CJHP JCPH

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

Vol. 56, AGM Supplement 3 • August 2003
Vol. 56, AGM Supplement 3 • Août 2003

"Setting the Course
Partnering with Patients
Striving for Excellence"

Experience the Edge... Where Old Meets New

56th AGM & Educational Sessions

55e AGA et séances éducatives

St. John's, Newfoundland & Labrador

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). These changes in HDL-C with HMG-CoA reductase inhibitors should be considered as modest when compared to those observed in LDL-C and do not play a primary role in the lowering of LDL-C/HDL-C and Total-C/HDL-C ratios.

See Prescribing Information for complete warnings, precautions, dosing and administration.

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.

The effects of atorvastatin-induced changes in lipoprotein levels, including reduction of serum cholesterol on cardiovascular morbidity, mortality, or total mortality have not been established.

‡ A patient-year represents the total time of exposure to LIPITOR as defined by the sum of each patient time on LIPITOR.[3]

¥ 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 randomized 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.[1]

Aiming beyond.

EFFICACY ➢ † A powerful demonstrated effect across key lipid parameters[1]

EXPERIENCE ➢ More than ~~44~~ 48 million patient-years of experience[2‡]

EVIDENCE ➢ Demonstrated delayed time to first ischemic event in stable CAD patients (n=164, p=0.03)[3¥]

LIPITOR has a leading edge clinical research program exploring new areas that may extend beyond lipid control[4]

Pfizer
Life is our life's work

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PAAB

Member R&D

LIPITOR*
atorvastatin calcium
tablets

Dear Colleague:

As we plan for the Canadian Society of Hospital Pharmacists' 56th Annual General Meeting and Educational Sessions, scheduled for August 16-19, 2003, we're 56 years strong. We celebrate a past of exceptional academic and professional contributions to the field of pharmacy, and we are anxious to discover a tomorrow of unprecedented activity and vision.

As we look forward, it is with great pleasure that we invite you to join us in the breathtaking city of St. John's, Newfoundland & Labrador for AGM 2003.

The Educational Services Committee, chaired by Judy Chong, has assembled a dynamic program. All sessions are designed to provide a contemporary insight into a wide range of practice-based topics, as well as broad professional issues such as dealing with staff shortages, responding to a SARS outbreak and the formulary system debate. Workshops will be focusing on the assessment of drug-induced adverse effects, the COPD guidelines, and neuropsychopharmacology. A special Canadian Hospital Pharmacy Residency Board workshop will be focusing on "learning styles" and the "development of self-directed learners". This year's program features a faculty of exceptional speakers and opportunities for learning that are both abundant and diverse.

Similarly, the exhibit program offers you the opportunity to interact with members of the pharmaceutical industry, gathering the latest information on their products and services. Please take the time to gain from their expertise and acknowledge the tremendous support they offer to our event.

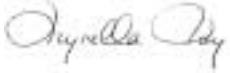
The 2003 Annual General Meeting (AGM) is scheduled for Sunday, August 17th from 15h00 until 17h00. The AGM is your opportunity to hear what your Society has been working hard for on your behalf over the last year. Reports from CSHP Council provide an overview of last year's initiatives and serve as a strategic framework as we move ahead. The Coffee and Chat immediately following the AGM offers you an informal opportunity to continue the discussion with the Council and staff of CSHP. As we work towards the development of a new strategic plan for the Society, we value your feedback and insight. It's important to make time in your busy AGM schedule to participate in the Coffee and Chat as Council needs to hear from you, our members.

Social events kick off Saturday, August 16th, with the eighth annual CSHP Research & Education (R&E) Foundation Fundraising Golf Event, to be held at The Wilds at Salmonier River Golf Club. All profits from the event will be donated to the R&E Foundation, supporting and promoting the practice-based research initiatives of CSHP's members. Register early as this event fills up fast!

The Newfoundland & Labrador Host Committee, chaired by Lisa Bishop, has organized an impressive itinerary of social activities including an early morning Fun Run/Walk, a Fun Night at Club One – Steak and Lobster Dinner, and the annual Past-Presidents' Dinner and Dance. The efforts of this year's Committee guarantee that you will never be far from the spectacular flavour of the east coast and our magnificent host city.

AGM 2003: ***Experience the Edge… Where Old Meets New.*** We look forward to sharing the adventure with you.

Mike Gaucher, BSP, MBA
CSHP President



Myrella Roy, Pharm.D., FCCP
CSHP Interim Executive Director

Chers collègues,

Voici bientôt venue la 56e Assemblée générale annuelle (AGA) et les séances éducatives de la Société canadienne des pharmaciens d'hôpitaux, qui sont prévues du 16 au 19 août 2003. À cette occasion, nous célébrerons nos 56 années de contributions exceptionnelles à la formation des pharmaciens et à l'exercice de la profession, et nous nous préparerons à des lendemains chargés d'activité et d'une vision dynamique de niveau encore inégalé.

C'est donc avec joie que nous vous invitons à l'AGA 2003 qui se tiendra dans la captivante ville de St John's, à Terre-Neuve & Labrador.

Le Comité des services éducatifs, présidé par Judy Chong, vous a préparé un programme dynamique. Toutes les séances ont été conçues pour vous livrer un contenu très actuel, sur une variété de sujets touchant tant les aspects pratiques que professionnels, comme la gestion de la pénurie de personnel, comment réagir face à la flambée de SRAS, et le débat sur le système de formulaire thérapeutique. Les ateliers traiteront principalement de l'évaluation des réactions indésirables d'origine médicamenteuse, des lignes directrices sur la MPOC, et de la neuropsychopharmacologie. Il y aura également un atelier spécial du Conseil canadien de résidence en pharmacie d'hôpital sur les «styles d'apprentissage» et sur la «formation d'apprenants autonomes». Le programme de cette année vous réserve une brochette de conférenciers exceptionnels et des occasions d'apprentissage aussi variées que nombreuses.

De même, le programme d'exposition vous offre la chance d'échanger avec les membres de l'industrie pharmaceutique et d'obtenir l'information la plus à jour sur leurs produits et services. Nous vous invitons à prendre quelques minutes de votre temps pour tirer profit de leur expertise et les remercier de leur généreux appui à cet événement.

L'Assemblée générale annuelle 2003 est prévue pour le dimanche 17 août, de 15 heures à 17 heures. C'est l'occasion de vous mettre au fait des travaux qu'a effectués la Société en votre nom. Les rapports du Conseil de la SCPH vous brosseront un tableau des projets de l'année précédente et serviront de cadre de travail stratégique à la poursuite des activités. Le «café-rencontre», immédiatement après l'AGA, se veut un cadre tout à fait informel, propice à la poursuite des discussions avec le Conseil et le personnel de la SCPH. Comme nous sommes en train d'élaborer le nouveau plan stratégique pour la Société, vos commentaires et suggestions sont donc les bienvenus. Nous croyons qu'il est important que vous preniez quelques minutes de votre temps durant l'AGA, pour participer à ce «café-rencontre», car le Conseil a besoin de connaître l'opinion de ses membres.

Quant aux activités sociales, elles débutent le 16 août, avec le 8e tournoi de golf-bénéfice annuel de la Fondation pour la recherche et l'éducation de la SCPH, qui aura lieu au Wilds at Salmonier River Golf Club. Tous les profits seront remis à la Fondation pour la recherche et l'éducation, pour appuyer et promouvoir les projets de recherche sur la pratique des membres de la SCPH. Inscrivez-vous sans tarder, car cette activité est très en demande!

Le Comité d'accueil de Terre-Neuve et du Labrador, présidé par Lisa Bishop, vous a concocté un impressionnant programme d'activités sociales, dont la «marche/course matinale amicale», une soirée endiablée au Club One – dîner steak et homard, et le dîner-dansant du président sortant. Le Comité d'accueil vous a préparé cette année un programme qui vous rappellera sans cesse les saveurs spectaculaires de la côte est et de notre magnifique ville hôte.

AGA 2003 : ***Venez explorer les confins… Où l'ancien se marie au nouveau.*** Nous vous attendons pour une expérience hors du commun.

Mike Gaucher,
B.Sc. Pharm., MBA
Président de la SCPH

Myrella Roy,
Pharm.D., FCCP
Directrice exécutive intérimaire, SCPH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NOW AVAILABLE

PMILRINONE

MILRINONE LACTATE INJECTION

Yet another testimony to our commitment to Hospital Pharmacists.

Good things are happening at Novopharm's Hospital Division. Our recent collaboration with Teva Pharmaceutical Industries, the world's largest generic drug company, means enhanced R&D and a product line on the cutting edge of innovation, for you.

Teva is committed to the development, production and marketing of generic and proprietary branded pharmaceuticals worldwide. Novopharm, as part of Teva, is committed to Canada.

Together with Teva, Novopharm's Hospital Division will continue to lead the way in innovation, technology and service, for our valued partner – the Hospital Pharmacist.

Now through the efforts of our entire team, we are pleased to introduce yet another new product in our continually expanding product line – Milrinone.

Today, more than ever, it makes sense to have such impressive product resources on your side. Contact your Novopharm Hospital Division Representative today.

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TWO FORCES. ONE MISSION

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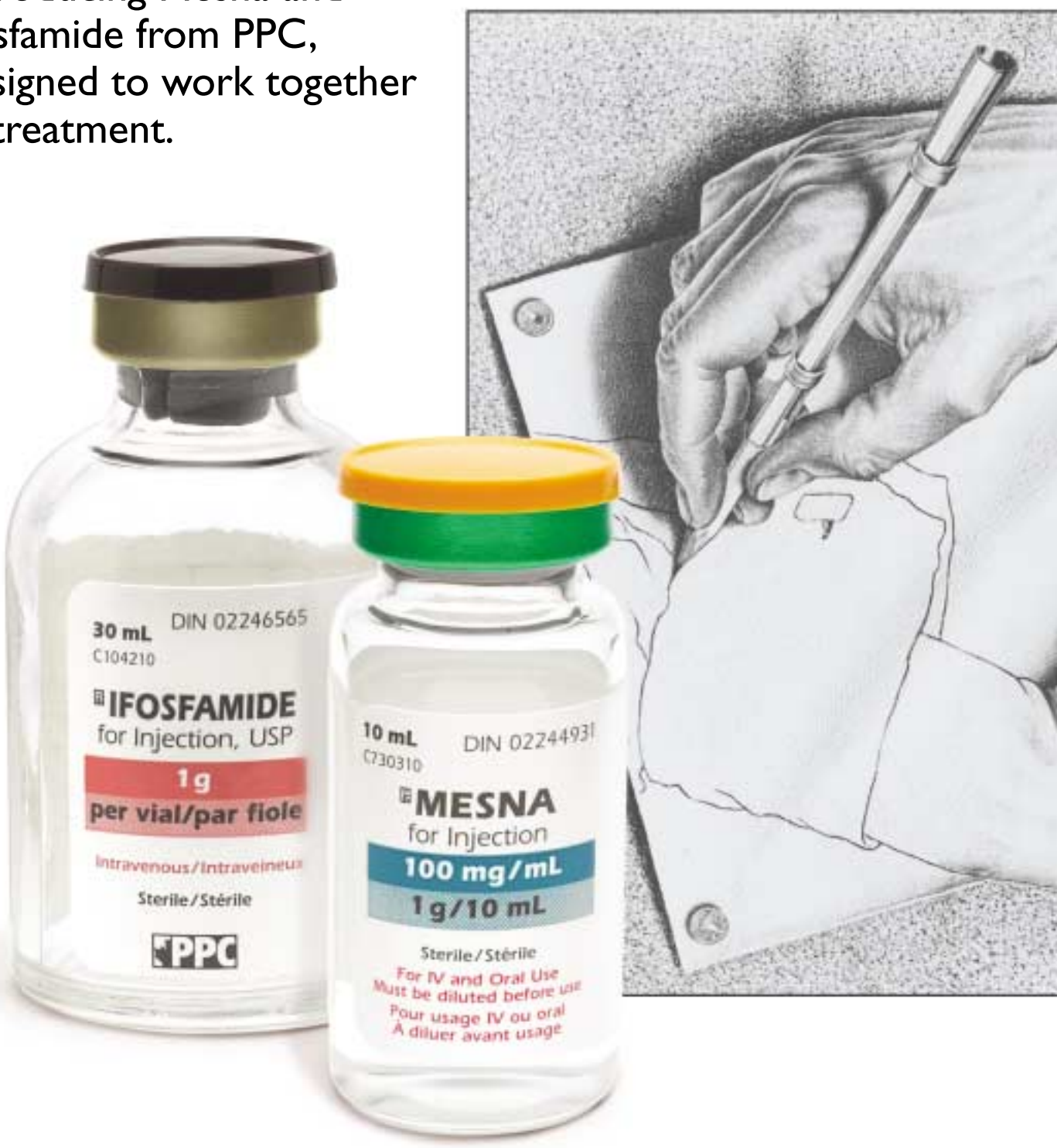
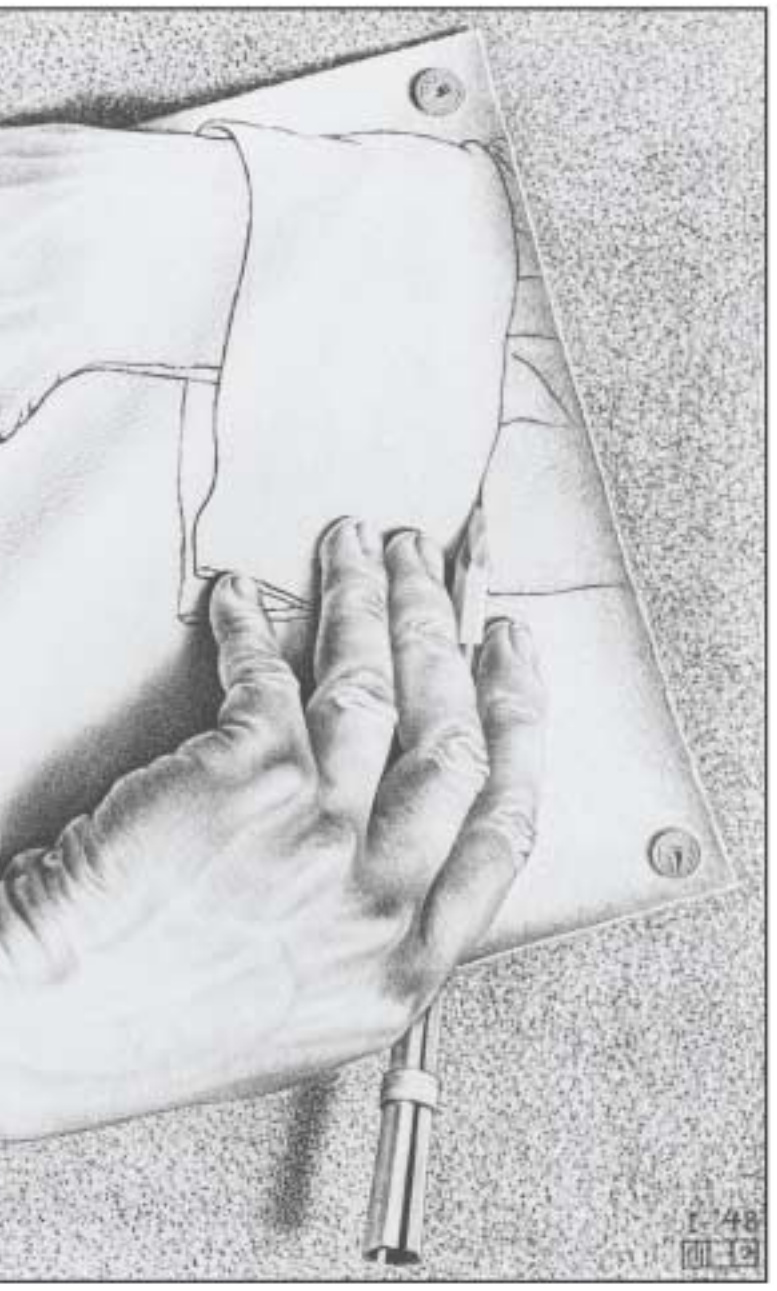
True partners give

Introducing Mesna and Ifosfamide from PPC, designed to work together in treatment.



each other a hand.



M.C. Escher's "Drawing Hands" © 2003 Cordon Art B.V. — Baarn — Holland. All rights reserved.

Mesna
now in a multi-dose vial.

Mesna for Injection from Pharmaceutical Partners of Canada Inc. (PPC) is a 100% latex-free uroprotective agent designed for use with the drug Ifosfamide. Only PPC makes Mesna available in a multi-dose 100 mg/ml size. The easy-to-use vial format also eliminates glass shards and the need for filters. Mesna is competitively priced and available in a 10-vial/case format from PPC.

