. In a clinical trial of Epoetin alfa treatment in hemodialysis patients with clinically evident cardiac disease, patients were randomized to a target hemoglobin of either 140 ± 10 g/L or 100 ± 10 g/L. Higher mortality (35% versus 29%) was observed in the 634 patients randomized to a target hemoglobin of 140 g/L than in the 631 patients assigned a target hemoglobin of 100 g/L. The reason for the increased mortality observed in this study is unknown; however, the incidence of nonfatal myocardial infarction, vascular access thrombosis, and other thrombotic events was also higher in the group randomized to a target hemoglobin of 140 g/L. In patients treated with Aranesp® or recombinant erythropoietins in Aranesp® CRF clinical trials, increases in hemoglobin greater than approximately 10 g/L during any 2-week period were associated with increased incidence of cardiac arrest, neurologic events (including seizures and stroke), exacerbations of hypertension, congestive heart failure, vascular thrombosis/ischemia/infarction, acute myocardial infarction, and fluid overload/edema. **It is recommended that the dose of Aranesp® be decreased if the hemoglobin increase exceeds 10 g/L in any 2-week period, because of the association of excessive rate of rise of hemoglobin with these events (see Dose Adjustment for CRF Patients).**

Hypertension
Patients with uncontrolled hypertension should not be treated with Aranesp®; blood pressure should be controlled adequately before initiation of therapy. Blood pressure may rise during treatment of anemia with Aranesp® or rHuEPO. In Aranesp® CRF clinical trials, approximately 40% of patients required initiation or intensification of antihypertensive therapy during the early phase of treatment when the hemoglobin was increasing. Hypertensive encephalopathy and seizures have been observed in patients with CRF treated with Aranesp® or rHuEPO.

Special care should be taken to closely monitor and control blood pressure in patients treated with Aranesp®. During Aranesp® therapy, patients should be advised of the importance of compliance with antihypertensive therapy and dietary restrictions. If blood pressure is difficult to control by pharmacologic or dietary measures, the dose of Aranesp® should be reduced or withheld (see **DOSAGE AND ADMINISTRATION: Dose Adjustment for CRF Patients**). A clinically significant decrease in hemoglobin may not be observed for several weeks.

Seizures
Seizures have occurred in patients with CRF participating in clinical trials of Aranesp® and rHuEPO. During the first several months of therapy, blood pressure and the presence of premonitory neurologic symptoms should be monitored closely. While the relationship between seizures and the rate of rise of hemoglobin is uncertain, it is recommended that the dose of Aranesp® be decreased if the hemoglobin increase exceeds 10 g/L in any 2-week period.

Thrombotic Events and Increased Mortality
An increased incidence of thrombotic events has been observed in patients treated with erythropoietic agents. Vascular access thrombosis occurred in CRF clinical trials at an annualized rate of 0.22 events per patient year of Aranesp® therapy. Rates of thrombotic events (e.g., vascular access thrombosis, venous thrombosis, and pulmonary emboli) with Aranesp® therapy were similar to those observed with rHuEPO therapy in these trials. Patients with pre-existing vascular disease should be closely monitored. In cancer patients, the incidence of thrombotic events was 6% for Aranesp®, 5% for r-HuEPO and 4% for placebo. Thrombotic events included pulmonary embolism, deep venous thrombosis, thromboembolism and thrombophlebitis. The median exposure was 12 weeks. Until further information is available, the recommended target hemoglobin should not exceed 120 g/L in men or women.

Albumin (Human)†
Aranesp® is supplied in 2 formulations with different excipients, one containing polysorbate 80 and another containing albumin (human), a derivative of human blood. Based on effective donor screening and product manufacturing processes, Aranesp® formulated with albumin carries an extremely remote risk for transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) also is considered extremely remote. No cases of transmission of viral diseases or CJD have ever been identified for albumin.

PRECAUTIONS
General
The safety and efficacy of Aranesp® (darbepoetin alfa) therapy has not been established in patients with underlying hematologic diseases (e.g., hemolytic anemia, sickle cell anemia, thalassemia, porphyria). In order to ensure effective erythropoiesis, iron status should be evaluated for all patients before and during treatment as the majority of patients will eventually require supplemental iron therapy. Supplemental iron therapy is recommended for all patients whose serum ferritin is below 100 mcg/L or serum transferrin saturation is below 20%.

Lack or Loss of Response to Aranesp®
A lack of response or failure to maintain a hemoglobin response with Aranesp® (darbepoetin alfa) doses within the recommended dosing range should prompt a search for causative factors. Deficiencies of folic acid, or vitamin B_{12} should be excluded or corrected. Depending on the clinical setting, intercurrent infections, inflammatory or malignant processes, osteofibrosis cystica, occult blood loss, severe aluminum toxicity, bone marrow fibrosis, insufficient dialysis and malnutrition may compromise an erythropoietic response.

If patients are hyporesponsive, or fail to respond to other erythropoietic proteins, Pure Red Cell Aplasia (PRCA) or anti-erythropoietin antibody formation should be excluded. Patients with confirmed antibody-mediated PRCA should not be switched to Aranesp®.

Allergic Reactions
There have been rare reports of potentially serious allergic reactions including skin rash and urticaria associated with Aranesp®. Symptoms have recurred with rechallenge, suggesting a causal relationship exists in some instances. If a serious allergic or an anaphylactic reaction occurs, Aranesp® should be immediately discontinued and appropriate therapy should be administered.