Ifosfamide
now competitively-priced

Ifosfamide for Injection is a new cancer therapy product line from Pharmaceutical Partners of Canada Inc. This 100% latex-free format is available at a highly competitive price from PPC, in a 1 gram 30 mL vial, and coming soon in a 3 gram 100 mL size.

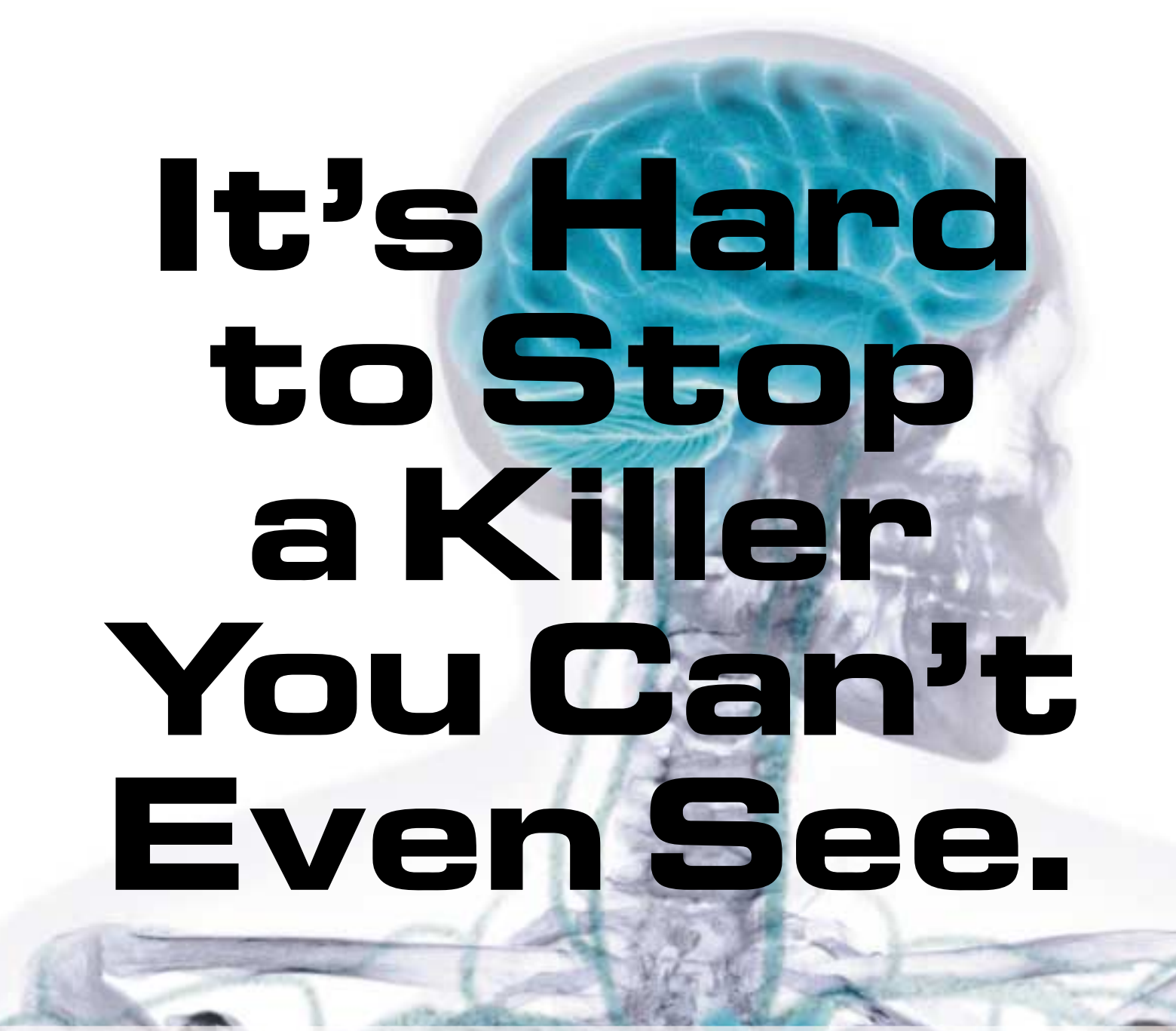
Pharmaceutical Partners of Canada Inc. is a growing multi-source company committed to providing high quality, cost-effective innovative products. For more information about the fine products from PPC, please call 1-877-821-7724.

Ifosfamide is indicated for soft tissue sarcoma, pancreatic carcinoma and cervical carcinoma.
Mesna is indicated for the reduction and prevention of urinary tract toxicity of oxazaphosphorines.
See prescribing information for full disclosure.

PPC PHARMACEUTICAL PARTNERS OF CANADA INC.
PARTENAIRES PHARMACEUTIQUES DU CANADA INC.

9050 Yonge Street, Suite 306, Richmond Hill, Ontario, Canada L4C 9S6, Telephone: (905) 707-7760 Fax: (905) 707-9309

PAAB



It's Hard to Stop a Killer You Can't Even See.

PLAVIX (clopidogrel bisulfate) is indicated for the secondary prevention of atherothrombotic events (myocardial infarction, stroke or vascular death) in patients with atherosclerosis documented by stroke, myocardial infarction or established peripheral arterial disease.[1]

PLAVIX is also indicated for the reduction of atherothrombotic events (myocardial infarction, ischemic stroke, cardiovascular death and/or refractory ischemia) in patients with acute coronary syndromes, unstable angina or non-Q-wave myocardial infarction without ST-segment elevation. 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 in those who were managed with percutaneous coronary intervention (with or without stent) or CABG (coronary artery bypass graft).[1]

PLAVIX is contraindicated in patients with a hypersensitivity to the drug substance or any component of the product and in patients with active bleeding such as peptic ulcers or intracranial hemorrhage. PLAVIX should not be used in patients who have lesions with a propensity to bleed. As with other antiplatelet agents, PLAVIX should be used with caution in patients who may be at risk of increased bleeding from recent trauma, surgery or other pathological conditions.[1]

PLAVIX should be used with caution in patients with severe or moderate renal impairment and in patients with moderate hepatic impairment who may have bleeding diatheses. PLAVIX is contraindicated in patients with severe liver impairment or cholestatic jaundice.[1]

The most common side effects of PLAVIX in CAPRIE included headache, flu-like symptoms and pain (7.6%, 7.5%, 6.4%).[1]

In CURE: Non-life-threatening major bleeding: PLAVIX + ASA, 1.6%; placebo + ASA, 1.0% ($p = 0.005$). Minor bleeding: PLAVIX + ASA, 5.1%; placebo + ASA, 2.4% ($p < 0.001$).[1]

It's the Clot that Kills.[2,3]

PLAVIX Offers Excellent Long-Term Protection from Further Atherothrombotic Events, Alone or With ASA.

IN CAPRIE,* A STUDY OF 19,185 PATIENTS WITH STROKE, MI OR PERIPHERAL ARTERIAL DISEASE (PAD):

- PLAVIX alone significantly reduced the combined risk of stroke, MI and vascular death by 8.7%† over and above the accepted 25% reduction provided by ASA‡ ($p = 0.045$)[1,4]
- Long-term risk reduction continued throughout the 3-year study period[1,4§]
- Simple, 75 mg once-daily dosing[1]

§The long-term comparative clinical significance of these findings beyond 3 years is unknown.

* Clopidogrel vs. Aspirin in Patients at Risk of Ischemic Events Trial.
CAPRIE dosing: PLAVIX 75 mg o.d. (n = 9,599), ASA 325 mg o.d. (n = 9,586).
† From CAPRIE. Absolute outcomes: PLAVIX (9.78%) vs. ASA (10.64%).
‡ From the Antiplatelet Trialists' Collaboration. Absolute outcomes: ASA (11.9%) vs. controls (15.2%).

IN CURE,¶ A STUDY OF 12,562 PATIENTS WITH UNSTABLE ANGINA OR NON-ST-SEGMENT ELEVATION MI:

- PLAVIX + ASA** significantly reduced the combined risk of stroke, non-fatal MI and cardiovascular death by 20%†† vs. placebo + ASA** ($p = 0.00009$)[1,5]
- Long-term risk reduction continued throughout the 12-month study period[1,5]
- PLAVIX + ASA had a beneficial, synergistic antiplatelet effect[6,7,8]

¶ Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial. CURE dosing: 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.
** Patients may also have received other standard cardiovascular therapies.
†† From CURE. Absolute outcomes: PLAVIX + ASA (9.3%) vs. placebo + ASA (11.4%).

Plavix®
clopidogrel 75mg

Bristol-Myers Squibb
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(at time of printing)

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Notice to Members – Changes to the CSHP Bylaws

Motion to change Bylaw Number 4.2 Setting of Fees

CSHP members will be asked to vote on the following motion: That the current CSHP Bylaw:

Article 4 Fees:

4.2 Setting of Fees

Council may set such annual fees as it may from time to time determine, but such fees shall not come into effect until approved by the members.

Be amended such that it now reads:

4.2 Setting of Fees

Council may set such annual fees as it may from time to time determine.

Continuing Education Credits/ Crédits de formation permanente

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

GOAL AND OBJECTIVES FOR THE CSHP AGM EDUCATION 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 support all practitioners in "Striving for Excellence" by presenting sessions related to the Vision Statement
- 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 ET DES SÉANCES ÉDUCATIVES

But :

Offrir des séances éducatives de qualité aux participants

Objectifs :

- Offrir aux participants des séances éducatives qui seront instructives et formatrices et qui motiveront les cliniciens et les gestionnaires
- Agir en meneur pour la pratique de la pharmacie hospitalière par des présentations sur des innovations en matière de rôles du pharmacien, de l'exercice de la pharmacie et de programmes en pharmacie
- Appuyer tous les praticiens à "Atteindre l'excellence" en présentant des séances inspirées de l'énoncé de la Vision 2003
- Promouvoir les aptitudes d'apprentissage perpétuel par la participation active à des ateliers de résolution de problèmes
- Donner aux participants la possibilité d'établir des réseaux professionnels et d'échanger par le truchement de programmes d'exposition et de séances d'affichage
- Donner la possibilité aux réseaux de pratique spécialisée de se rencontrer

AGM Social Events

In order to provide accurate dinner numbers to our host facilities, we encourage registrants to purchase tickets for both the Fun Night at Club One – Steak and Lobster Dinner on Sunday and the Past Presidents' Dinner on Monday prior to arrival at AGM 2003. Order forms are included on the AGM 2003 registration form. Tickets may be available on-site. Absolutely no tickets will be sold after 5 p.m. on Saturday, August 16. Thank you for your cooperation.

Where to Stay for AGM?

Delta St. John's Hotel and Conference Centre

CSHP is pleased to offer a special room rate of $156.00-single or double occupancy at the Delta St. John's Hotel. All CSHP official conference related meetings will take place at this property. The conference rate of $156.00 will be guaranteed until July 13, 2003. Don't miss out! Make your reservation early. You may make your reservations by telephoning the hotel directly at 709-739-6404 or 1-800-268-1133. When making reservations please remember to make reference to CSHP AGM 2003 for your conference rate.

How to Get to AGM

Air Canada has been appointed the official airline for CSHP's Annual General Meeting and Educational Sessions 2003. Please quote Reference Number CV454796 when making your travel arrangements.

As an AGM 2003 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 CV454796 in reference to your ticket and you could receive up to 50% off. Remember – YOU will continue to accumulate your travel plan points while supporting 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 favorite travel agent quoting the above Reference Number.
4. By ensuring CV454796 appears on your ticket, you help support your organization – in advance, we thank you.

AGM 2003 at a Glance

Educational Sessions

Sunday, August 17	8:30 – 15:00
Monday, August 18	8:15 – 15:15
Tuesday, August 19	8:15 – 16:00

Annual General Meeting

Sunday, August 17	15:00 – 17:00

Registration

Saturday, August 16	15:00 – 17:30
Sunday, August 17	07:30 – 17:00
Monday, August 18	07:30 – 17:00
Tuesday, August 19	08:00 – 16:00

Exhibits

Sunday, August 17	09:00 – 15:00
Monday, August 18	09:00 – 15:00

Lunch with Exhibitors

Sunday, August 17	12:15 – 14:15
Monday, August 18	12:30 – 14:30

Posters

Presentations:

Sunday, August 17	12:15 – 14:15
Monday, August 18	12:30 – 14:30

Viewing:

Sunday, August 17	10:15 – 10:45
Monday, August 18	10:00 – 10:30

SOCIAL EVENTS

Saturday, August 16

06:00 Breakfast

07:00 – 17:00 Research and Education Foundation Fundraising Golf Event
The Wilds at Salmonier River Golf Club
Limit: 80 golfers

18:00 – 19:30 CSHP Residency Mentorship Program Reception
Salon C

20:00 – 23:00 Opening Reception
Delta St. John's Hotel Crush Lobby

Sunday, August 17

06:30 – 08:00 Fun Run/Walk Event
Delta St. John's Lobby

17:00 – 18:00 Coffee and Chat
Conception Bay Room

18:00 – 24:00 Fun Night at Club One – Steak and Lobster Dinner
Dress: Casual

Monday, August 18

17:30 – 01:00 Past President's Dinner and Dance
Memorial University R. Gushue Hall
Buses provided for arrival and departure trips

Satellite Symposia

(breakfast/lunch included, limit of 100 participants)

Monday, August 17 - Hosted by Bayer Inc.
Salon CD

Tuesday, August 18 – breakfast
Hosted by Merck Frosst Canada Inc.
Salon CD

Tuesday, August 18 – luncheon
Hosted by Organon-Sanofi-Synthelabo
Salon A

Tuesday, August 18 – luncheon
Hosted by Amgen Canada
Salon B

Upcoming Events / Événements à venir

Professional Practice Conference (PPC)
January 31 – February 4, 2004
Sheraton Centre Toronto Hotel, Toronto, Ontario

Professional Practice Conference (PPC)
February 5 – February 9, 2005
Westin Harbour Castle Hotel, Toronto, Ontario

Annual General Meeting (AGM)
August 14 – August 17, 2004
The Westin Edmonton, Edmonton, Alberta

Annual General Meeting (AGM)
August 2005, Montreal, Quebec

Annual General Meeting (AGM)
August 2006, Ottawa, Ontario

Annual General Meeting (AGM)
August 2007, Saskatchewan

Annual General Meeting (AGM)
August 2008, New Brunswick

For further information, please contact:
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email: ddavidson@cshp.ca

AGM Registration Form

2003 Annual General Meeting • August 16th - 19th, 2003 • St. John's, Newfoundland & Labrador
Canadian Society of Hospital Pharmacists • Société canadienne des pharmaciens d'hôpitaux

350 – 1145 Hunt Club Road, Ottawa, ON K1V 0Y3 • Phone: (613) 736-9733 • Fax: (613) 736-5660 • www.cshp.ca

Please complete the following form and send to CSHP by **Friday, August 11, 2003**. After this date, we request that you bring your registration form and payment with you to the conference. Please note the early bird date of **July 13, 2003.**

Registration Information: Name badge will indicate this information. Please print clearly.

CSHP Membership Number (printed on address label): _____

First Name: _____ Initial: _____ Last Name: _____

Preferred Mailing Address: ❑ Business ❑ Home

City: _____ State/Province: _____ Postal Code: _____

Telephone (W): _____ Fax: _____ Telephone (H): _____

Email (to ensure membership database is up-to-date): _____

Workshop Information: Select **only one** workshop/day. For shared registrations, please indicate name of attendees.

Monday, 10:30 a.m. – 12:30 p.m.
- ❑ How to Assess Drug-Induced Adverse Effects
- ❑ What the COPD Guidelines Do Not Tell Us
- ❑ Neuropsychopharmacology: Predicting Clinical Profiles of Antidepressants

Tuesday, 10:45 a.m. – 12:45 p.m.
- ❑ How to Assess Drug-Induced Adverse Effects
- ❑ What the COPD Guidelines Do Not Tell Us
- ❑ Neuropsychopharmacology: Predicting Clinical Profiles of Antidepressants

Please indicate order of preference (1-3) in the boxes above. While every effort is made to accommodate first choices, we will assign you to your next indicated preference in the event of a full session.

Shared Registration: Please indicate name of registrants & day(s) attending along with workshop preference

Name(s)/Position(s)	Day(s) attending

Canadian Hospital Pharmacy Residency Board Preceptor Workshop • Monday 9:15 am – 12:30 pm.