Chronic Renal Failure Patients
Patients With CRF Not Requiring Dialysis
Patients with CRF not yet requiring dialysis (pre-dialysis patients) may require lower maintenance doses of Aranesp® than patients receiving dialysis. Though pre-dialysis patients generally receive less frequent monitoring of blood pressure and laboratory parameters than dialysis patients, pre-dialysis patients may be more responsive to the effects of Aranesp,® and require judicious monitoring of blood pressure and hemoglobin. Renal function and fluid and electrolyte balance should also be closely monitored.

Dialysis Management
Therapy with Aranesp® results in an increase in the number of red blood cells and a decrease in plasma volume, which could reduce dialysis efficiency; patients who are marginally dialyzed may require adjustments in their dialysis prescription. The importance of compliance with a prescribed diet should be reinforced. Notably hyperkalemia is not uncommon in this patient population.

Cancer Patients
Tumor Growth Factor Potential
Aranesp® is a growth factor that primarily stimulates RBC production. Like all growth factors, the possibility that Aranesp® can act as a growth factor for any tumor type, particularly myeloid malignancies, cannot be excluded. To assess this potential, the effect of Aranesp® on tumor progression and survival was evaluated through long-term surveillance of patients treated in the pivotal clinical study. After a median observation period of approximately 1 year, the median time to disease progression in the Aranesp® group (n = 155) was 29 weeks (95% CI: 22, 33) compared with 22 weeks (95% CI: 18, 25) in the placebo group (n = 159). The median time to death in the Aranesp® group (n = 155) was 43 weeks (95% CI: 37, not estimable) compared with 35 weeks (95% CI: 29, 48) in the placebo group (n = 159). Statistically significant differences in time-to-progression (TTP) or overall survival (OS) were not observed. However, the study was not designed to detect or exclude clinically meaningful differences in either TTP or OS.

Geriatric Use
Chronic Renal Failure Patients
The results of clinical trials with Aranesp® suggest no increased safety risk with increasing age. Of more than 1500 patients with CRF treated with Aranesp,® 43% were 65 years of age or older. Of these geriatric patients, 35% were 75 years of age or older. Regardless of age, the administration of Aranesp,® either IV or SC, resulted in a dose-dependent and sustained increase in hemoglobin. No differences in dose requirements between geriatric and younger adults were observed. No overall differences in safety or efficacy were observed between these subjects and younger subjects. A greater sensitivity in older patients cannot be ruled out.

Cancer Patients
Of the 873 cancer patients in clinical studies receiving Aranesp® and concomitant chemotherapy, 45% were age 65 and over, while 14% were 75 and over. No overall differences in safety or efficacy were observed between these patients and younger patients.

Impairment of Fertility
No data are available from human studies with regard to impairment of fertility. When administered to rats before mating, reproductive performance, fertility, and sperm assessment parameters were not affected at any doses evaluated (up to 10 mcg/kg/day). An increase in post-implantation fetal loss was seen with Aranesp® doses of 0.5 mcg/kg/day and higher.

Use in Pregnancy
There are no adequate and well-controlled studies in pregnant women. Aranesp® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Reproductive studies in rats showed no significant placental transfer of Aranesp.® Studies in rats and rabbits, in which Aranesp® was administered during gestation, showed no evidence of direct embryotoxic, fetotoxic, or teratogenic properties at doses up to 40 times the human dose. The only adverse effect observed was a slight reduction in fetal weight, which was seen at doses causing exaggerated pharmacological effects in the dams. No treatment effects on uterine implantation were seen in either species.

Nursing Mothers
It is not known whether Aranesp® is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Aranesp® is administered to a nursing woman.

Use in Children
The safety and efficacy of Aranesp® in pediatric patients has not been established.

Laboratory Monitoring
Chronic Renal Failure Patients
After initiation of Aranesp® therapy, the hemoglobin should be determined weekly until it has stabilized and the maintenance dose has been established (see **DOSAGE AND ADMINISTRATION: Chronic Renal Failure Patients**). After a dose adjustment, the hemoglobin should be determined weekly for at least 4 weeks until it has been determined that the hemoglobin has stabilized in response to the dose change. The hemoglobin should then be monitored at regular intervals, in order to ensure effective erythropoiesis; iron status should be evaluated for all patients before and during treatment, as the majority of patients will eventually require supplemental iron therapy. Supplemental iron therapy is recommended for all patients whose serum ferritin is below 100 mcg/L or whose serum transferrin saturation is below 20%.

Cancer Patients
The hemoglobin concentration after initiation of Aranesp® therapy should be monitored at regular intervals to assess the need to modify dose based on the individual patient's response (see **DOSAGE AND ADMINISTRATION: Cancer Patients Receiving Chemotherapy**).

Drug Interactions
No formal drug interaction studies of Aranesp® with other medications commonly used in CRF or cancer patients have been performed.

Carcinogenesis, Mutagenesis
Carcinogenicity
Aranesp® was not evaluated in standard carcinogenicity bioassays. Aranesp® did not alter the proliferative response of non-hematological cells in vitro or in vivo. In chronic toxicity studies, no tumourogenic or unexpected mitogenic responses were observed in any tissue type. In toxicity studies of approximately 6 months duration in rats and dogs, no tumourogenic or unexpected mitogenic responses were observed in any tissue type. Using a panel of human tissues, the in vitro tissue binding profile of Aranesp® was identical to rHuEPO. Neither molecule bound to human tissues other than those expressing the EPO receptor.