WHO SHOULD ATTEND: Pharmacists who are residency directors, coordinators, current preceptors, or those who are interested in becoming a preceptor, for undergraduate or residency rotations. There is a **limit of 50 participants.**

❑ I wish to attend the CHPRB Preceptor Workshop

AGM Fees: Full Program and One-Day Programs include all educational sessions, exhibits and luncheons

	Full Program		Daily Rates	
	On/Before July 13/03	**After/on site**	**On/Before July 13/03**	**After/on site**
CSHP Member	$420.00	$495.00	$235.00	$271.00
Non-member	$614.00	$689.00	$300.00	$348.00
Shared Member	$481.00	$567.00	n/a	n/a
Non-member	$675.00	$761.00	n/a	n/a
Student Member	$170.00	$197.00	$57.00	$66.00
Non-member	$210.00	$237.00	$70.00	$79.00
AIT Member	$170.00	$197.00	$57.00	$66.00

AGM Registration Form

AGM Social Events (Optional)

Event	Date & Time	Place	Fees		Qty	Total
Research & Education Foundation Fundraising Golf Event Note: all golf fees/ rentals are HST exempt	Saturday, August 16 7:00 am – 5:00 pm	The Wilds at Salmonier River Golf Club *Transportation provided * Please note event limit of 80 golfers	Green Fees: $50.00			
			Club Rentals: $30/set Please specify: ❑ Left-handed ❑ Right-handed			
Opening Reception	Saturday, August 16 8:00 pm – 11:00 pm	Delta St. John's Hotel (Crush Lobby)	Complimentary			
Fun Run/Walk	Sunday, August 17 6:30 am – 8:00 am	Delta St. John's Hotel (Lobby area)	Complimentary			
Fun Night at Club One – Steak & Lobster Dinner	Sunday, August 17 6:00 pm – Midnight	Club One (George Street)	Early Bird $55.00	On Site $60.00		
Past Presidents' Dinner & Dance	Monday, August 18 5:30 pm – 1:00 am	Memorial University (R. Gushue Dining Hall)	$45.00	$50.00		

Non-member full program AGM rates include a one-year CSHP membership (national fee).

Did you remember to renew your CSHP membership – June 30, 2003?

Registration Fee	$ _____
R&E Foundation Golf Event	$ _____
Club One	$ _____
Past Presidents' Dinner	$ _____
15% HST (GST # R106866940)	$ _____
Total Enclosed:	**$** _____

❑ I am enclosing a cheque payable to the Canadian Society of Hospital Pharmacists (CSHP).

❑ Please charge my VISA / MASTERCARD or AMEX number (circle one): _____

Expiry Date: _____ Signature of Cardholder: _____

If you have a dietary restriction, please specify: _____

Emergency Contact: _____

AGM: Registration and Fee Information

- Fees are payable to the Canadian Society of Hospital Pharmacists by cheque, VISA, MasterCard or AMEX and MUST accompany this form. All fees are subject to 15% HST.
- CSHP accepts faxed registrations for those wishing to pay by credit card (in this case, please do not mail original form). To qualify for the early bird fees, registrations must be post-marked or faxed (with payment) on or before July 13, 2003. Cheques post-dated after this date will not be eligible for the early bird fee. Confirmations will be mailed within two weeks of receipt of registration.
- AGM registration fees include lunch on Sunday and Monday.
- Students are defined as undergraduate students. Graduate student members (including PharmD) must register using the Active-In-Training fees.
- Poster presenters attending sessions other than their own will be charged the applicable daily fee. Early bird fees apply to all accepted poster applicants.
- An institution may purchase a 3-day shared registration and use it for one individual ONLY per day. There are no shared registrations for students or residents.
- To qualify for the shared registration member rate, ALL of the individuals listed must be current CSHP members.
- The name of each shared registrant must be indicated on the shared application form and must be accompanied by payment in full.
- Individual name badges, tickets for luncheons and on-site registration kits will be provided for each shared registrant.

Cancellation Policy

Registrations may be cancelled in writing without penalty up to July 31, 2003. Cancellations after August 1st will be assessed an administration fee of $50.00. No refunds will be made after August 8, 2003. Individuals who wish to designate an alternate registrant for one or more of their days must first upgrade to a Shared Registration. Please note: There will be a $10.00 administration fee to transfer registrations.

Please return registration to the Canadian Society of Hospital Pharmacists
1145 Hunt Club Road, Suite 350, Ottawa, ON K1V 0Y3
For all Registration Enquires please contact Laurie Carquez at lcarquez@cshp.ca or by phone (613) 736-9733 ext 226 and for General Enquires please contact Desarae Davidson at ddavidson@cshp.ca or by phone (613) 736-9733 ext 229

CSHP 56th AGM and Educational Sessions

SATURDAY, AUGUST 16

07:00- 17:00 **Research & Education Foundation Fundraising Golf Event**

Salmonier River Golf Club

The Wilds at Salmonier River Golf Club (buses departing from the Delta)

15:00 – 17:30 **Registration**

Delta Lobby

18:00 – 19:30 **CSHP Residency Mentorship Program Reception**

Salon C

20:00 – 23:00 **Opening Night/Reception**

Delta Crush Lobby

Dress: casual

Meet and greet one another at a traditional Newfoundland Kitchen Party complete with entertainment by fiddler Stan Picket. Sample some tasty local treats while you relax and "make yourself at home"… we'll even bring along a Newfoundland dog to welcome you.

SUNDAY, AUGUST 17

06:30 – 08:00 **Fun Run/Walk Event**

Delta Lobby

Come along and enjoy the fresh air of a St. John's morning on our fun/run walk through historic downtown. Participants will receive a T-shirt and a complimentary hot/cold breakfast at Fireside Eatery. You may want to pack a sweatshirt, it may be a little cool at 6:30 am.

07:00 – 17:00 **Registration**

Delta Lobby

08:30 – 08:45 **Opening Remarks**

Salon B

08:45 – 09:30 **Herbal Products and the Hospital Pharmacist**

Salon B

Tannis Jürgens, PhD
Dalhousie University, Halifax, NS

09:30 – 10:15 **Response to the SARS Outbreak – The Ontario Experience**

Salon B

Linda Dresser, PharmD
Mount Sinai Hospital, Toronto,ON

10:15 – 10:45 **Exhibit Break/Pause**

Salon A

10:45 – 11:30 **Concurrent Sessions**

1. **Therapeutic Alternatives for Pulmonary Hypertension**

   Salon C

   Reem Haj, BScPharm
   St Michael's Hospital, Toronto, Ontario

2. **Dealing with Staff Shortages**

   Salon B

   Patricia Lefebvre, BPharm, MSc
   McGill University Health Centre, Montréal, QC

   Juan Edwards, BScPharm
   St. Clare's Mercy Hospital, St. John's, NL

11:30 – 12:15

1. **Breathing Easy: COPD Management for Pharmacists**

   Salon C

   Christine Folia, PharmD
   Agro Health Associates Inc., Flamborough, ON

2. **Is the Patient Delirious or is it His Baseline? Detecting and Managing Delirium**

   Salon B

   Lisa Burry, PharmD, FCCP
   Mount Sinai Hospital, Toronto, ON

12:15 – 14:15 **Lunch with Exhibitors/Poster Presentations**

Salon A

14:15 – 15:00 **Formularies – Cornerstone for Rational Drug Therapy or Barrier to Seamless Care?**

Salon CD

Bob Nakagawa, BScPhm, FCSHP
Fraser Health Authority, Port Moody, BC

Tom Paton, PharmD
Sunnybrook and Women's College HSC, Toronto, ON

15:00 – 17:00 **Annual General Meeting**

Salon B

17:00 – 18:00 **Coffee and Chat**

Conception Bay

18:00 – 24:00 **Fun Night at Club One**

Off-Site

Steak and Lobster Dinner

Dress: casual

Club One (part of the famous George Street) is all ours for an evening of fun and is located just down the street from the Delta. We'll start off the night with steak

and lobster and "dinner theatre" style entertainment with Spirit of Newfoundland. Following dinner, we'll have a "scruff" (otherwise known as dance) with a traditional Newfoundland band. It's bound to be a great time!

MONDAY, AUGUST 18

06:15 – 08:00 **Satellite Symposium (breakfast included)**

Salon CD

PK/PD Overview of Fluoroquinolones: Predictors of Antibiotic Efficacy and Resistance

hosted by: Bayer Inc.

07:00 – 17:00 **Registration**

Delta Lobby

08:15 – 08:30 **Announcements**

Salon B

CHPRB Residency Workshop:

08:30 – 09:15 **Learning Styles**

Salon B

Zubin Austin, BScPhm, MBA, MIS, PhD
University of Toronto, Toronto, ON

09:15 – 10:45 **Learning Styles: Teaching to Learn and Learning to Teach**

Salon C

Zubin Austin, BScPhm, MBA, MIS, PhD
University of Toronto, Toronto, ON

10:45 – 11:00 **Break**

Crush Lobby

11:00 – 12:30 **How to "Grow" a Self-Directed Learner**

Salon C

Donna Woloschuk, PharmD, FCSHP
Winnipeg Regional Health Authority, Winnipeg, MB

Educational Program:

08:30 – 09:15 **Learning Styles**

Salon B

Zubin Austin, BScPhm, MBA, MIS, PhD
University of Toronto, Toronto, ON

09:15 – 10:00 **Concurrent Sessions**

1. **The Use of Antiepileptic Drugs in the Treatment of Pain**

   Salon B

   Tejal Patel, PharmD
   Regina Qu'Apelle Health Region, Regina, SK

2. **The Pandemic of Preventable Drug-Related Morbidity: Our Medication Use System in Crisis**

   Salon D

   Neil MacKinnon, PhD
   Dalhousie University, College of Pharmacy, Halifax, NS

10:00 – 10:30 **Exhibits/Pause/Posters**

Salon A

10:30 – 12:30 **Workshops**

1. **How to Assess Drug-Induced Adverse Effects**

   Salon D

   Sandra Knowles, BScPhm
   Sunnybrook and Women's College HSC, Toronto, ON

2. **What the COPD Guidelines Do Not Tell Us**

   Conception Bay

   Charles Bayliff, PharmD, FCSHP
   London Health Sciences Centre, London, ON

3. **Neuropsychopharmacology: Predicting Clinical Profiles of Antidepressants**

   Salon B

   Leslie Phillips, PharmD
   Memorial University of Newfoundland, St. John's, NL

12:30 – 14:30 **Lunch with Exhibitors**

Salon A

14:30 – 15:15 **Hypertension – New Guidelines and Recent Trials**

Salon B

TBA

17:30 – 01:00 **Past-Presidents' Dinner and Dance**

Off-Site

Memorial University – R. Gushue Hall

Dress: Smart Casual. Bus provided from the Delta with return transportation starting at 23:30.

This evening is planned to honour CSHP Past Presidents. We'll enjoy a salmon dinner at Memorial's lovely Gushue Hall. Following dinner, we'll kick up our heels again with the help of one of the province's best live bands. (Please note the hall has no access to an ATM and the bar is cash only.)

TUESDAY, AUGUST 19

06:15 – 08:00 **Satellite Symposium (breakfast included)**

Salon CD

Innovation in the Treatment of Community Acquired Intra-Abdominal Infections

hosted by: Merck Frosst Canada Ltd.

08:00 – 16:00 **Registration**

Delta Lobby

08:15 – 08:30 **Announcements**

Salon B

08:30 – 09:30 **Antibiotic Consumption Measurement**

Salon B

Jim Hutchinson, MD, FRCP(C)
Memorial University of Newfoundland,
St. John's, NL

09:30 – 10:15 **Concurrent Sessions**

1. **Upper Gastrointestinal Bleeding Peptic Ulcer Disease: Pharmacotherapy Issues in Acute Management and Secondary Prevention**

   Salon B

   Peter Zed, PharmD
   Vancouver General Hospital,
   Vancouver, BC

2. **Seamless Care**

   Salon CD

   Scott Edwards, BScPharm
   Newfoundland Cancer Treatment &
   Research Foundation,
   St. John's, NL

10:15 – 10:45 **Break**

Crush Lobby

10:45 – 12:45 **Workshops**

1. **How to Assess Drug-Induced Adverse Effects**

   Conception Bay

   Sandra Knowles, BScPhm
   Sunnybrook and Women's College HSC,
   Toronto, ON

2. **What the COPD Guidelines Do Not Tell Us**

   Salon C

   Charles Bayliff, PharmD, FCSHP
   London Health Sciences Centre,
   London, ON

3. **Neuropsychopharmacology: Predicting Clinical Profiles of Antidepressants**

   Govenor Gower

   Leslie Phillips, PharmD
   Memorial University of Newfoundland,
   St. John's, NL

10:45 – 12:45 **ID – PSN**

Vancomycin Monitoring: Should it be Done, Why, When and How?

Salon D

Luc Bergeron, BPharm, MSc
CHUL du CHUQ, Québec City, QC

C. difficile Disease: Not Just the Runs

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

12:45 – 14:15 **Satellite Symposiums (lunch included)**

Advances in Management of VTE Prevention: Cost-Efficacy Considerations

Salon A

hosted by: Organon-Sanofi-Synthelabo

"Early Aggressive Therapy of Rheumatoid Arthritis: Capturing a Window of Opportunity

Salon B

hosted by: Amgen Canada Inc. &
Wyeth Pharmaceuticals

14:15 – 15:00 **Short and Snappies**

The "Heart Ache" of Selective COX-2 Inhibitors: Do They Increase the Risk of Myocardial Infarction?

Salon CD

Deborah Kelly, PharmD
Memorial University & Health Care
Corporation of St. John's, St. John's, NL

Rosuvastatin, New Statin on the Block

Stephanie Young, BScPharm, Pharm.D.
Health Care Corp of St John's,
St. John's, NL

A Novel Use for Atypical Antipsychotics – Nonpsychotic Unipolar Depression

Carla Dillon, BScPharm
Memorial University, NL

15:00 – 16:00 **New Antithrombotic Agents**

Salon CD

Margaret Ackman, PharmD
Capital Health Authority, Edmonton, AB

16:00 **Close of CSHP Educational Sessions**

Organized through the collaborative efforts of CSHP's National Educational Services Committee, Host Committee Task Force AGM 2003 and staff.

Sunday, August 17

Herbal Products and the Hospital Pharmacist

Tannis Jurgens, BSc(Pharm), PhD (Pharmacognosy), College of Pharmacy, Dalhousie University, Halifax NS.

A significant number of Canadians report using herbal products as a part of their health care. The ability to self select these products, their long "history of safe use" as well as the thought that "natural" drugs are safer then synthetic drugs are reasons patients give for choosing herbs. The scientific evaluation of herbs is beginning to show trends towards therapeutic value for some products. However, the current lack of consistency in product content, as well as other factors unique to herbal products, makes it difficult to reach firm conclusions as to their efficacy. The current and new regulations of herbal products in Canada will be discussed.

The use of herbal products by the inpatient population presents additional issues to the hospital pharmacist. It is essential that the pharmacist ask if a patient is taking an herbal product as well as determining if they plan to continue taking the product while in the hospital. A review of policies and approaches taken by hospitals regarding the use of herbs by their patients will be presented. Clinically important herb/drug interactions and herbs that should be avoided prior to surgery will be reviewed.

Goals and Objectives of Presentation

1. To provide pharmacists with an appreciation of issues unique to herbal products that affect our ability to determine their safety and efficacy
2. To enable pharmacists to determine when an herbal product should not be taken with a drug therapy.

Self Assessment Questions

1. What herbal products should not be taken prior to surgery?
2. What herbal products should a patient on anticoagulant therapy not take?

Response to the SARS Pandemic – The Ontario Experience

Linda Dresser BScPhm, Pharm D, Mt Sinai Hospital, Toronto, Ontario

Severe acute respiratory syndrome (SARS) is an emerging infectious disease that has disseminated globally following its appearance in China, November, 2002. As of May 30, 2003 8,317 cases of SARS including, 755 deaths have been reported to the World Health Organization. In Canada, as of June 1, 203 a total of 393 cases (198 probable, 195 suspect), including 30 deaths have been reported. The vast majority of cases reported in Canada have occurred in Toronto, and the Greater Toronto Area (GTA); 194 probable cases, 136 suspect cases as of June 1, 2003. The first awareness that there was a cluster of patients with a respiratory illness of unknown etiology in Toronto was March 13, 2003 following the death of 2 family members and the identification of respiratory illness in 5 of the remaining 8 household members. The response to this cluster and the ensuing epidemic or pandemic when considered globally has been both fascinating and frightening. I will discuss in this presentation background information regarding the known etiology, pathophysiology, and transmissibility, of the novel coronavirus responsible for SARS. I will focus on the infection control measures instituted to control the spread of the illness, and on the treatment strategies that have been explored to date or are currently under investigation. I will highlight the role of the hospital pharmacist in the development of recommendations for treatment, monitoring and reporting adverse events, research protocol design and implementation, and how all this information was disseminated and shared through utilization of the ID PSN.