Mutagenicity
Aranesp® was negative in the in vitro bacterial and CHO cell assays used to detect mutagenicity and in the in vivo mouse micronucleus assay to detect clastogenicity.

ADVERSE REACTIONS
General
Immunogenicity
As with all therapeutic proteins, there is a potential for immunogenicity. Radioimmunoprecipitation assays were performed on sera from 1534 CRF patients and 833 cancer patients treated with Aranesp® High-titer antibodies were not detected, but assay sensitivity may be inadequate to reliably detect lower titers. Since the incidence of antibody formation is highly dependent on the sensitivity and specificity of the assay, and the observed incidence of antibody positivity in an assay may additionally be influenced by several factors including sample handling, concomitant medications, and underlying disease, comparison of the incidence of antibodies to Aranesp® with the incidence of antibodies to other products may be misleading. Pure red cell aplasia, in association with antibodies to erythropoietin, has been reported on rare occasions in patients treated with other recombinant erythropoietins. Due to the close relationship of Aranesp® to endogenous erythropoietin, such a response is a theoretical possibility with Aranesp® treatment, but has not been observed to date.

Chronic Renal Failure Patients
In all studies with CRF patients, the most frequently reported serious adverse reactions with Aranesp® were vascular access thrombosis, congestive heart failure, sepsis, and cardiac arrhythmia. The most commonly reported adverse reactions were infection, hypertension, hypotension, myalgia, headache, and diarrhea (see **WARNINGS: Cardiovascular Events, Hemoglobin, and Rate of Rise of Hemoglobin/Hypertension**). The most frequently reported adverse reactions resulting in clinical intervention (e.g., discontinuation of Aranesp,® adjustment in dosage, or the need for concomitant medication to treat an adverse reaction symptom) were hypotension, hypertension, fever, myalgia, nausea, and chest pain. The data described below reflect exposure to Aranesp® in 1598 CRF patients, including 675 exposed for at least 6 months, of whom 185 were exposed for greater than 1 year. Aranesp® was evaluated in active-controlled (n = 823) and uncontrolled studies (n = 775). The rates of adverse events and association with Aranesp® are best assessed in the results from studies in which Aranesp® was used to stimulate erythropoiesis in patients anemic at study baseline (n = 348), and, in particular, the subset of these patients in randomized controlled trials (n = 276). Because there were no substantive differences in the rates of adverse reactions between these subpopulations, or between these subpopulations and the entire population of patients treated with Aranesp,® data from all 1598 patients were pooled. The population encompassed an age range from 18 to 91 years. Fifty-seven percent of the patients were male. The percentages of Caucasian, Black, Asian, and Hispanic patients were 83%, 11%, 3%, and 1%, respectively. The median weekly dose of Aranesp® was 0.45 mcg/kg (20th, 75th percentiles: 0.29, 0.66 mcg/kg). Some of the adverse events reported are typically associated with CRF, or recognized complications of dialysis, and may not necessarily be attributable to Aranesp® therapy. No important differences in adverse event rates between treatment groups were observed in controlled studies in which patients received Aranesp® or other recombinant erythropoietins.

The data in Table 1 reflect those adverse events occurring in at least 5% of CRF patients treated with Aranesp®

Table 1. Adverse Events Occurring in ≥ 5% of CRF Patients

Event	CRF Patients Treated With Aranesp® (n = 1598)
APPLICATION SITE	
Injection Site Pain	7%
BODY AS A WHOLE	
Peripheral Edema	11%
Fatigue	9%
Fever	9%
Death	7%
Chest Pain, Unspecified	6%
Fluid Overload	6%
Access Infection	6%
Influenza-like Symptoms	6%
Access Hemorrhage	6%
Asthenia	5%

Table continued on page 2

†Note: Albumin formulation not currently available in Canada.

Table 1. *(continued)* Adverse Events Occurring in ≥ 5% of CRF Patients

Event	CRF Patients Treated With Aranesp® (n = 1598)
CARDIOVASCULAR	
Hypertension	23%
Hypotension	22%
Cardiac Arrhythmias/Cardiac Arrest	10%
Angina Pectoris/Cardiac Chest Pain	8%
Thrombosis Vascular Access	8%
Congestive Heart Failure	6%
CNS/PNS	
Headache	16%
Dizziness	8%
GASTROINTESTINAL	
Diarrhea	16%
Vomiting	15%
Nausea	14%
Abdominal Pain	12%
Constipation	5%
MUSCULO-SKELETAL	
Myalgia	21%
Arthralgia	11%
Limb Pain	10%
Back Pain	8%
RESISTANCE MECHANISM	
Infection[a]	27%
RESPIRATORY	
Upper Respiratory Infection	14%
Dyspnea	12%
Cough	10%
Bronchitis	6%
SKIN AND APPENDAGES	
Pruritus	8%

[a] Infection includes sepsis, bacteremia, pneumonia, peritonitis, and abscess.

The incidence rates for other clinically significant events are shown in Table 2.