Goals and Objectives

1. To provide pharmacists with a first-hand description of the SARS outbreak in Ontario.
2. To describe the infection control measures utilized to control spread of illness, and the pharmaceutical options tried to therapeutically manage the illness.
3. To describe the potential role of the pharmacist in responding to an emerging infectious disease.

Self Assessment Questions

1. What are the essential components of personal protective barriers to minimize transmission of virus?
2. Based on our knowledge to date what therapeutic strategies are reasonable?
3. List 3 ways a hospital pharmacist may be involved in directly responding to an emerging infectious disease.

Therapeutic Alternatives for Pulmonary Hypertension

Reem Haj BScPharm, St. Michael's Hospital, Toronto

Pulmonary hypertension can complicate the care of hospitalized patients especially those in the intensive care unit. The management of patients with pulmonary hypertension provides a therapeutic challenge for the health care team as patients often present with nonspecific cardiorespiratory signs and symptoms.

Systemic hypotension can limit the use of intravenous vasodilators which have traditionally been used first line. Delivery of vasodilators via nebulization have been investigated and found to have an acceptable hemodynamics but varying effects on the pulmonary artery pressures.

An ideal agent would be a selective pulmonary vasodilator. Sildenafil™ is now being investigated as a selective pulmonary vasodilator for the management of both primary and secondary pulmonary hypertension. Other novel therapies for the treatment of pulmonary hypertension include the endothelin-receptor antagonist, Bosentan.

Goals and Objectives

1. Describe the pathophysiology of pulmonary hypertension and pharmacological principles of treatment.

2. List the therapeutic alternatives for the management of pulmonary hypertension and their advantages and disadvantages.
3. Describe the potential place in therapy of newer therapeutic alternatives in the management of pulmonary hypertension.

Self-Assessment Questions

1. List two complications of pulmonary hypertension
2. List two limitations of current pharmacological options
3. Describe the characteristics of an ideal pulmonary vasodilator

Dealing with Staff Shortages

Patricia Lefebvre, B. Pharm, M.Sc, McGill University Health Centre, Montréal, Québec

The goal of this session is to share the McGill University Health Centre (MUHC) recruitment and retention strategic plan and its results from a manager's perspective.

In November 2000, five pharmacy departments merged to become the MUHC Pharmacy Department. The merger presented the opportunity to develop the MUHC mission, vision, goals and objectives of the newly created pharmacy department. The shortage of pharmacists was identified as the most significant issue facing the pharmacy department.

To be successful in the currently highly competitive environment, the MUHC had to attract highly qualified pharmacists and develop strategies to retain them.

Our first step was to conduct a pharmacist satisfaction survey and individual interviews with pharmacist. The results of the survey and the interviews were presented at the department meeting in December at which time priorities were identified.

A Recruitment and Retention Committee was created in collaboration with Human Resources Department. Their first task was to identify, by conducting focus groups, guiding principles for the management of our professional staff. The pharmacists identified 4 key principles: equity and transparency of the working conditions (current and newly recruited staff), to avoid overwork and to always put safety of our services as a priority.

Those principles guided our choices of services, our redesign of the scheduling (service hours, rotation clinical, distribution, weekend and on-call shifts) and our teaching commitment. In addition to the restructuring of our services, retention initiatives identified in the survey were implemented: organization-sponsored events such as continuing-education sessions, on-site training in a specialty area at another institution, award presentations, hand-held devices (Palm Pilot).

As for the recruitment strategies, our highly motivated group of pharmacists made the MUHC attractive. During the summer of 2002, the pharmacy department welcomed 20 pharmacy students from the Québec, 2 out of province pharmacy students and 3 out of the country pharmacists. By September 2002, Preceptors, of their own will, opened their clinical rotations 10 months/year. This summer, we are welcoming 22 students, 6 pharmacy residents and 9 pharmacists.

The impact of the measures implemented is captured, our indicators include: staff turnover, sick days/absenteeism, participation in social events, participation in recruitment events, complaints.

Goals and Objectives of Presentation

1. To assist pharmacy managers in the development of a strategic plan for recruitment and retention
2. To share the MUHC experiences in our recruitment and retention, its results and the role of our managers

Self Assessment Questions

1. Identify guiding principles of the pharmacy department taking into consideration the pharmacists and the organization needs.
2. Identify performance indicators to measure the success of the recruitment/retention initiatives.

Dealing with the Stress of Staff Shortages

Juan J. Edwards, BScPharm, Health Care Corporation of St. John's, St. John's, NL

The goal of this session is to discuss some of the stresses that pharmacists face in dealing with the problem of staff shortages and frequent staff turnover. There are many examples of how we have dealt with and continue to deal with these problems within our organization. Examples of how others have chosen to deal with these problems will also be provided.

Each year, we try to maintain staffing levels to provide the same quality of service that patients, nursing and medical staff, and other health care providers have come to expect. This is a challenge in itself. In addition to this, the role of the pharmacist is ever expanding with more demands being placed on each of us. Clinical services need to expand but are hindered due to the lack of human resources. This lack of human resources is due to both a lack of funding for new positions as well as a lack of available pharmacists to fill the positions that are available.

I hope to provide insight into this problem by choosing examples for discussion from my own experience and the experience of my co-workers within the organization, and I will expand on this by using examples from the literature. The goal is to identify strategies that reduce stress levels among staff.

Goals and Objectives of Presentation

1. To provide examples of stresses that we face in dealing with staff shortages.
2. To provide insight into this problem by discussing examples of how to deal with these stresses so that they are less damaging to the staff, with the goal of eliminating some of these stresses altogether.

Self Assessment Questions

1. What are some of the stresses that affect pharmacists working in environments where there are insufficient human resources?
2. Which stresses are we able to overcome and how?
3. How should we deal with stresses that cannot be eliminated?

Breathing Easy - COPD Management for Pharmacists

Beena Kuriakose, BScPhm, PharmD and David Millar, BScPhm.

Presented by: Christine Folia, BScPhm, PharmD.

The goal of this session is to provide pharmacists with an overview of the risk factors and symptoms of COPD. Current treatment guidelines, highlighting the place in therapy of key pharmacologic agents, will be discussed.

The morbidity and mortality associated with COPD is substantial, with the World Health Organization reporting an estimated 2.7 million COPD-related deaths in 2000. To date, no pharmacologic agents appear capable of affecting progression of the disease; however, the appropriate use of bronchodilators is important for alleviating symptoms and improving quality of life. Slowing the rate of decline of decline of lung function via smoking cessation represents the single-most important intervention for patients with COPD.

The role of inhaled corticosteroids in COPD management remains controversial. Candidates for ongoing therapy with inhaled corticosteroid include those demonstrating a significant response to a trial of inhaled corticosteroids, or those with moderate-severe disease who are experiencing repeated exacerbations necessitating treatment with oral glucocorticoids and antibiotics.

Goals and Objectives of Presentation

1. Identify patients with COPD.
2. Describe options to prevent the onset or worsening of COPD.
3. Describe the overall treatment approach to managing the patient with stable COPD.

Self-Assessment Questions

1. What pathological features distinguish chronic bronchitis from emphysema?
2. Why don't all smokers develop COPD?
3. Why are anticholinergics preferable as maintenance bronchodilators?

Is the Patient Delirious or is it his Baseline? Detecting and Managing Delirium.

Lisa D. Burry, BScPharm, PharmD, FCCP Mount Sinai Hospital, Toronto, ON

Delirium, or acute confusion, is a clinical syndrome affecting on average 1/3 of all hospitalized elderly patients. Studies have shown that patient outcomes are substantially worsened as a direct result, with higher mortality rates, longer length of stays, increased post-operative complications, and overall increased expenditures.

Despite increased awareness of this clinical syndrome, patient outcomes remain unchanged largely due to failure to recognize delirium on the part of health care providers. Reasons for under recognition include lack of routine, standardized cognitive assessment, especially when patients are critically ill and mechanically ventilated. Insufficient knowledge about delirium and methods of cognitive assessment that focus exclusively on the level of alertness and degree of orientation also contribute to misdiagnosis. In one study, health care professionals failed to recognize delirium in as many as 70-85% of their patients.

Agitation and anxiety are commonly associated with delirium and are difficult to manage. The difficulty stems from the lack of data to direct the use of various therapies. It has recently been proposed that prevention is a key factor in reducing the associated morbidity and mortality. Drugs may be the most frequent cause of delirium and, very often, they are a critical element in a multifactorial aetiology. A combined approach using pharmacologic and nonpharmacologic techniques maybe useful for the prevention and management of delirium. However, since no one regimen will achieve the desired goals for every patients, therapy must be tailored to the needs of individuals. The complexities associated with diagnosing and managing delirium requires a multidisplinary approach.

Goals and Objectives of Presentation

1. to provide pharmacists with the tools to detect or diagnosis of delirium in their patients,
2. to review the risk factors for delirium in the hospitalized/institutionalized patient,
3. to review drug therapies that typically worsen or improve symptoms, and adjunctive therapies that minimize the associated morbidity and mortality.

Self Assessment Questions

1. How is delirium different than dementia?
2. What are the key risk factors for developing dementia in a hospitalized patient?
3. List 5 behavioral interventions that may help prevent or minimize delirium?
4. What pharmacotherapeutic options are available to manage delirium?

Formularies – Cornerstone for Rational Drug Therapy or Barrier to Seamless Care?

Bob Nakagawa, BScPhm, FCSHP, Fraser Health Authority, Port Moody, BC and Thomas Paton, PharmD, Sunnybrook and Women's College HSC, Toronto, ON

Formularies have been the cornerstone of hospital pharmacy practice and one of many tools available to assist with responsible drug use. When formularies were originally conceived, they represented the drugs that were necessary to meet the therapeutic needs of patients in the hospital with the focus primarily on acute care hospital stays. At the time, most all drugs in the community were covered by the provincial pharmacare programs. In recent years, the focus has been on caring for patients in their communities. The publicly funded drug programs have implemented criteria based drug plans that restrict the drugs to those patients who could benefit the most from expensive therapies. On many occasions these do not match the hospital formularies. In these cases patients may be switched from the medications that they have received at home with uncertain consequences. Recently, hospital

pharmacy departments have adopted more open formulary practices in order to facilitate seamless transitions for their patients. The presentation will highlight the arguments for either a closed or open formulary.

Learning Objectives:

1. Identify 3 reasons for maintaining a strict formulary;
2. Identify 3 reasons for adopting an open formulary
3. Balance the arguments heard for each of the approaches and determine the best approach for application within the context of their own environment

Monday, August 18

Learning Styles

Zubin Austin BScPhm, MBA, MIS, PhD, Faculty of Pharmacy, University of Toronto, Toronto, ON

The goal of this session is to provide pharmacist-educators with new tools for providing effective feedback to students, using the theory and principles of learning styles.

This session will review principles of educational psychology and learning sciences as they apply to teaching and learning in health care environments. Models will be presented to illustrate the different ways in which individuals acquire, process, and apply information in highly context-specific ways. Critical issues related to learning and human development will be discussed to provide participants with an opportunity to understand the principles of learning styles theory.

Learning styles theory provides descriptions of four major learning types: divergers, assimilators, convergers, and accommodators. Each of these learning types typically demonstrates unique ways of receiving information, processing it, and applying it to real-life situations. By understanding these learning types, pharmacist-educators can develop responsive teaching situations and feedback opportunities to provide optimal benefit for their students.

Goals and Objectives of this Session:

1. Describe principles of educational psychology as they apply to learning styles theory.
2. Apply learning styles theory to describe education needs of students.

Self-Assessment Questions:

1. Define the term "learning styles".
2. Describe major attributes of divergers, assimilators, convergers and accommodators.
3. Identify three strategies for incorporating learning styles theory into clinical teaching of pharmacy students and residents.

Learning Styles: Teaching to Learn and Learning to Teach

Zubin Austin BScPhm, MBA, MIS, PhD, Faculty of Pharmacy, University of Toronto, Toronto, ON

The goal of this workshop is to apply learning styles theory in practice using the Pharmacists' Inventory of Learning Styles (PILS) tool.

During this session, participants will have an opportunity to complete the PILS to identify their own learning styles. Through group discussion, participants will learn about the various preferences of different learning styles and discuss approaches to optimizing teaching and learning. Working in small group, participants will have the opportunity to discuss their own experiences as teachers and as learners and will use their own examples of effective – and less-than-effective – teaching and learning moments.

By applying the principles of learning theory, and using the PILS tool for self-assessment and reflection, participants will begin a process of critical evaluation of their own strengths and challenges as teachers and learners. Through this evaluation, new opportunities for personal and professional development will emerge that will allow individuals to acquire a broader range of skills related to clinical instruction.

Goals and Objectives of this Session:

1. Identify and describe their personal learning styles.
2. Apply learning styles theory to describe and deliver effective feedback to students.

Self-Assessment Questions:

1. Describe three strategies for applying learning styles to self-assessment and reflective practice.
2. Describe three feedback strategies that are most effective for each learning style.
3. Describe three feedback strategies that are least effective for each learning style.

How to "Grow" a Self-Directed Learner

Donna M.M. Woloschuk, PharmD, Winnipeg Regional Health Authority, Winnipeg, MB

It is a tremendous challenge to precept learners. Not only do learners exhibit different learning styles, but they may also exhibit differing abilities to engage in self-directed learning. Self-directed learning requires (minimally) that learners have the self-confidence, experience, motivation, knowledge and skills to complete the required learning objectives. Most learners do not enter experiential learning rotations as fully self-directed learners. Learning style, teaching style and learning self-direction are inter-related. Unfortunately, preceptors often default to a teaching style that favors personal learning style, with little reflection about the effect that this choice will have on the evolution of learner self-direction. It is clear that some learner-preceptor style mismatches lead to anger, frustration, uncooperative behavior, or a lack of motivation to learn. Preceptors can successfully guide learners toward self-direction in experiential settings if they are prepared to modify their teaching approach within a rotation or across a series of rotations. This workshop will

introduce preceptors to Grow's Staged Self-Direction model of instruction. Participants will use the model to design learning experiences that "grow" learner self-direction within and across experiential rotations.

Learning Objectives

1. Differentiate between dependent, interested, involved and fully self-directed learners.
2. Use the self-directed learning model to plan practice-based learning experiences that encourage learner self-direction within and across rotations.

Self-Assessment Questions

1. What kind of learner-preceptor mismatch is associated with learners that respond to a preceptor with anger and/or frustration?
   a. interested learner + authoritarian/coach precepting style
   b. dependent learner + mentor/colleague precepting style
   c. involved learner + motivational precepting style
   d. self-directed learner + facilitator precepting style
2. At which point in a four week rotation is the authoritarian coach/expert precepting style most appropriately used, if self-directed learning is to be encouraged?
   a. first week
   b. second week
   c. third week
   d. fourth week
3. What kind of learner-preceptor mismatch is associated with a preceptor who views the learner as uncooperative, unprepared to learn ("personality conflict")?
   a. interested learner + facilitator precepting style
   b. involved learner + mentor/colleague precepting style
   c. dependent learner + motivational precepting style
   d. self-directed learner + authoritarian/coach precepting style

The Use of Antiepileptic Drugs in the Treatment of Pain

Tejal Patel, PharmD, Regina Qu'Appelle Health Region, Regina, Saskatchewan

The goal of this presentation is to review the similarities between epilepsy and pain and to discuss the rationale and evidence for the use of antiepileptic agents in the treatment of pain.

The mechanisms of action of antiepileptic drugs in the treatment of neuropathic pain and migraine are not completely understood. However, neuronal hyperexcitability, a characteristic of neuropathic pain, may be due to several proposed mechanisms, including upregulation of sodium channels and altered GABA-ergic inhibition. These changes have similarities with epilepsy. Migraine occurs more frequently in patients with epilepsy. Both disorders can present with auras, and focal, sensory and motor symptoms.

The first published report of the use of an antiepileptic drug in the treatment of neuropathic pain was in 1942. Since then, there have been numerous publications on the use of first and second generation anti-epileptic drugs for the treatment of trigeminal neuralgia, diabetic neuropathy, post-herpetic neuralgia, HIV associated sensory polyneuropathy and for prophylaxis of migraines. However, many of these reports are anecdotal in nature or fraught with poor study design, and conflicting results.

Carbamazepine is approved for treatment of trigeminal neuralgia, while there is evidence for the use of gabapentin in diabetic neuropathy and postherpetic neuralgia. Randomized controlled studies have established efficacy of divalproex sodium in the prophylaxis of migraines.

Goals and Objectives

1. To review the pathophysiology of epilepsy and different pain syndromes and to discuss the similarities between them.
2. To review the rationale behind the use of antiepileptic agents in the treatment of pain.
3. To review the evidence supporting the use of different antiepileptic agents in the treatment of pain syndromes such as neuropathic pain and migraines.

Self Assessment Questions

1. What clinical symptoms commonly occur in both patients with epilepsy and migraines?
2. Which antiepileptic agents have been shown to be efficacious in the management of migraines?
3. How do antiepileptic agents alleviate neuropathic pain?

The Pandemic of Preventable Drug-Related Morbidity: Our Medication Use System in Crisis

Neil J. MacKinnon, BSc(Pharm), MSc(Pharm), Ph.D., Dalhousie University College of Pharmacy, Halifax, NS

Medications have long been considered a double-edged sword. They can effectively be used to control diseases, reduce symptoms and improve health-related quality of life. At the same time, adverse consequences of medication use have been well-recognized, including adverse drug reactions and adverse drug events. Recently, patient safety efforts have focused on reporting and reducing medication errors.

Unfortunately, many of these efforts have ignored one of the main types of adverse consequences of medication use: preventable drug related morbidity (PDRM). PDRM and its origins from pharmaceutical care will be reviewed in detail. Studies that have developed quality indicators of PDRM and have reported on the incidence of PDRM in the US and UK will be discussed. Canadian research initiatives which have quantified these problems in the impatient setting in one hospital in New Brunswick and in the ambulatory setting in Nova Scotia will be reviewed. Additionally, risk factors for PDRM and the estimated cost of PDRM in Canada will be addressed.

Fortunately, many strategies do exist which can help to reduce PDRM, both at the global health plan level and at the individual patient level. These include the provision of seamless care programs, the use of quality indicators in continuous quality improvement cycles, computerized decision

support tools, neural networks and other tools and techniques. The benefits of these strategies and the costs of inaction will be reviewed.

Goals and Objectives of Presentation

1. To provide pharmacists with an understanding of the magnitude of the problem of preventable adverse consequences of medication use.
2. To enable pharmacists to improve the medication use system by discussing strategies that foster a safer and more effective medication use system.

Self Assessment Questions

1. What evidence exists to support the assertion that the medication use system is in crisis?
2. Which global strategies can be used to improve the medication use system at a health plan or health system level?
3. Which practical strategies can be used to improve the medication use system in the daily practice of a pharmacist for individual patients?

How to Address Drug-Induced Adverse Effects

Sandra Knowles, BScPhm, Sunnybrook & Women's College Health Sciences Centre, Toronto, ON

Adverse drug reactions occur in 10 to 20 percent of all patients, and can range from common side effects to rare and potentially life-threatening idiosyncratic reactions. There are many challenges in managing patients who develop a potential drug-induced adverse effect, including patient evaluation and causality assessment.

A patient with a potential adverse drug reaction should be evaluated using a systematic approach. The first step in this process is determination of a specific diagnosis with consideration given to the differential diagnosis. A thorough evaluation of the drug exposure including all over-the-counter and prescription medications is paramount in the assessment of the patient. A literature search may provide information regarding treatment, testing and possible cross-reactivity. Although confirmation of the adverse drug reaction would be helpful, diagnostic tests are only available for a few selected medications. Appropriate management of the patient, including treatment and counseling, is essential. Finally, if warranted, the adverse drug reaction should be reported to federal health officials (e.g., Health Canada) and/or the drug manufacturer.

In this case-based workshop, anticonvulsant-induced drug reactions and other adverse drug reactions, will be used to highlight this systematic approach.

Goals and Objectives

1. to outline and describe a systematic approach in the evaluation of patients with adverse drug reactions
2. to evaluate various anticonvulsant-induced drug reactions, including anticonvulsant hypersensitivity syndrome, using the systematic approach

Self Assessment Questions

1. What diagnostic tests are available in the assessment of a patient with an adverse drug reaction?
2. What information should be provided to the patient who developed an anticonvulsant-induced drug reaction?

What the COPD Guidelines Do Not Tell Us

Charles D. Bayliff, PharmD., London Health Sciences Centre, London, Ontario, Canada

The goal of this session is to enhance the pharmacist's knowledge of COPD management so that appropriate judgments and recommendations can be made to enhance outcomes for the patient with COPD. To do so, the clinical trials and the evidence from which COPD guidelines are derived will be reviewed. The areas for which the guidelines are non-existent or unclear will be highlighted. The benefits and limitations of the various therapeutic modalities including systemic and inhalational corticosteroids, beta agonists, both short acting and long acting formulations, combination products, anticholinergics, theophylline and antibiotics in patients with COPD will be reviewed. With background medical history and pertinent laboratory information, a case of an elderly patient with an acute exacerbation of COPD requiring hospital admission will be used to illustrate where the guidelines should be followed and when changes, which appear to be at odds with the guidelines, need to be made. The selection of medications, monitoring of therapy, and identification of common drug related problems, including drugs to avoid, will be highlighted. Documentation of care in the health record and education of individual patients regarding disease and drug therapy management will also be discussed.

Goals and Objectives

1. To provide a review of current drug therapy management for COPD
2. To provide the pharmacist with information on drug therapy management that can be used in practice to enhance the care of the patient with COPD.

Self-assessment Questions

1. Should long-acting bronchodilators be continued during hospitalization?
2. What information should be conveyed to patients who are being discharged home on systemic corticosteroids?

Neuropsychopharmacology: Turning science into art - Predicting Clinical Profiles of Antidepressants

Leslie Phillips, B.Sc. (Pharm), Pharm. D., Memorial University and Health Care Corporation of St. John's, St. John's, NL

The goal of this workshop is to help pharmacists develop a rational approach to selecting antidepressant therapies for individual patients.

Depression is a highly prevalent and disabling disorder. Approximately 1 in 20 Canadians are suffering from major depression at any point in time. The WHO Global Burden of

Disease Study ranked it as the 4th leading cause of disability as measured by disability-adjusted life years (DALYs) in 2000. By the year 2020, the WHO has predicted depression to be second only to ischemic heart disease as a contributor to disease burden. Depression is an illness that knows no boundaries. Regardless of where we practice or what specialty area we may choose, we will all encounter patients with this devastating disorder.

There are seven main classes of antidepressant medications currently available to treat depression, representing in excess of 2-dozen agents. With no demonstrable difference in efficacy among these agents (approximately 70% of individuals with major depressive disorder will obtain a response by 8 weeks to monotherapy with any antidepressant), the pharmacist must turn his/her attention to other considerations when individualizing therapy.

This session will review key neurotransmitter-receptor systems targeted by antidepressant therapies. Following a discussion on how these agents might interact with various receptors to produce their clinical effects, workshop participants will begin to apply this knowledge to develop a rational approach to selecting antidepressant therapy.

Goals and Objectives of the Works

1. To understand the pharmacologic profiles of antidepressants
2. To be able to predict the clinical profile of an antidepressant based on its pharmacologic profile
3. To use this knowledge as a guide to making rational decisions in the selection of antidepressant therapy for individual patients.

Self Assessment Questions

1. What are the presynaptic mechanisms via which the action of norepinephrine and serotonin can be terminated?
2. What are the clinical consequences of stimulation and/or antagonism of postsynaptic receptors in noradrenergic and serotonergic neurons?
3. For each antidepressant class:
   a. Identify which neurotransmitter system(s) is/are targeted
   b. Describe how the neurotransmitter-receptor system is affected
   c. Predict clinical profiles based on the above
   d. Develop theoretical preferred or least preferred uses based on clinical profile.

Tuesday, August 19

The Importance of Measuring Antibiotic Consumption in the Fight Against Antibiotic Resistance - Focus on ATC/DDD Methodology

Jim Hutchinson MD FRCPC Medical Director – Antibiotic Utilization Team, Healthcare Corporation of St. John's

Background: Antibiotic resistance is a growing worldwide public health problem. It is most acute in hospitals where rapidly increasing rates of resistance in many nosocomial pathogens is occurring in Canada. Driven primarily by the immediate concerns of intravenous antimicrobial costs, clinical pharmacy programs in Canada have focused on influencing the selection of antimicrobial agents and their route of administration. Little has been done to quantify overall antibiotic consumption or to determine desirable amounts.

Thesis: You must know how much is used to start to determine how much is good.

Measurement Tools: The ATC/DDD classification system is the most widely used and best tool for measuring and comparing drug consumption. Application to hospital antibiotics affords the antibiotic utilization pharmacist the ability to compare patterns of consumption between areas and over time. Benchmarking becomes feasible and graphical reports to prescribers with comparisons to benchmarks or other areas can be used educationally. As more prescribers "buy in" to the importance of population antibiotic consumption it should be easier to encourage and reinforce conservative prescribing behavior.

Practical Applications: A display of work done in Newfoundland and elsewhere demonstrating the utility, approaches to displaying information and future directions.

Objectives

1. have had at least one good laugh
2. be aware of the WHO's ATC/DDD system of drug classification and measurement and its application to antibiotics
3. be introduced to some of the practical considerations of using administrative data to create consumption statistics
4. understand the importance of population antibiotic consumption and its relationship to resistance development and sustenance
5. understand the term benchmark as it pertains to antibiotic consumption rates
6. know where to find help in applying ATC/DDD
7. run immediately back to their institution and get started!

Self-assessment question

1. What is a "reasonable" overall level of consumption of ATC DDD category J01 antibiotics on a general medical ward of your institution? (I'm not thinking of the specific answer but the ability to tackle this question rationally would be a good measure of the understanding of the concepts)

Upper Gastrointestinal Bleeding Peptic Ulcer Disease: Pharmacotherapy Issues in Acute Management and Secondary Prevention.

Peter J. Zed, B.Sc., B.Sc.(Pharm), Pharm.D., Pharmacotherapeutic Specialist – Emergency

Medicine, CSU Pharmaceutical Sciences, Vancouver General Hospital, Clinical Assistant Professor, Faculty of Pharmaceutical Sciences & Associate Member, Department of Surgery, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada

Peptic ulcer is the most common cause of acute upper gastrointestinal bleeding (GIB), accounting for up to 50% of cases. Bleeding stops spontaneously within 72 hours in up to 80% of patients; however, recurrent bleeding during this time period in patients hospitalized for bleeding peptic ulcer increases the need for surgery and the risk of death. Endoscopic treatment for high risk bleeding peptic ulcers reduces recurrent bleeding, need for surgery and death. However, despite these advances, overall mortality of acute upper GIB is approximately 10-15% and has not changed significantly over the past 4 decades.

The role of antisecretory therapy in the acute management of GIB has previously focused on the use of histamine receptor antagonists (H2RA). However, results of RCTs have confirmed that H2RA do not appear to be of any benefit in reducing recurrent bleeding, need for surgery or mortality. Most recently the focus of antisecretory therapy has shifted away from H2RA to the proton-pump inhibitors (PPI). Proton-pump inhibitors have gained widespread use as antisecretory agents for a number of gastrointestinal disorders and appear to be beneficial in a select population of patients with acute GIB secondary to peptic ulcer diseases.

The purpose of this session will be to review the current pharmacotherapy advances in the acute management of acute GIB secondary to peptic ulcer disease. In addition, secondary prevention strategies which should be considered following acute stabilization will be discussed.

Goals and Objectives:

1. To discuss the acute management of upper GI bleeding peptic ulcers with a focus on antisecretory therapy.
2. To discuss secondary prevention strategies following acute stabilization of acute GI bleeding peptic ulcers.

Self-Assessment Questions:

1. What is the role of H2-receptor antagonists and proton-pump inhibitors in the acute management of bleeding peptic ulcers.
2. What secondary prevention issues must be considered following acute stabilization of bleeding peptic ulcers?

Seamless Care

Scott Edwards, BSc(Pharm), Newfoundland Cancer Treatment and Research Foundation, St. John's, NL

Seamless Care is defined as the desirable continuity of care delivered to a patient in the health care system across the spectrum of caregivers and their environments. Pharmacy care is carried out without interruption such that when one pharmacist ceases to be responsible for the patient's care, another pharmacist or health care professional accepts responsibility for the patient's care.

The health care system of Canada's increasing effort to transfer patients from the institutional care setting back into an ambulatory setting once their acute illness is managed, but before patients are stable is leading to an increased number of drug related problems. This problem is heightened in rural Newfoundland where many patients live in remote areas, far removed from direct patient care. The Seamless Care program discussed here will emphasize the importance of a seamless care practice for Newfoundland, and emphasize by examples the impact a program like this can have on patient outcomes.

Rural pharmacists in Newfoundland are often asked to prepare chemotherapy regimens in less than ideal conditions. Newfoundland does not have an online communication link between all sites, therefore rural pharmacists are required to collect and interpret pertinent clinical data, and assume personal accountability for successful drug therapy outcomes without being provided with the background information on the patient, pertinent lab values, number of cycles of regimen already given, cumulative doses, or reason for regimen changes. The oncology seamless care program described here should help to bridge the gap between the rural hospital pharmacists and the ambulatory oncology clinic by advancing the specialized knowledge and skills of our provincial oncology pharmacy service in addition to developing enhanced safeguards against drug misadventures to further meet the drug related needs of our cancer patients.

Goals and Objectives of Presentation

1. To define Seamless Care.
2. To provide an overview of the implementation of a seamless care practice in a rural setting.
3. To discuss the transition of a seamless care practice from a rural setting to an outpatient oncology clinic.
4. To provide specific examples of patients who have benefited from our seamless care practice.

Self Assessment Questions

2. What are some of the mechanisms to overcome the barriers to practicing Seamless Care?
2. Is Seamless Care something most pharmacists can incorporate into their practice?

Vancomycin Monitoring: Should It Be Done, Why, When, And How?

Luc Bergeron, B.Pharm, M.Sc., C.H. Universitaire de Québec, Québec City, QC

At the beginning of the last decade a number of important papers have been published, revisiting the need for therapeutic drug monitoring (TDM) of vancomycin. The authors had uniformly concluded that routine TDM of vancomycin is of very, if any limited value, and recommended to monitor only trough levels in selected patients. However, many practitioners still routinely monitor peaks and troughs of vancomycin.

Moreover, new threats have emerged since then, such as vancomycin (or glycopeptide) intermediate-susceptible Staphylococcus aureus (VISA or GISA) and penicillin-resistant Streptococcus pneumoniae (PRSP). Vancomycin being a concentration-dependent killer (and a slow one, to begin with), it is of utmost importance in this context to ascertain that adequate concentrations of the drug are maintained throughout the entire dosing interval.

The evidences available indicate that vancomycin TDM should not routinely be done. However, trough levels between 5-15 µg/ml should be aimed in the following patient populations:

- Patients infected with VISA/GISA strains (trough 10-20µg/ml)
- Anephric patients undergoing hemodialysis, especially when high-flux membranes are used
- Patients with meningitis (peak levels might be useful as well, although no specific target has been proposed)
- Patients with changing renal function or with inadequate therapeutic response to vancomycin
- Morbidly obese patients
- Patients treated concomitantly with vancomycin and aminoglycosides or other known nephrotoxic drug

Goals and Objectives of Presentation

1. To review evidences regarding the usefulness and relevance of vancomycin serum concentration monitoring
2. To enable pharmacists to apply available evidence-based data on vancomycin TDM in their daily clinical practice

Self Assessment Questions

1. What is the rationale for vancomycin TDM in 2003?
2. Which patient population would benefit most from monitoring vancomycin serum concentration?

C. difficile Disease: Not Just the Runs

Alfred Gin, Pharm.D, Winnipeg Health Sciences Centre, Winnipeg, MB

Nosocomial C. difficile diarrhea is common in Canada with epidemics reported in acute care hospitals and long term care facilities. Damage to the intestinal lining is attributed to the production of toxins A and/or B. Significant morbidity and mortality have associated with C. difficile diarrhea/disease (CDAC). The cost of this disease is estimated to be $1 billion in the US annually resulting is financial burden to institutions. Examples of risk factors include exposure to antibiotics, underlying disease severity, age and colonization with C. difficile. Standard treatment approaches have included discontinuing the offending antimicrobial agent, supportive care and use of metronidazole or vancomycin. Alternative agents although not widely used in Canada have included cholestyramine, bacitracin, lactobacillus spp. and Sacchromyceses bouladii. Infection control procedures have included intensive environmental cleaning, patient cohorting or isolation, hand washing and education. Despite these treatment approaches, outbreaks as well as persistent or recurrent CDAC remains difficult to manage. This presentation will review available data pertaining to C. difficile and its management.