Table 2. Percent Incidence of Other Clinically Significant Events in CRF Patients

Event	CRF Patients Treated With Aranesp® (n = 1598)
Acute Myocardial Infarction	2%
Seizure	1%
Stroke	1%
Transient Ischemic Attack	1%

Cancer Patients Receiving Chemotherapy

The data described below reflect the exposure to Aranesp® in 873 cancer patients. Aranesp® was evaluated in seven studies that were active-controlled and/or placebo-controlled studies of up to 6 months duration. The Aranesp®-treated patient demographics were as follows: median age of 63 years (range of 20 to 91 years); 40% male; 88% Caucasian, 5% Hispanic, 4% Black, and 3% Asian. Over 90% of patients had locally advanced or metastatic cancer, with the remainder having early stage disease. Patients with solid tumors (e.g., lung, breast, colon, ovarian cancers), and lymphoproliferative malignancies (e.g., lymphoma, multiple myeloma) were enrolled in the clinical studies. All of the 873 Aranesp®-treated subjects also received concomitant cyclic chemotherapy. The most frequently reported serious adverse events included death (10%), fever (4%), pneumonia (3%), dehydration (3%), vomiting (2%), and dyspnea (2%). The most commonly reported adverse events were fatigue, edema, nausea, vomiting, diarrhea, fever, and dyspnea (see **Table 3**). Except for those events listed in Tables 3 and 4 the incidence of adverse events in clinical studies occurred at a similar rate compared with patients who received placebo and were generally consistent with the underlying disease and its treatment with chemotherapy. The most frequently reported reasons for discontinuation of Aranesp® were progressive disease, death, discontinuation of the chemotherapy, asthenia, dyspnea, pneumonia, and gastrointestinal hemorrhage. No important differences in adverse event rates between treatment groups were observed in controlled studies in which patients received Aranesp® or other recombinant erythropoietins.

Table 3. Adverse Events Occurring in ≥ 5% of Patients Receiving Chemotherapy

Event	Aranesp® (n = 873)	Placebo (n = 221)
BODY AS A WHOLE		
Fatigue	33%	30%
Edema	21%	10%
Fever	19%	16%
CNS/PNS		
Dizziness	14%	8%
Headache	12%	9%
GASTROINTESTINAL		
Diarrhea	22%	12%
Constipation	18%	17%

Table 3. *(continued)* Adverse Events Occurring in ≥ 5% of Patients Receiving Chemotherapy

Event	Aranesp® (n = 873)	Placebo (n = 221)
METABOLIC/NUTRITION		
Dehydration	5%	3%
MUSCULO-SKELETAL		
Arthralgia	13%	6%
Myalgia	8%	5%
SKIN AND APPENDAGES		
Rash	7%	3%

Table 4. Incidence of Other Clinically Significant Adverse Events in Patients Receiving Chemotherapy

Event	All Aranesp® (n = 873)	Placebo (n = 221)
Hypertension	3.7%	3.2%
Seizures/Convulsions[a]	0.6%	0.5%
Thrombotic Events	6.2%	4.1%
Pulmonary Embolism	1.3%	0.0%
Thrombosis[b]	5.6%	4.1%

[a] Seizures/Convulsions include the preferred terms: Convulsions, Convulsions Grand Mal, and Convulsions Local.

[b] Thrombosis includes: Thrombophlebitis, Thrombophlebitis Deep, Thrombosis Venous, Thrombosis Venous Deep, Thromboembolism, and Thrombosis.

Thrombotic and Cardiovascular Events

Overall, the incidence of thrombotic events was 6.2% for Aranesp® and 4.1% for placebo. The following events were reported more frequently in Aranesp®-treated patients than in placebo controls: pulmonary embolism, thromboembolism, thrombosis, and thrombophlebitis (deep and/or superficial). In addition, edema of any type was more frequently reported in Aranesp®-treated (21%) patients than in patients who received placebo (10%). (See **Table 4**.)

DOSAGE AND ADMINISTRATION

IMPORTANT: Aranesp® dosing regimens are different for each of the indications described in this section of the product monograph. Be sure to reference the appropriate section below. Due to the longer serum half-life, Aranesp® should be administered less frequently than Epoetin alfa (for example, where Epoetin alfa is administered three times a week, Aranesp® should be administered weekly). Aranesp® should be administered under the supervision of a healthcare professional.

Chronic Renal Failure Patients

Aranesp® is administered either IV or SC as a single injection administered weekly or once every two weeks. The dose should be started and slowly adjusted as described below based on hemoglobin levels. If a patient fails to respond or maintain a response, other etiologies should be considered and evaluated (see **PRECAUTIONS: General/Laboratory Monitoring**). When Aranesp® therapy is initiated or adjusted, the hemoglobin should be followed weekly until stabilized and monitored at least monthly thereafter. For patients who respond to Aranesp® with a rapid increase in hemoglobin (e.g., more than 10 g/L in any 2-week period), the dose of Aranesp® should be reduced (see **DOSAGE AND ADMINISTRATION: Dose Adjustment for CRF Patients**) because of the association of excessive rate of rise of hemoglobin with adverse events (see **WARNINGS: Cardiovascular Events, Hemoglobin, and Rate of Rise of Hemoglobin**). The "Clinical Practice Guidelines of the Canadian Society of Nephrology for Treatment of Patients with Chronic Renal Failure" recommend that patients' hemoglobin levels should not plateau below 100 g/L or above 130 g/L. To achieve this, the Canadian Society of Nephrology recommends to target hemoglobin between 110 to 120 g/L.

Correction of Anemia in Chronic Renal Failure Patients

The recommended starting dose of Aranesp® for the correction of anemia in CRF patients is 0.45 mcg/kg body weight, administered as a single IV or SC injection once weekly. Because of individual variability, doses should be titrated to a target not to exceed a hemoglobin concentration of 120 g/L (see **Dose Adjustment for CRF Patients**). For many patients, the appropriate maintenance dose will be lower than this starting dose. Predialysis patients, in particular, may require lower maintenance doses. Also, some patients have been treated successfully with a SC dose of Aranesp® administered once every 2 weeks.

Conversion to Aranesp® from Recombinant Human Erythropoietin in CRF Patients

The clinical studies demonstrated that the relationship between baseline rHuEPO and maintenance Aranesp® is nonlinear across the dosing spectrum. Consequently, the starting weekly dose of Aranesp® should be estimated on the basis of the weekly Epoetin alfa dose at the time of substitution (see **Table 5**). Due to the longer serum half-life, Aranesp® should be administered less frequently than rHuEPO. Patients receiving rHuEPO 2 or 3 times weekly should change to once weekly Aranesp® at a dose equivalent to their total weekly dose of rHuEPO. Patients receiving rHuEPO once per week should change to Aranesp® once every 2 weeks at a dose that is equivalent to the sum of 2 weekly doses of rHuEPO. The same route of administration should be used. For patients prescribed prefilled syringes the calculated dose should be rounded upward to the next available syringe strength.

Table 5. Estimated Aranesp® Starting Dose (mcg/week) Based on Previous Epoetin alfa Dose (Units/week) for CRF Patients

Previous Weekly Epoetin alfa Dose (CRF Patients) (Units/week)	Weekly Aranesp® Dose (CRF Patients) (mcg/week)
< 2,500	6.25
2,500 to 4,999	12.5
5,000 to 10,999	25
11,000 to 17,999	40
18,000 to 33,999	60
34,000 to 89,999	100
≥ 90,000	200

Patients should be carefully monitored to ensure appropriate dose adjustments in order to maintain appropriate hemoglobin levels (see **Dose Adjustment for CRF Patients**). Data from approximately 800 patients receiving Aranesp® in clinical studies were analysed to assess the dose required to maintain hemoglobin; no difference was observed between the average weekly dose administered by the IV or SC routes of administration. Because of intersubject variability, titration to the optimal therapeutic Aranesp® dose is required for individual patients. When a patient's hemoglobin is stabilized within the target range it should be monitored monthly and adjustments made as described below (see **Dose Adjustment for CRF Patients**).

Dose Adjustment for CRF Patients

The dose should be adjusted for each patient to achieve and maintain a target hemoglobin not to exceed 120 g/L. Because of the time required for erythropoiesis and the red cell half-life, an interval of 2 to 6 weeks may occur between the time of a dose adjustment and a significant change in hemoglobin. Increases in dose should not be made more frequently than once a month. If the hemoglobin is increasing and approaching the upper limit of the target hemoglobin range, the dose should be reduced by approximately 25%. If the hemoglobin continues to increase, and exceeds the target hemoglobin range, doses should be temporarily withheld until the hemoglobin begins to decrease, at which point therapy should be reinitiated at a dose approximately 25% below the previous dose. If the hemoglobin increases by more than 10 g/L in a 2-week period, the dose should be decreased by approximately 25%. After Aranesp® initiation or dose increase, if the increase in hemoglobin is less than 10 g/L over 4 weeks and iron stores are adequate (see **PRECAUTIONS: General**), the dose of Aranesp® may be increased by approximately 25% of the previous dose. Further increases may be made at 4-week intervals until the desired response is attained.

Maintenance Dose for CRF Patients

Aranesp® dosage should be adjusted to maintain a target hemoglobin not to exceed 120 g/L. If the hemoglobin exceeds 120 g/L, the dose may be adjusted as described above. Doses must be individualized to ensure that hemoglobin is maintained at an appropriate level for each patient.

Cancer Patients Receiving Chemotherapy

The recommended starting dose of Aranesp® is 2.25 mcg/kg administered as a single weekly SC injection. The dose should be adjusted for each patient to achieve and maintain a target hemoglobin of 120 g/L. If the increase in hemoglobin is inadequate (≤ 10 g/L) or if the response is not satisfactory in terms of reducing RBC transfusion requirements after approximately 6 weeks of therapy, the dose of Aranesp® should be increased up to 4.5 mcg/kg/week. For patients prescribed prefilled syringes the calculated dose should be rounded upward to the next available syringe strength. If hemoglobin increases by more than 10 g/L in a 2-week period or if the hemoglobin exceeds 120 g/L, the dose should be reduced by approximately 25%. If the hemoglobin exceeds 130 g/L, doses should be temporarily withheld until the hemoglobin falls to 120 g/L. At this point, therapy should be reinitiated at a dose approximately 25% below the previous dose.

AVAILABILITY OF DOSAGE FORMS

The following dosage forms are available for Aranesp® (darbepoetin alfa):

Table 6. Single-dose Prefilled Syringes

Quantity of Aranesp®	Volume	Aranesp® Concentration
10 mcg	0.4 mL	25 mcg/mL
15 mcg	0.38 mL	40 mcg/mL
20 mcg	0.5 mL	40 mcg/mL
30 mcg	0.3 mL	100 mcg/mL
40 mcg	0.4 mL	100 mcg/mL
50 mcg	0.5 mL	100 mcg/mL
60 mcg	0.3 mL	200 mcg/mL
80 mcg	0.4 mL	200 mcg/mL
100 mcg	0.5 mL	200 mcg/mL
130 mcg	0.4 mL	325 mcg/mL
150 mcg	0.3 mL	500 mcg/mL
200 mcg	0.4 mL	500 mcg/mL
250 mcg	0.5 mL	500 mcg/mL
300 mcg	0.6 mL	500 mcg/mL
400 mcg	0.8 mL	500 mcg/mL
500 mcg	1.0 mL	500 mcg/mL

Table 7. Single-dose Vials

Quantity of Aranesp®	Volume	Aranesp® Concentration
15 mcg	1.0 mL	15 mcg/mL
25 mcg	1.0 mL	25 mcg/mL
40 mcg	1.0 mL	40 mcg/mL
60 mcg	1.0 mL	60 mcg/mL
100 mcg	1.0 mL	100 mcg/mL
200 mcg	1.0 mL	200 mcg/mL
325 mcg	1.0 mL	325 mcg/mL
500 mcg	1.0 mL	500 mcg/mL

Product Monograph available upon request.