Objectives of Presentation

1. The pharmacist should be familiar with the etiology and pathogenesis of C. difficile disease
2. The pharmacist should be familiar with the risk factors and epidemiology of C. difficile disease
3. The pharmacist should be familiar with the current and alternative treatment modalities for managing C. difficile disease.

Self Assessment Questions

1. Is diarrhea the only presentation of C. difficile disease?
2. What diagnostic test is used at your institution?
3. What is the supportive data for alternative treatment regimens?

The "Heart Ache" of Selective COX-2 Inhibitors: Do They Increase the Risk of Myocardial Infarction?

Deborah V. Kelly, B.Sc.(Pharm), Pharm.D., Memorial University and Health Care Corporaton of St. John's, St. John's, NL

The goal of this session is to provide pharmacists with an understanding of the proposed risk of myocardial infarction (MI) associated with the use of selective COX-2 inhibitors, and to review the evidence surrounding this issue.

Recent publications have suggested that the selective COX-2 inhibitors, celecoxib and rofecoxib, may be associated with an increased risk of MI. Theoretical reasons for this increased cardiovascular risk include a possible direct prothrombotic effect of these agents, as well as via their tendency to cause high blood pressure.

To date, no study has conclusively demonstrated an increased risk of MI due to selective COX-2 inhibitor use. Nevertheless, reanalyses of clinical trials, meta-analyses, and adverse event reporting data exist, which suggest this association may be significant. These indirect data merit attention and review to help put this issue in perspective until better data become available. Questions exist regarding the limitations of existing data, and how to use this information to guide clinical decision-making.

Goals and Objectives of this Presentation

1. To discuss the theoretical reasons why selective COX-2 inhibitors may be associated with an increased risk of myocardial infarction.
2. To review the evidence regarding the association between selective COX-2 use and myocardial infarction.

Self Assessment Questions

1. What are the theoretical mechanisms by which selective COX-2 inhibitors may increase the risk of myocardial infarction?
2. Does the evidence support the hypothesis that celecoxib and rofecoxib are associated with an increased risk of myocardial infarction?
3. Should patients with cardiovascular risk factors avoid using selective COX-2 inhibitors?

Rosuvastatin: New Statin on the Block

Stephanie Young, BScPharm, Pharm.D., Health Care Corporation of St. John's

Rosuvastatin is the newest addition to the HMG-CoA reductase inhibitor family. The issues of safety and efficacy are critical to its role in the treatment of lipid abnormalities, given the availability of other drugs in the same class. Safety is a particularly important consideration, with the prior withdrawal of cerivastatin from most countries because of the risk of severe myositis.

Clinical trials have compared rosuvastatin to atorvastatin, pravastatin and simvastatin in durations of up to 52 weeks, and have examined the effects on LDL-C, HDL-C, apolipoprotein B, and triglycerides. Data from these trials will be discussed, with an emphasis on comparative efficacy of rosuvastatin versus these other agents. From a safety perspective, experience with regard to patient years treated with rosuvastatin is limited. Safety data currently available will be reviewed.

Goals and Objectives

1. To review the current efficacy profile of rosuvastatin based on clinical trial data.
2. To review the current safety profile of rosuvastatin.

Self-Assessment Questions

1. How effective is rosuvastatin for lowering LDL-C compared to the other statins currently available?
2. What is currently known of the safety profile of rosuvastatin?

A Novel Use for Atypical Antipsychotics – Nonpsychotic Unipolar Depression

Carla M. Dillon, BSc(Pharm), Memorial University of Newfoundland, St. John's, NL

The goal of this session is provide pharmacists with an overview of the literature concerning the use of atypical antipsychotics in nonpsychotic unipolar depression.

Compared to traditional antipsychotics, atypicals have unique mechanisms of action and favourable adverse effect profiles. Due to these advantages, clozapine, olanzapine, quetiapine and risperidone are being increasingly used in disorders outside of their traditional indications of schizophrenia and psychosis.

Up to 30 to 50% of depressed patients do not respond to initial treatment with antidepressants. For patients who do benefit, significant response is generally not seen until after 4 to 6 weeks of treatment with an adequate dose. In those who have a partial or no response, the antidepressant may be switched to an agent of another class, an agent may be added to boost the antidepressant response or ECT may be considered. A number of these treatment strategies may be attempted prior to finding an effective therapy. Such patients are often considered to be treatment-resistant or refractory. Due to the delayed onset of current therapies and the significant number of patients who fail initial treatment, are treatment resistant and/or relapse, there is a desire for more effective therapies with a faster onset of action.

Initial case reports of atypicals as adjunct therapy in nonpsychotic depression have shown promise. This session will review the current literature in this emerging field.

Goals and Objectives of Presentation

1. To provide pharmacists with an overview of the literature concerning atypical antipsychotics in nonpyschotic unipolar depression.
2. To inform pharmacists of the potential drug interactions and adverse effects that may be seen when atypical antipsychotics and antidepressants are used in combination.

Self Assessment Questions

1. What is the strength of the evidence for the use of atypical antipsychotics in nonpsychotic unipolar depression?
2. Which atypical antipsychotic/antidepressant combinations have been studied for this disorder?
3. What are the potential problems of combined use of atypical antipsychotics and antidepressants?

New Antithrombotic Agents

Margaret L. Ackman, BSc(Pharm), PharmD, Capital Health, Edmonton AB

The limitations of traditional anticoagulants, such as heparin and warfarin, have led to the development of agents that interact with different sections of the coagulation cascade.

Fondaparinux is a synthetic pentasaccharide that enhances the rate of Factor Xa inactivation and blocks the generation of thrombin. No monitoring is required and there is no risk of thrombocytopenia. In randomized controlled trials, it compares favourably with enoxaparin for prophylaxis of thromboembolism in various orthopedic procedures.

There are a number of direct thrombin inhibitors available. They inhibit both free thrombin and thrombin bound to fibrin. All are parenteral products and require monitoring. They are currently marketed for the treatment of heparin induced thrombocytopenia. However, there is trial evidence for these agents in acute coronary syndromes and percutaneous coronary intervention. It is apparent that this class of agents is quite heterogeneous with respect to both efficacy and bleeding risk for these indications. One of the direct thrombin inhibitors under development, ximelagatran, is orally bioavailable and is being investigated as a replacement for warfarin, as no monitoring is required.

These agents have many potential advantages over traditional anticoagulants. However, there are a number of issues concerning the combination of or comparison between these agents and the newer antiplatelet agents, clopidogrel and/or the glycoprotein IIb/IIIa receptor inhibitors.

Goals and Objectives of Presentation:

1. Discuss the advantages of the new antithrombotic agents in comparison to traditional agents.
2. Address dosage adjustment and monitoring for these new agents.

Self-Assessment Questions:

1. Should fondaparinux replace low molecular weight heparin for thromboembolic prophylaxis in orthopedic procedures?
2. Which patients undergoing percutaneous coronary intervention should be considered for bivalirudin?
3. What monitoring is required for ximelagatran?

Sunday, August 17

12:15 – 14:15 – Avalon Ballroom (Salon A)

1. Variation in Carbamazepine Serum Concentration Following Morning and Evening Administration, E.J. Bustillo Vidal, Guantanamo Children's Hospital, "Pedro A. Perez", Guantanamo Cuba
2. Analysis of Pharmacological Prescription of Antimicobials in Children with Pneumonia During 2002, E.J. Bustillo Vidal, Guantanamo Children's Hospital "Pedro A. Perez", Guantanamo Cuba
3. Pharmacoeconomic Analysis of Fondaparinux for the Prevention of Thromboembolic Events in Orthopedic Surgical Patients, Carmine Stumpo, SusanKahn, Josee Martineau, Reginald Smith, Tom Paton, Jeff Ginsberg and George Dranitsaris, The Fondaparinux Canadian Health Economic Study Group,oronto, ON
4. Readmission Rates for Lower Respiratory Tract Infections and Levofloxacin Use, B. Church, M. Wrobel and C. Stumpo Toronto East General Hospital, Toronto, ON
5. Outcomes on Pharmacy Practice after Participation in Pharmacist Certificate Programs, Karen Cameron, Sandra Winkelbauer and Kris Wichman, Drug Information and Research Centre & Ontario Pharmacists' Association, Toronto, ON
6. The Impact of Pharmacists on Adequacy of Allergy Information Upon Admission to Hospital, C. Bayliff, D. Arboin, J. Baskette and N. Badner, London Health Sciences Centre, London, ON
7. The Evolution of Experiential Learning for Canadian Forces Pharmacists, R. Vaillancourt and F. Hall, Deputy Chief of Staff Medical Policy and Standards, Canadian Forces, Ottawa ON
8. Provision of Non-Prescription Medications to Canadian Forces Members Through Civilian Pharmacies: A Pilot Project, Regis Vaillancout, Michel Trottier, Alan Gervais, Deputy Chief of Staff Medical Policy Pharmacy Policy and Standards, Canadian Forces, Ottawa, ON, Rosemin Kassam, University of British Columbia, Vancouver, BC
9. Development of a Learning Module on Chemoprophylaxis for Occupational Exposure to Blood-Borne Viruses, R. Vaillancourt and J. Ma, Canadian Forces Health Services, Directorate of Medical Policy, Pharmacy Policy & Standards, Ottawa, ON
10. Outcomes Associated with the Inclusion of Sildenafil as a Benefit Item on the Canadian Forces Drug Plan, Regis Vaillancourt, Alan Gervais and Cora Fisher, Deputy Chief of Staff, Medical Policy, PharmacyPolicies and Standards, Canadian Forces Health Services, Ottawa, ON
11. Impact of Bronchoalveolar Lavage on Antimicrobial Use in an Adult Intensive Care Unit, B. McTaggart, Hamilton Health Sciences, Hamilton, ON and J. Nagge, University Health Network, Toronto, ON
12. A Review of Linezolid Use in a Tertiary Care Hospital, B. McTaggart and K. To, Hamilton Health Sciences, Hamilton, ON
13. A Multi-Centre, Retrospective Comparison of the Nephrotoxic Effects of Amphotericin B Lipid Complex and Liposomal Amphotericin B, B. McTaggart, C. Rotstein and M. McKechnie, Departments of Pharmacy and Medicine, Hamilton Health Sciences, Hamilton, ON

VARIATION IN CARBAMAZEPINE SERUM CONCENTRATION FOLLOWING MORNING AND EVENING ADMINISTRATION

E.J.Bustillo Vidal. B.Sc. M.Sc., Department of Pharmacy, Guantánamo Children's Hospital, "Pedro A. Pérez" Guantánamo. Cuba

Background: Chronopharmacokinetic variations (Hartley et al., Clin. Pharmacokinet. 20(1991)237-44), and correlation with its side effects (Riva et al., Epilepsia 25(1984)476-81) have been reported for carbamazepine (CBZ) in children. The question whether the undesired effects of CBZ exhibit circadian variation has not been studied extensively. The aim of this study was to determine the administration-time-dependent variations in the serum concentration of (CBZ) in epileptic children with tonoclonic seizures.

Methods. Twenty-two pediatric epileptic patients (12 boys / 10 girls; Age 6.75±3.22 years; Weight- 24.4±5.0 kg) were randomly chosen from the neurological care room at the Teaching Pediatric Hospital "Pedro A. Pérez", Guantanamo City, Cuba. All patients were continuously under therapy, for at least one year, ingesting 10.85 mg/kg CBZ (Carbamazepina, 200 mg tablets, national production) twice a day (at 08:00 h and at 20:00 h). During that time they were exposed to a 14:10 L:D lighting schedule (lights on at 07:00 h). Blood samples were obtained by venous puncture, fifteen minutes before drug ingestion. Serum carbamazepine concentrations were measured by High Performance Liquid Chromatography. Hemoglobin, total leukocyte count and differential count were also assessed at these time using conventional methods.

Results. The average morning CBZ serum concentration was higher (5.6±2.5 mg/L), than that determined at 19.45 h (4.7±2.5 mg/L) ($p<0.05$, paired t-test).

Hemoglobin levels and polymorphonuclear leukocytes and eosinophils counts were also higher at 07:45 h than those measured at 19:45 h, ((119±7.7 g/L vs. 113±8.5 g/L) (0.46±0.1 vs. 0.42±0.1) and (0.06±0.03 vs. 0.05±0.03) respectively, ($p<0.05$, paired t-test). Total leukocytes and lymphocytes count were higher at 19:45 h as compared to the count at 07:45 h. (8.45±2.06 x 109 /L vs. 7.8±1.97 x 109/ L) (0.49±0.12 vs. 0.45±0.12) ($p<0.05$, paired t-test), respectively. All differences were independent of age, gender and weight (Pearson correlation).

Conclusion. We have shown a significant time-dependent variation in CBZ trough levels (12 hours after a dose). We have also observed time-dependent variation in some hematological variables. Whether these variations are related is unknown.

ANALYSIS OF PHARMACOLOGICAL PRESCRIPTION OF ANTIMICROBIALS IN CHILDREN WITH PNEUMONIA DURING 2002.

Bustillo Vidal, Emilio J. B.Sc. M.Sc., Guantánamo Children's Hospital. "Pedro A. Pérez". Service of Pharmacy. Guantanamo. Cuba.

Introduction: One of the diseases that require the use of antimicrobials for treatment and cure is pneumonia, which constitutes one of the main health problems in underdeveloped countries.

Objectives: The objective of this work is the evaluation of antimicrobials in children with pneumonia, the quality of its prescription and its influence in hospital stay.

Methods: A one-year prospective study was performed. The sample was formed by 112 randomised patients and characterized both, demographically and clinically. Most frequent antibiotic determination, their combination and added drugs for treatment, were performed by observation of indicates therapeutical schedules. For the evaluation of prescription quality, indication, dosage, interval of dosage, administration pathway, drug interaction and microbiological cultures were taken in consideration. From all this, categories were established for adequate or inadequate prescription.

Results: Major antibiotic prescription was constituted by Sodium Penicillin G (57.14%), followed by cephalosporins and antimicrobial combinations. Adequate prescriptions represented 78.58 %. Risk drug interactions were observed in 6.25 % of cases (n=7). Hospital stay was longer (8.08±5.8 days) in these patients with non-adequate prescriptions, as compared to 5.06±3.2 days in those with adequate prescriptions. (p<0..05).

Conclusion: Adequate prescriptions were predominant and main use of Sodium Penicillin G was outstanding. Lack of microbiological backup related to causal agent is nevertheless questionable. Mostly affected prescription quality indications were, administration pathway and indication. Inadequate prescriptions led to longer hospital stay, negative consequences related to drug consumption costs and patients quality of life.

PHARMACOECONOMIC ANALYSIS OF FONDAPARINUX FOR THE PREVENTION OF THROMBOEMBOLIC EVENTS IN ORTHOPEDIC SURGICAL PATIENTS

Carmine Stumpo, Susan Kahn, Josee Martineau, Reginald Smith, Tom Paton, Jeff Ginsberg and George Dranitsaris; on behalf of The Fondaparinux Canadian Health Economic Study Group

Background: Fondaparinux is a novel synthetic antithrombotic, which has been evaluated for the prevention of venous thromboembolism (VTE). In four large trials of patients who underwent major hip or knee surgery, fondaparinux was found to be safe and more effective than enoxaparin. To generate Canadian pharmacoeconomic data for fondaparinux, an internationally-developed cohort simulation model was used to estimate the costs and consequences of prophylaxis with fondaparinux compared to enoxaparin in the Canadian orthopedic surgical setting.

Methods: A health economic advisory group was assembled to guide the pharmacoeconomic evaluation. Efficacy and safety data for fondaparinux relative to enoxaparin were abstracted from a meta analysis of the four randomized trials. Canadian cost data to populate the model were obtained from a resource use survey of four large Canadian hospitals, from the Canadian Institute for Health Information (CIHI) and from the Canadian economic literature. Case-mix information obtained from CIHI was incorporated into the cohort simulation model, which predicted the number of VTEs and bleeds following prophylaxis with fondaparinux or enoxaparin within 90 days of surgery, and the associated overall cost difference. The stability of the base case findings were evaluated with sensitivity analyses.

Results: Assuming a case-mix of 50,693 major hip or knee surgeries performed in Canada in 1999/2000 (as reported by CIHI), the simulation model predicted that prophylaxis with fondaparinux would avoid an additional 16 VTEs per 1000 patients over the first 90 days, with an average cost savings of $55 per patient. These findings were stable with variations in key economic and clinical parameters.

Conclusions: Our results suggest that prophylactic fondaparinux compared to enoxaparin avoids VTEs and is associated with lower costs in Canadian patients who would undergo major hip or knee surgery.

READMISSION RATES FOR LOWER RESPIRATORY TRACT INFECTIONS AND LEVOFLOXACIN USE

Church B (BSc Pharm), CAE, Wrobel M, and Stumpo C (BSc. Phm, Pharm.D.), Toronto East General Hospital

Background: The treatment of lower respiratory tract infections (LRTIs) such as acute exacerbations of COPD and pneumonia has changed. At Toronto East General Hospital (TEGH), there has been a dramatic increase in levofloxacin use since 1997. Given the enhanced activity of levofloxacin against pathogens such as S. pneumonia and improved bioavailability over beta-lactam and macrolides, improved patient outcomes may be realized with increased levofloxacin use

Purpose: To determine the association between levofloxacin use and hospital readmission rates for the treatment of LRTIs.

Methods: Patients discharged between January 1, 1997 and December 31,2001 with a most responsible diagnosis of community acquired pneumonia (as defined by the Ontario Hospital Association) or chronic bronchitis were included. During the same time period, patients readmitted within 1 month from those discharged with a most responsible diagnosis or pre-admission diagnosis of community acquired pneumonia or chronic bronchitis were identified. Readmission rates were calculated based on these values for each calendar year. Levofloxacin usage was determined from total dollars issued per fiscal year.

Results: A total of 5382 patients were identified as LRTI admissions from Jan 1, 1997 to Dec 31,2001. A trend towards lower readmission rates was noted. The annual readmission rate dropped from 8.3% in 1997 to 5.1% in 2001. During the same time period a steady increase in levofloxacin use was noted. Levofloxacin use increased from $0 during the April 1997 –March 1998 fiscal year to $229,741 during the April 2001- March 2002 fiscal year.

Conclusion: We have seen a decrease in readmission rates for LRTI's that may be linked to an increase use of levofloxacin at our institution. A decrease in readmission rates may represent a positive, measurable indicator of treatment success.

OUTCOMES ON PHARMACY PRACTICE AFTER PARTICIPATION IN PHARMACIST CERTIFICATE PROGRAMS

Karen Cameron, B.Sc.Phm, Sandra Winkelbauer, B.Sc.Phm, and Kris Wichman, B.Sc.Phm. Drug Information and Research Centre & Ontario Pharmacists' Association, Toronto, Ontario

Rationale: A Certificate Program is a formally organized educational program that awards a certificate to those who meet its predefined requirements. Certificate programs in four therapeutic areas (Women's Health, Cardiovascular, Psychiatry and Diabetes) have been developed and implemented over the past three years. The ultimate goal is to provide the education necessary to allow pharmacists to enhance the level of care that they provide to their patients beyond the provision of medications. Although evaluation forms indicate satisfaction with the program content and delivery in meeting learning needs, the impact these programs have on the practice of program participants in unknown.

Description: The goal of this project is to gather information as to the impact of the Certificate programs on the number and types of practice changes, over the long-term, attributable to the Certificate programs.

Development and Implementation: A questionnaire was developed and distributed to approximately 500 pharmacists who participated in one or more of the Certificate Programs held over the 3 year period. Based on the written responses, follow-up by telephone was performed in a sub group that indicated a change, to further explore the impact on pharmacy practice that the educational programs provided.

Results and Evaluation: Data received over 3 months was analyzed (in progress). Preliminary feedback indicates practice change for some of the participants. Factors facilitating change are identified as well.

Importance and Impact: It is known through program evaluations, that participation in Certificate programs meets the subjective learning needs of the participants. However this study was undertaken to explore whether this educational program can have an impact on changing practice – an important consideration for educational providers. Additional benefits from the survey include the

identification of pharmacists who are providing enhanced patient care. These pharmacists can then be utilized for future presentations, considered for professional awards and serve as role models and mentors for other members of the profession.

THE IMPACT OF PHARMACISTS ON ADEQUACY OF ALLERGY INFORMATION UPON ADMISSION TO HOSPITAL

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Background: Patient care may be compromised in situations where patient information, including allergy status, is insufficient, inaccurate or absent.

Objectives: The overall objective was to determine the completeness of allergy documentation at 1 site of our facility. Specifically we wished to determine1) the proportion of orders with allergy information provided (ie NKDA or specific allergies cited); 2) the proportion of orders with incomplete allergy information(ie NKDA not checked off and no information on a specific drug(s) indicated); 3) the number of patients with single or multiple allergies as indicated on the form; and 4) the proportion of patients who received allergy augmentation or alteration according to pharmacy records.

Methods: All new patient orders containing a front allergy section were reviewed over a 2 week period for above information. Pharmacist augmented allergy documentation was assessed by reviewing 40 patients chosen at random from those with documented allergies.

Results:

# Initial Orders	489
# NKDA reported %Total	248 51%
# Allergies reported %Total	156 32%
# Incomplete allergy information %Total	85 17%
# Multiple allergies reported	51

Sixteen patients (40% of those assessed) had allergy information altered or augmented by the pharmacist.

Conclusions: Our review shows that:

1. a substantial proportion of original orders do not have required allergy documentation;
2. allergies are commonly reported by patients with approximately 1 in 3 patients reporting some allergy; and
3. pharmacists often alter allergy status information.

THE EVOLUTION OF EXPERIENTIAL LEARNING FOR CANADIAN FORCES PHARMACISTS

LCol R Vaillancourt Pharm. D., F. Hall BSc Pharm, MBA, Deputy Chief of Staff Medical Policy Pharmacy Policy and Standards, Canadian Forces, Ottawa, ON.

Canadian Forces pharmacists are faced with unique challenges related to maintenance of clinical skills. Innovative solutions are required to address the gaps identified.

The concept of maintenance of clinical skills program was initially formalized in 1997 to support operational readiness. The Canadian Forces have also downsized over recent years and moved to a new Health-Care delivery model. Pharmacy officers can no-longer experience tertiary- care services within a Canadian Forces facility and now require to complete rotations in Civilian health care facilities.

Any experiential training program designed required to address both the skills gaps identified and pertinent disease states and therapeutics. These areas were validated from a number of information sources of the Canadian Forces. It was also a priority to ensure care of Canadian Forces members both in-garrison and on deployment, comparable to that in the civilian sector.

The requirements of operational readiness served as the initial driving forces for the concept of the maintenance of clinical skills. Once in place the rotations acted as a catalyst to identify other areas of practice within the clinical skill spectrum.

This has resulted in a number of initiatives such as re-evaluation of the Canadian Forces Pharmacy Residency program, alternate rotation selection for the maintenance of clinical skills and exploration of the options for credentialing for certain disease states. All these initiatives are intended both to support operational readiness and enhance care of CF members.

The intended Outcomes of the program are:
- Increased operational readiness
- Enhanced care of CF members
- Retention of officers
- Development of expertise within the CF

PROVISION OF NON-PRESCRIPTION MEDICATIONS TO CANADIAN FORCES MEMBERS THROUGH CIVILIAN PHARMACIES: A PILOT PROJECT

Régis Vaillancourt, BPharm, PharmD. Michel Trottier, BScPhm. Alan Gervais, BSP. Deputy Chief of Staff Medical Policy Pharmacy Policy and Standards, Canadian Forces, Ottawa, ON. Rosemin Kassam, BScPharm, PharmD,University of British Columbia, Vancouver, BC.

Background: Although non-prescription (OTC) medications are approved for all Canadian Forces (CF) members, access is compromised for members without a base pharmacy. As the CF endeavors to provide equitable access to both medication and pharmacy services, an alternative method of providing OTC drugs was designed.

Description: In this pilot project, wallet cards were provided to patients to facilitate access to OTC drugs directly from community pharmacies.

Implementation: Wallet cards and information sheets were sent to eligible members, encouraging them to obtain OTC drugs from a civilian pharmacy. Wallet cards list approved OTC products and provide instructions for reimbursement of drug costs and cognitive service fees.

Evaluation: Preliminary evaluation involved assessing feasibility and member satisfaction with this alternative process. Electronic records on OTC drug claims were reviewed monthly. Members who obtained OTC medications were contacted to participate in a telephone survey.

Results: Wallet cards were issued to 583 members. By July 31 2002, 222Between 01 May and 31 October 2002, 400 transactions were identified. Of these, 142 217 were excluded (9659 lost to follow-up, 6645 prescriptions, 5435 cancelled, 2 did not consult pharmacist, and 1 declined survey). These results are based on 80 183 transactions from 12956 encounters members with the pharmacist.

Most members (8275%) were "very satisfied" with the process. However, more time was spent on technical tasks: while 734% of members spent only 1-5 minutes discussing symptoms, 6548% reported that 10 minutes or moremore than 6 minutes were spent processing the claim. Two-thirdsEighty percent of members were asked about their medical history, and 5764% were counseled to see a physician if symptoms did not resolve. Total symptom resolution was reported in 8271% of cases surveyed. Only one member required physician follow-up. Our pharmacoeconomic model proved that direct access to the pharmacist for OTCs is cost effective. Compared to a prescription-only reimbursement model, a saving of $25.91 per transaction could be realized.

Impact: Members appear to be satisfied initiating contact with pharmacists to obtain OTC medications. Allowing CF members direct access to the pharmacist for the provision of OTCs is the most cost-effective option.

DEVELOPMENT OF A LEARNING MODULE ON CHEMOPROPHYLAXIS FOR OCCUPATIONAL EXPOSURE TO BLOOD-BORNE VIRUSES

LCol R. Vaillancourt, BPharm, PharmD; J. Ma, BScPhm, PharmD. Canadian Forces Health Services, Directorate of Medical Policy, Pharmacy Policy & Standards. Ottawa, ON.

Background: In June 2001, the Center for Disease Control and Prevention (CDC) issued new guidelines for management of occupational exposures to hepatitis B, hepatitis C, and HIV. Although the new recommendations for drug therapy do not differ dramatically, more information is now provided about individual risk assessment and overall case management. A learning module is thus being developed to inform health care providers about current management strategies for post-exposure prophylaxis (PEP).

Description of the Learning Module: The module will be available in both electronic and written format. Material covered will include updated information on PEP for blood-borne viruses from new CDC guidelines, and case-based questions to stimulate and assess learning.

Development of the Learning Module: A pharmacy consultant with specialized expertise in the field of PEP identified differences between current CDC guidelines and our existing policies, and suggested relevant learning objectives. For each objective, didactic information and case-based questions were developed. The final module is organized into three separate sections, one for each of the three viruses of concern.

Evaluation: The module also includes a series of multiple-choice questions for formal evaluation of knowledge acquisition. A separate evaluation form will allow for audience feedback on structure and content of the module. The module will be submitted for formal accreditation.

Impact: This module will serve to educate pharmacists and other health care providers about CDC recommendations for management of occupational exposures to blood-borne viruses. Information in this module will also aid the revision of institutional policies regarding PEP.

OUTCOMES ASSOCIATED WITH THE INCLUSION OF SILDENAFIL AS A BENEFIT ITEM ON THE CANADIAN FORCES DRUG PLAN

L Col R Vaillancourt BPharm, Pharm D., Alan Gervais BSP., Cora Fisher MD, Deputy Chief of Staff, Medical Policy, Pharmacy Policies and Standards, Canadian Forces Health Services, Ottawa, ON

Purpose: Sildenafil was included as a special authorization item on the Canadian Forces drug plan in July 2000. Reimbursement was provided for prescriptions written by physicians with expertise in erectile dysfunction (ED), with up to 12 tablets reimbursed every 2 months. This study evaluated the impact of reimbursement criteria on usage of sildenafil.

Methods: Between July 2000 and March 2001, 163 patients were reimbursed for sildenafil prescriptions. Data was collected from patient charts to identify factors potentially associated with sildenafil use, including: patient demographics, cause of ED identified by general practitioner (GP) and ED specialist, number of physician visits, and length of time for specialist referral.

Results: There was poor correlation between ED etiology attributed by specialists and by GPs. However, sildenafil was equally likely to be prescribed, regardless of ED etiology. Between 3.3 - 7.5 weeks elapsed between referral and actual visit to the ED specialist. In patients with chronic illness, visits to physicians declined after sildenafil was prescribed.

Conclusion: The CF no longer requires patients to see a specialist to be reimbursed for sildenafil. However, patients with unknown ED etiology will continue to be referred to specialists for further investigations. The quantity limit remains unchanged.

IMPACT OF BRONCHOALVEOLAR LAVAGE ON ANTIMICROBIAL USE IN AN ADULT INTENSIVE CARE UNIT

B. McTaggart BSc Phm, Hamilton Health Sciences, Hamilton, Ont.; J. Nagge BSc Phm, University Health Network, Toronto, Ont.

Rationale: Pneumonia in the ICU setting poses serious diagnostic challenges. Invasive diagnostic techniques including bronchoalveolar lavage (BAL) have been developed in an attempt to improve the sensitivity and specificity of diagnosis. Clinical trials evaluating the impact of BAL in hospitalized patients with pneumonia have produced discordant conclusions. Consequently, we decided to evaluate the impact of BAL on the antimicrobial management of patients in our adult ICU.

Objectives: To describe the impact of BAL results on the use of antimicrobials in the ICU. To identify the characteristics of patients undergoing BAL in our ICU.

Methods: Retrospective chart review of ICU pts >18 yrs of age who underwent BAL from Jan 1999 to Apr 2000.

Results: Fifty-four BALs were performed in 40 patients. Sixty-three potential pathogens were isolated from 43 BALs (35 bacteria, 23 fungi, 5 viruses). The most frequently identified organisms were C. albicans (13 pts), MRSA (8 pts), and S. maltophilia (5 pts). The majority (81%) of patients were receiving antibiotics at the time of the procedure. Overall antibiotic regimens were modified as a direct result of the BAL in 10 patients (25%). In patients with pathogens identified, changes in antimicrobial therapy directly attributable to the BAL occurred in 9 cases (12 additional agents, 4 agents discontinued). For patients with negative BALs streamlining of antimicrobials occurred in a single patient.

Conclusions: The use of BAL was associated with a modest impact on the use of antimicrobial agents in this cohort of adult ICU patients. Additional work is required to identify how to maximize the benefits of BAL in this patient population.

A REVIEW OF LINEZOLID USE IN A TERTIARY CARE HOSPITAL

B. McTaggart BScPharm and K. To BScPharm, Hamilton Health Sciences, Hamilton, Ontario

Rationale: The emergence of resistant gram positive bacteria is a growing concern worldwide that calls for the judicious use of antibiotics. A review of linezolid use in a large tertiary care hospital was performed due its rate of usage, high cost, and the potential for misuse.

Objectives: To describe the pattern of linezolid use. To evaluate linezolid use for compliance with proposed hospital guidelines.

Methods: A retrospective chart review was performed for all inpatients treated with linezolid from January 1 to December 31, 2002. Compliance was assessed against proposed hospital guidelines developed by the infectious diseases (ID) pharmacist in collaboration with ID physicians.

Results: A total of 58 courses of therapy in 54 patients were evaluated. The total acquisition cost of linezolid was $97,506 for the study period. The ID service was consulted for 51 (87.9%) of the 58 courses. Linezolid was prescribed for empiric therapy in 17 courses, specific therapy in 40 courses, and surgical prophylaxis in 1 course. Of the 40 specific courses, 15 cultured MRSA, 13 cultured coagulase negative Staphylococcus spp., 9 cultured Enterococcus spp. (none VRE). Sixteen courses (27.6%) were in compliance with the proposed guidelines. Of the 16 appropriate courses, 13 courses were prescribed for intolerance or salvage to vancomycin therapy. Inappropriate use was associated with $64,862 in linezolid drug costs.

Conclusions: A significant proportion of linezolid use should have been discouraged. The pharmacy department will continue to work collaboratively with the Pharmacy and Therapeutics Committee and ID physicians to improve linezolid use.

A MULTI-CENTRE, RETROSPECTIVE COMPARISON OF THE NEPHROTOXIC EFFECTS OF AMPHOTERICIN B LIPID COMPLEX AND LIPOSOMAL AMPHOTERICIN B.

B. McTaggart BSc Phm, C. Rotstein MD, M. McKechnie BSc Phm, Departments of Pharmacy and Medicine, Hamilton Health Sciences, Hamilton, Ontario.

Rationale: The two lipid formulations of amphotericin B available in Canada, amphotericin B lipid complex (ABLC, Abelcet®) and liposomal amphotericin B (L-AmB, Ambisome®) have been shown to be associated with less nephrotoxicity in comparison to amphotericin B deoxycholate. It is unclear as to whether there are differences in the renal sparing effects of the two lipid formulations.