Amgen Canada
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AMGEN CANADA INC.

Member PAAB R&D

Venofer®

iron sucrose injection

20 mg elemental iron/mL
Therapeutic Class: Hematinic

DESCRIPTION

VENOFER (Iron Sucrose Injection) is a brown, viscous, sterile, nonpyrogenic aqueous solution containing 20 mg/mL elemental iron in the form of an iron(III)-hydroxide sucrose complex as the active ingredient, and water for injection. NaOH may be used to adjust the pH to 10.5 - 11.1. The sterile solution has an osmolarity of 1250 mOsmol/L.

Iron(III)-hydroxide sucrose complex has a molecular weight of approximately 43,200 daltons and a molecular formula as follows:

$$[Na_2Fe_5O_8(OH)\bullet 3(H_2O)]_n\bullet m(C_{12}H_{22}O_{11})$$

where: n is the degree of iron polymerization and m is the number of sucrose molecules in complex with the iron(III)-hydroxide. VENOFER is available in 5 mL single dose vials. The product contains no preservatives or dextran polysaccharides.

ACTION AND CLINICAL PHARMACOLOGY

VENOFER (Iron Sucrose Injection) consists of polynuclear ferric hydroxide cores surrounded by noncovalently bound sucrose molecules. Following intravenous administration of VENOFER, iron sucrose is dissociated by the reticuloendothelial system into iron and sucrose.

In 22 hemodialysis patients on erythropoietin therapy treated with iron sucrose at 100 mg of iron three times weekly for three weeks, significant increases in serum iron and serum ferritin and significant decreases in total iron binding capacity occurred four weeks from the initiation of iron sucrose treatment.

In healthy adults treated with intravenous doses of VENOFER, the iron component exhibits first order kinetics with an elimination half-life of 6 h, total clearance of 1.2 L/h, non-steady state apparent volume of distribution of 10.0 L and steady state apparent volume of distribution of 7.9 L. Since iron disappearance from serum depends on the need for iron in the iron stores and iron utilizing tissues of the body, serum clearance of iron is expected to be more rapid in iron deficient patients compared to healthy individuals. The effects of age and gender on the pharmacokinetics of VENOFER have not been studied.

In healthy adults treated with intravenous doses of VENOFER, the iron component appears to distribute mainly in blood and to some extent in extravascular fluid. In a study evaluating VENOFER at 100 mg of iron labelled with $^{52}Fe/^{59}Fe$ in patients with iron deficiency, it was found that a significant amount of the administered iron distributes in the liver, spleen and bone marrow. The bone marrow is an iron trapping compartment and not a reversible volume of distribution.

The sucrose component of VENOFER is eliminated mainly by urinary excretion. In a study evaluating a single intravenous dose of VENOFER containing 1510 mg of sucrose and 100 mg of iron in 12 healthy adults, 68.3% of the sucrose was eliminated in urine in 4 h and 75.4% in 24 h. About 5% of the iron was eliminated via renal excretion over 24 h.

INDICATIONS AND CLINICAL USE

VENOFER (Iron Sucrose Injection) is indicated in the treatment of patients with dialysis-associated anemia.

CONTRAINDICATIONS

The use of VENOFER (Iron Sucrose Injection) is contraindicated in patients with evidence of iron overload, patients with known hypersensitivity to VENOFER, and patients with anemia not caused by iron deficiency.

WARNINGS

HYPERSENSITIVITY REACTIONS

POTENTIALLY FATAL HYPERSENSITIVITY OR ANAPHYLACTIC-TYPE REACTIONS CHARACTERIZED BY SHOCK, LOSS OF CONSCIOUSNESS, COLLAPSE, HYPOTENSION, DYSPNEA, OR CONVULSION HAVE BEEN REPORTED RARELY IN PATIENTS RECEIVING VENOFER (IRON SUCROSE INJECTION) (SEE ADVERSE REACTIONS). FATAL IMMEDIATE HYPERSENSITIVITY REACTIONS HAVE BEEN REPORTED IN PATIENTS RECEIVING THERAPY WITH A VARIETY OF PARENTERAL PREPARATIONS CONTAINING IRON CARBOHYDRATE COMPLEXES. FACILITIES FOR CARDIOPULMONARY RESUSCITATION MUST BE AVAILABLE DURING DOSING IN CASE OF SERIOUS ANAPHYLACTOID REACTIONS (SEE ADVERSE REACTIONS). PHYSICIAN VIGILANCE IS REQUIRED WHEN ADMINISTERING ANY INTRAVENOUS IRON PRODUCT.

HYPOTENSION

HYPOTENSION HAS BEEN REPORTED FREQUENTLY IN PATIENTS RECEIVING INTRAVENOUS IRON. HYPOTENSION FOLLOWING ADMINISTRATION OF VENOFER MAY BE RELATED TO RATE OF ADMINISTRATION AND TOTAL DOSE ADMINISTERED. CAUTION SHOULD BE TAKEN TO ADMINISTER VENOFER AS RECOMMENDED (SEE DOSAGE AND ADMINISTRATION).

PRECAUTIONS

General

Because body iron excretion is limited and excess tissue iron can be hazardous, caution should be exercised in the administration of parenteral iron formulations, and treatment should be withheld when there is evidence of tissue iron overload. Patients receiving VENOFER (Iron Sucrose Injection) require periodic monitoring of hematologic parameters, including hemoglobin, hematocrit, serum ferritin and transferrin saturation. Generally accepted guidelines recommend withholding administration of intravenous iron formulations from patients demonstrating a transferrin saturation >50% or serum ferritin >800 ng/mL (see DOSAGE AND ADMINISTRATION and SYMPTOMS AND TREATMENT OF OVERDOSAGE). Transferrin saturation values increase rapidly after IV administration of iron sucrose; thus, serum iron values may be reliably obtained 48 hours after IV dosing.

Local Reactions

Care must be taken to avoid paravenous infiltration. If this occurs, the infusion of VENOFER should be discontinued immediately. Ice may be applied to cause local vasoconstriction and decrease fluid absorption; massage of the area should be avoided.

Oral Iron Use

Oral iron should not be administered concomitantly with parenteral iron preparations. Like other parenteral iron preparations, VENOFER may be expected to reduce the absorption of concomitantly administered oral iron preparations.

Pregnancy

Teratology studies performed in rats at IV doses up to 13 mg iron/kg/day (more than 9 times the maximum recommended human dose for a 70 kg person) and rabbits at IV doses up to 13 mg iron/kg on alternate days (approximately 9 times the maximum recommended human dose for a 70 kg person) have not revealed definitive evidence of impaired fertility. Fetal growth effects at these doses appeared related to low maternal food consumption and low body weight gain. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, VENOFER should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. When iron sucrose was administered at deliberate overdoses to rabbit dams (up to 215 mg/kg/day) marked fetal/placental iron overload was noted. It is unlikely that significant fetal iron overload would occur in iron deficient pregnant women receiving therapeutic doses of VENOFER to correct iron deficiency (see PRECAUTIONS - General).

Nursing Mothers

VENOFER is excreted in the milk of rats. It is not known whether VENOFER is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when VENOFER is administered to nursing women.

Pediatric Use

The safety and effectiveness of VENOFER in pediatric patients has not been established.

Geriatric Use

Clinical studies of VENOFER did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting with lower doses, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Drug Interactions

Drug interactions involving VENOFER have not been studied.

ADVERSE REACTIONS

The safety of VENOFER (Iron Sucrose Injection) has been documented in 231 chronic renal failure patients exposed to doses of 100 mg iron IV as iron sucrose given up to three times weekly for up to ten doses in three separate clinical trials.

The following adverse events, whether or not related to VENOFER administration, were reported by >5% of those patients: hypotension (36%), cramps/leg cramps (23%), nausea, headache, vomiting, and diarrhea.

Adverse events, whether or not related to VENOFER administration, reported by >1% of these patients are categorized below by body system and ranked in order of decreasing frequency within each body system. Some of these symptoms are seen in dialysis patients not receiving intravenous iron.

Body as a Whole: headache, fever, pain, asthenia, malaise.
Cardiovascular: hypotension, chest pain, hypertension, hypervolemia.
Gastrointestinal: nausea, vomiting, abdominal pain.
Central and Peripheral Nervous Systems: dizziness.
Musculoskeletal: cramps/leg cramps, musculoskeletal pain.
Respiratory: dyspnea, cough.
Skin and appendages: pruritus, application site reaction.

Anaphylactoid reactions were not observed in these clinical studies, but have been reported with iron sucrose, generally at doses higher than 100 mg and/or with fast infusion rates.

Post-Marketing Experience: From the spontaneous reporting system, 46 out of an estimated more than 787,361 patients exposed to VENOFER between 1992 and 2000 reported anaphylactoid reactions, including 15 patients who experienced serious or life-threatening reactions associated with VENOFER administration (see WARNINGS – HYPERSENSITIVITY REACTIONS). Almost all of these patients received single doses greater than 100 mg iron.

Other adverse events, in order of decreasing frequency, reported rarely with VENOFER use, were: hypotension, nausea, headache, edema, metallic taste/taste perversion, vomiting, abdominal pain, phlebitis, urticaria, flushing, dyspnea, pyrexia, rash, dizziness, tachycardia, tachypnea and wheezing. Doses higher than 100 mg are associated with a higher incidence of adverse events. Necrotizing enterocolitis, not necessarily causally associated with VENOFER use, has been reported rarely in very low birth weight premature infants.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Dosages of VENOFER (Iron Sucrose Injection) in excess of iron needs may lead to the accumulation of iron in storage sites, resulting in hemosiderosis. Periodic monitoring of iron parameters such as serum ferritin and transferrin saturation may assist in recognizing iron accumulation. VENOFER should not be administered to patients with iron overload and should be discontinued when serum ferritin levels exceed usual norms (see PRECAUTIONS – General).

Symptoms associated with overdosage or infusing VENOFER too rapidly include hypotension, headache, vomiting, nausea, dizziness, joint aches, paresthesia, abdominal and muscle pain, edema, and cardiovascular collapse. Most symptoms have been successfully treated with IV fluids, corticosteroids and/or antihistamines.

DOSAGE AND ADMINISTRATION

The dosage of VENOFER (Iron Sucrose Injection) is expressed in terms of mg of elemental iron. Each 5 mL vial contains 100 mg of elemental iron (20 mg/mL).

The recommended dosage of VENOFER for the repletion treatment of iron deficiency in dialysis patients is 5 mL of VENOFER (100 mg of elemental iron) delivered slowly by the intravenous route during the dialysis session. Frequency of dosing should be not more than three times weekly. Most anemic patients will require a minimum cumulative dose of 1000 mg of elemental iron, administered over 10 sequential dialysis sessions, to achieve a favourable hemoglobin or hematocrit response. Patients may then continue to require therapy at the lowest dose necessary to maintain target levels of hemoglobin, hematocrit and iron storage parameters within acceptable limits. Doses of iron sucrose at 20-50 mg iron have been shown to result in clinically meaningful responses in some patients in the maintenance phase.

Administration: VENOFER must only be administered intravenously, by slow injection or infusion, generally into the dialysis line.

Slow Intravenous Injection: In chronic renal failure patients, VENOFER may be administered by slow intravenous injection at a rate of not more than 1 mL (20 mg iron) undiluted solution per minute [i.e., 5 minutes per vial] not exceeding one vial of VENOFER [100 mg iron] per injection. Discard any unused portion.

Intravenous Infusion: VENOFER may also be administered by infusion. This mode of administration may be preferable to minimize the risk of hypotensive episodes (see WARNINGS – HYPOTENSION). The content of each vial must be diluted exclusively in a maximum of 100 mL of 0.9% NaCl immediately prior to infusion. Use immediately after diluting in saline. Unused diluted solution should be discarded.

PHARMACEUTICAL INFORMATION

Proper Name: Iron Sucrose
Chemical Names: Iron (III)-hydroxide sucrose complex
Ferric-hydroxide Sucrose Complex
Saccharated Iron Oxide
Structural Formula: Exact structural formula not known.
Molecular Weight: Approximately 43,200 daltons

Reconstitution Table

Vial Size	Volume of Diluent to be Used per Vial	Nominal Concentration per mL
5 mL	Maximum 100 mL 0.9% NaCl	1 mg/mL (when the maximum of 100 mL NaCl is used).

When prepared as an infusion, use immediately. Do not store.

NOTE: Do not mix VENOFER with other medications or add to parenteral nutrition solutions for intravenous infusion. As with all parenteral drug products, intravenous admixtures should be inspected visually for clarity, particulate matter, precipitate, discolouration and leakage prior to administration, whenever solution and container permit. Solutions showing haziness, particulate matter, precipitate, discolouration or leakage should not be used. Discard unused portion.

STABILITY AND STORAGE RECOMMENDATIONS

Store at 15-25°C. Do not freeze. Discard unused portion.

PARENTERAL PRODUCTS

VENOFER must only be administered intravenously by slow injection or infusion (see DOSAGE AND ADMINISTRATION).

AVAILABILITY OF DOSAGE FORMS

VENOFER (Iron Sucrose Injection) is available in 5 mL single dose vials, sold in boxes of 10. Each 5 mL contains 100 mg (20 mg/mL) of elemental iron as an iron(III)-hydroxide sucrose complex in water for injection.

REFERENCES

National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease, 2000. *Am J Kidney Dis* 37:S182-S238, (suppl 1) 2001. Charytan C, Levin N, Al-Saloum M, *et al.* Efficacy and safety of iron sucrose for iron deficiency in patients with dialysis-associated anemia: North American clinical trial. *Am J Kidney Dis* 37 (2): 300-307, 2001. Van Wyck DB, Cavallo G, Spinowitz BS, *et al.* Safety and efficacy of iron sucrose in patients sensitive to iron dextran: North American clinical trial. *Am J Kidney Dis* 36 (1): 88-97, 2000. Danielson BG, Salmonson T, Derendorf H, *et al.* Pharmacokinetics of iron (III)-hydroxide sucrose complex after a single intravenous dose in healthy volunteers. *Arznein-Forsch/Drug Res* 46(I); 6: 615-621, 1996. Beshara S, Lundqvist H, Sundin J, *et al.* Kinetic analysis of ^{52}FE-labeled iron (III)-hydroxide sucrose complex following bolus administration using positron emission tomography. *Brit J of Haematology* 104: 288-295, 1999. Pribilla W. Animal experiments investigating the iron transfer between mother and fetus after the intravenous administration of iron. *Acta Haemat* 12:371-384, 1954. Wöhler F. The iron supply to the fetus. Reprinted from *Archiv für Kinderheilkunde* 155 (3); 1957.

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What does it take to stand out in a crowd?

PPC's support of Pharmacy is one way we make a difference you can see.

You don't always have to be a big fish to make a big difference.

At Pharmaceutical Partners of Canada, we're proud to have supported Pharmacy in Canada for more than 20 years, with special educational grants, awards, and funding that allows Pharmacy students to achieve their full potential. We also believe in the research and other contributions made by Hospital Pharmacy. Across the province and throughout the country, we are privileged to give back to an industry that has given so much to us.

We may not be the biggest fish in the pond, but supporting Hospital Pharmacy, and worthy health care organizations, is a proud part of our culture at PPC. Because we believe that how much you stand apart depends on what you stand behind.

we're privileged to sponsor grants that help pharmacy students like gillian joyce expand their education.

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