Objective: To compare the nephrotoxic effects of ABLC and L-AmB when used in routine practice.

Methods: A retrospective and concurrent study at 12 tertiary care and one community hospital. Patients 2 years of age or older, receiving a minimum of 4 doses of ABLC or L-AmB and not receiving dialysis were enrolled with subsequent data collected.

Results: One hundred and fifty patients were prescribed ABLC and 104 patients received L-AmB. The mean net change from baseline to peak serum creatinine was 47 umol/L for patients treated with ABLC and 43.5umol/L for patients treated with L-AmB ($p>0.05$). An increase of at least 50% in serum creatinine was experienced by 45 (30%) of ABLC treated patients and 31(29.8%) of patients in the L-AmB arm; 20 (13.3%) of ABLC and 14 (13.5%) of L-AmB patients had a doubling in creatinine and 3 (2%) of ABLC and 4 (3.8%) of L-AmB patients had a tripling of baseline serum creatinine ($p>0.05$). Four (2.7%) ABLC patients and 7 (6.7%) L-AmB patients required dialysis ($p>0.05$).

Conclusion: We were unable to demonstrate any significant differences in nephrotoxicity rates between ABLC and L-AmB when used according to current clinical practices.

Monday, August 18

12:30 – 14:30 – Avalon Ballroom (Salon A)

1. Metoclopramide Toxicity, MaryBeth Blokker, St Joseph's Health Care London, London, ON
2. Evaluation of Physician Adherence to a Chemotherapy-Induced Febrile Neutropenia Treatment Algorithm, Christine Howe, Linda Dresser and Allison McGeer, Mount Sinai Hospital, Toronto, ON
3. Development of an Institutional Perioperative Anticoagulation Management Guideline, Chris Fan-Lun, Lisa Burry, Cristina Zanchetta, Yun Wong, Ioanna Tzianetas, Yasmin Rajmohamed, May Musing, Holly Leung, Stacie Harley and Pavan Gill, Mount Sinai Hospital, Toronto, ON
4. Meropenem-Induced Hepatic Injury, Toni Bailie and Jenny Chiu, Mount Sinai Hospital, Toronto, ON
5. Measuring Antibiotic Activity in the Treatment of Peritoneal Dialysis-Related Peritonitis, Sheryl Zelenitsky, Christine Strijack and Robert Ariano, Faculty of Pharmacy, University of Manitoba and St. Boniface General Hospital, Winnipeg, MB
6. Expression of Antibiotic Utilization Data and it's Utility in a Newfoundland Hospital, Kristi Parmiter and Andrea Woodland, Health Care Corporation of St. John's, J.M. Hutchinson, Memorial University of Newfoundland, St. John's, NL
7. Developing Prescribing Indicators Using the Who AT/DDD System, Donna Wheeler-Usher, Pharmacy Consultant, Sarah Maaten, Dalhousie University Faculty of Medicine, Department of Community Health and Epidemiology and Ingrid Sketris, Dalhousie University College of Pharmacy, Halifax, NS
8. The Development of Perioperative Medication Guidelines for the Pre-Admission Unit, May Musing, Liz, Mahon, Lisa Burry, Chris Fan-Lum, Pavin Gill, Stacie Harley, Holly Leung, Yasmin Rajmohamed, Ioanna Tzianetas, Yun Wong and Cristina Zanchetta, Mount Sinai Hospital, Toronto, ON
9. Treatment of Ectopic Pregnancy Using Pre-Filled Syringes of Methotrexate Significantly Reduces Length of Stay in the Emergency Department and Results in Overall Costs Savings, Michael Ritchie and Frank Brommecker, Sunnybrook and Women's College Health Sciences Centre-Women College Campus, Toronto, ON
10. Implementation of the Canadian Forces Drug Exception Centre, Regis Vaillancour and Alan Gervais, Deputy Chief of Staff Medical Policy, Pharmacy Policies and Standards, Canadian Forces Health Services, Ottawa, ON
11. Provision of Non-Prescription Medications to Canadian Forces Members without Access to a Base Pharmacy: a Pharmacoeconomic Analysis, Regis Vaillancourt, Michel Trottier, Alan Gervais, Deputy Chief of Staff Medical Policy Pharmacy Policy and Standards, Canadian Forces, Ottawa, ON, Rosemin Kassam, University of British Columbia, Vancouver, BC
12. Provision of Non-Prescription Medications by Pharmacists in The Canadian Armed Forces, Regis Vaillancourt, Michel Trottier, Alan Gervais and Melanie St-Hilaire, Deputy Chief of Staff Medical Policy Pharmacy Policy and Standards, Canadian Forces, Ottawa, ON
13. Pre-Testing of Pictograms used in Medicines Dispensed in Missions of Humanitarian Relief, Regis Vaillancourt, Kath Ryan, Gordon Becket and Sulakshi de Silva

METOCLOPRAMIDE TOXICITY

MaryBeth Blokker, BSc. Phm, St. Joseph's Health Care London, London, Ontario

Rationale: The prokinetic agent metoclopramide is sometimes added to narcotic infusions to treat nausea in terminally ill patients. Metoclopramide toxicity occurs if its concentration is not reduced as the infusion rate increases.

Case Presentations: A 54-year-old man with lung cancer and a 53-year-old man with pancreatic cancer were admitted to the Palliative Care Unit in the summer of 2002. Both patients had initially been treated with long acting oral narcotics. Both were switched to continuous subcutaneous hydromorphone infusions for increasing pain. Metoclopramide was added to control nausea. Their symptoms worsened. Infusion rates were increased without adjusting the metoclopramide concentration. On admission, the second patient was receiving more than 100mg of metoclopramide daily. Both had severe myoclonus and constant pain. Hydromorphone infusions without metoclopramide were started. No additional medications were prescribed for myoclonus. Their symptoms subsided over 3 days. Pain was well controlled. The first patient was discharged home.

Both patients developed signs and symptoms of metoclopramide toxicity when they received excessive amounts of metoclopramide.

Analysis: Care providers for terminally ill patients often respond to signs and symptoms of pain and agitation by increasing analgesics. Reversible causes for symptoms are sometimes overlooked. As pharmacists, we must anticipate, identify and help resolve this type of drug related problem.

Importance of Case to Pharmacists: Pharmacists have a key role in anticipating and preventing this type of error. Pharmacists should be aware of the potential for metoclopramide toxicity when it is added to a narcotic infusion and take steps to prevent it.

EVALUATION OF PHYSICIAN ADHERENCE TO A CHEMOTHERAPY-INDUCED FEBRILE NEUTROPENIA TREATMENT ALGORITHM

Howe, Christine BSc Phm, Dresser, Linda Pharm D, McGeer Allison MD, Mt Sinai Hospital, Toronto Ontario

At our institution, a 2001 retrospective review found intravenous cefazolin plus intravenous tobramycin (CT) to be an appropriate empiric regimen for the majority of our chemotherapy-induced febrile neutropenia (CIFN) patients. CT was subsequently incorporated into an algorithm that required validation. We assessed physician adherence with the algorithm and patient outcomes.

Adults with a discharge diagnosis of CIFN between 8/01 and 8/02 were retrospectively identified. The first 51 patients meeting inclusion criteria were reviewed. Exclusion criteria included failure to meet diagnostic criteria (ANC < 0.5x109/L and a single oral temperature ≥ 38.3∞C or ≥ 38.0∞C for ≥1 hour) and transfer from another institution.

Prescribing was in accordance with the algorithm in 73% of cases and 75% of patients had successful outcomes. Failure rates (defined as lack of antimicrobial coverage, persistent fever or death) may have been overestimated due to possible contaminant-positive cultures and co-infection with organisms not sensitive to CT for which clinically significant infection would have been identified on exam and thus covered according to the algorithm's recommendations.

Cultures were positive for 22 patients (12 gram-negative, 8 gram-positive, 1 viral, 1 anaerobe) –12 were bacteremias. Gram-positive organisms included CNST (4 cases – 1 sensitive to cefazolin and 3 likely contaminants), Enterococci (3 patients), Viridans Group Streptococci and Staphylococcus aureus (2 patients each). Gram-negative organisms included Escherichia coli (3 patients) and Pseudomonas aeruginosa (2 patients).

In conclusion, physicians adhere to the algorithm and patients continue to have successful outcomes when managed according to its recommendations. Thus, we continue to endorse its use.

DEVLOPMENT OF AN INSTITUTIONAL PERIOPERATIVE ANTICOAGULATION MANAGEMENT GUIDELINE

Chris Fan-Lun, BScPhm; Lisa Burry, BScPharm, PharmD; Cristina Zanchetta, BScPhm; Yun Wong, BScPhm, Ioanna Tzianetas, BScPhm; Yasmin Rajmohamed, BScPhm, MSc; May Musing, BScPhm; Holly Leung, BPharm; Stacie Harley, BScPhm; Pavan Gill, BScPharm, Mount Sinai Hospital, Toronto, ON.

Optimizing thromboprophylaxis regimens in the perioperative setting requires identifying and assessing both surgical and patient-specific risk factors for venous thromboembolism (VTE). In addition, the risks of interrupting anticoagulation must be considered in the management of patients already receiving warfarin. When pharmacists at our hospital began seeing patients in the Pre-Admission Unit (PAU), we noted a lack of consistency for anticoagulation assessment and prescribing at our institution. The purpose of this project was to develop a perioperative anticoagulation management guideline for our institution.

A comprehensive literature search for anticoagulation in the perioperative setting was conducted using MEDLINE, EMBASE and the Cochrane Database (1966 – 2003). Based upon the best available evidence, anticoagulation guidelines and a prescribing tool were developed. Feedback was incorporated from Anaesthesia, Surgery, and Medicine (Internal and Hematology). The draft was revised and submitted to the Pharmacy & Therapeutics Committee for approval.

The guideline consists of a tool to stratify patients according to risk, suggestions for patients on anticoagulation prior to their procedure, as well as thromboprophylaxis regimens for anticoagulant-naïve patients. The guideline will be utilized not only in the PAU but also throughout the institution. We anticipate greater consistency in screening, prescribing, and information provision to our patients.

The next phase of the study is twofold: 1) implementation of the guideline; and 2) assessing patient outcomes and validating the guideline for efficacy and safety after implementation.

MEROPENEM-INDUCED HEPATIC INJURY

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Meropenem has a reported incidence of increased hepatic enzymes of 1.5-4.3%. A Med-line search revealed no reported cases of acute hepatic injury.

Our patient was a 56 y.o.year-old man who, after workup for his admitting symptoms, was diagnosed with plasmacytoid non-Hodgkin's lymphoma. He developed numerous complications including seizures and infections with multi-drug resistant hospital-acquired pneumonia (HAP).organisms On day 90 of admission, phenytoin was started for the seizures. On day 92, ciprofloxacin was changed to meropenem for his HAP.He was started on phenytoin for his seizures. Two days later his antibiotic coverage for HAP was changed to meropenem. On day 95, liver function tests were significantly elevated and he was clinically jaundiced. CT of the abdomen ruled out any structural abnormality. Phenytoin and meropenem were held on day 97 and amikacin was started. GGT, ALP, total bilirubin peaked at 34, 16 and 11 times normal respectively. , Lliver function began to resolve and, 2 days later phenytoin was restarted on day 99. Liver parameters continued to improve despite verified therapeutic levels of phenytoin. The patient succumbed on day 112.

Meropenem and phenytoin, temporally, were both implicated for the acute liver toxicity. However, the patient did not exhibit the typical pattern for phenytoin-induced hepatotoxicity (e.g. no rash or fever, only cholestasis and negative rechallenge). GGT, ALP and bilirubin all

promptly resolved upon withdrawal of meropenem. Meropenem-induced acute hepatic injury was considered to be probable according to the Naranjo probability scale.

The authors believe this to be the first reported case of meropenem-induced acute hepatic injury. Evaluation of each suspected agent by the pharmacist identified the most probable offending agent. Early recognition of probable toxicity may have prevented irreversible damage.

MEASURING ANTIBIOTIC ACTIVITY IN THE TREATMENT OF PERITONEAL DIALYSIS-RELATED PERITONITIS

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Rationale: Peritonitis is a common and potentially serious infection in patients undergoing peritoneal dialysis (PD). It is most commonly treated with intra-peritoneally administered antibiotics which significantly affects antibacterial activity in vivo. Our goal was to measure and compare antibacterial effects in dialysate using peritoneal fluid titres.

Methods: Spent dialysate from six patients with microbiologically confirmed peritonitis were processed and analyzed biochemically. Dialysate was spiked with antibiotic to simulate intra-peritoneal concentrations achieved with standard regimens of cefazolin plus tobramycin (empiric) and cefazolin alone (targeted). Four clinically relevant bacterial peritoneal pathogens including Staphylococcus epidermidis, Staphylococcus aureus, Escherichia coli and Enterobacter cloacae were tested. Dialysate was serially diluted, inoculated with bacteria and incubated for 24 h. The inhibitory titre was the highest dilution that was visually clear of bacterial growth. Test reproducibility was measured and dialysate-related effects were assessed. Titres for cefazolin plus tobramycin and cefazolin alone were compared.

Results: Titres were reproducible with an accuracy >95% within one dilution. Titre results were moderately influenced by different dialysate. There were characteristic bacteria-related ranges which were highest for S.aureus (median 1/128, interquartile range 1/80 - 1/128) and lowest for E.cloacae (1/32, 1/20 - 1/32). Titres were significantly higher for the combination compared to cefazolin alone against the Gram negative bacteria.

Conclusion: Pertioneal titres offer significant potential as a measure of overall antibacterial activity in the dialysate of patients being treated for PD-related peritonitis. These results warrant further investigation of this test as an index of antibacterial activity in the clinical setting.

EXPRESSION OF ANTIBIOTIC UTILIZATION DATA AND ITS UTILITY IN A NEWFOUNDLAND HOSPITAL

Kristi Parmiter, B.Sc.(Pharm); Andrea Woodland, B.Sc.(Pharm), Health Care Corporation of St. John's; J.M.Hutchinson, M.D., F.R.C.P.C., Memorial University of Newfoundland, St. John's, NL

Rationale: A clinical-pharmacy based Antibiotic Utilization Team is in place at our institution and staffing shortages have resulted in interruptions in service. A method of expressing antibiotic use to illustrate the impact of the team is an objective. The WHO Anatomical Therapeutic Chemical (ATC) classification system and Defined Daily Dose (DDD) were the desired means of expression.

Description: The hospital computer system is incapable of expressing drug utilization in DDD. The pharmacy information is downloaded into a database. It is then converted to express antibiotic use in DDD and cost per 100 bed days.

Development and Implementation: The data is then compiled to provide total antibiotic consumption for the institution or by hospital service. It can be expressed by drug class, individual drug or dosage form. Data from other hospitals has been added to the database and allows comparison across the province.

Results: From January 2000 to March 2003 total ciprofloxacin use on a urology ward was expressed in DDD and cost per 100 bed days. This was then stratified into IV and oral. There has been a trend toward increased consumption over this time frame which may correspond to an interruption in clinical service.

Importance and Future: The development of this database provides a method to measure and compare antibiotic utilization in our institution and across the province. This information will be used to evaluate clinical pharmacy impact and to identify future areas for intervention.

DEVELOPING PRESCRIBING INDICATORS USING THE WHO ATC/DDD SYSTEM

Donna Wheeler-Usher, M.Sc. Pharm, Pharmacy Consultant, Sarah Maaten, B.Sc., Dalhousie University Faculty of Medicine, Department of Community Health and Epidemiology, Ingrid Sketris, PharmD MPA(HSA), Dalhousie University College of Pharmacy, Halifax, Nova Scotia

Rational of Study: A number of health institutions in Canada are incorporating hospital information systems for data management. These systems provide significant opportunities for health practitioners to extract valuable information regarding patient diagnosis and drugs used during the delivery of patient care. The province of Nova Scotia is implementing a hospital information system vended by MEDITECH in 34 community and regional hospitals.

Objective of Study: In order to determine the usefulness of the information system in pharmacy practice a study was designed to determine if prescribing indicators could be developed utilizing the data extracted from the system.

Methods: This study was conducted at the IWK Grace Hospital a 308 bed hospital in Halifax, Nova Scotia following research and ethics approval. All pharmacy records for patients receiving ciprofloxacin were reviewed between the years 1997-2002. Data fields reviewed were patient age, dosage, route of administration, duration, frequency and clinical indication. The WHO Anatomical Therapeutic Classification/Defined Daily Dose (ATC/DDD) system was applied to calculate the DDDs/100 Occupied Bed Days, average DDDs/Patient, and IV/Total drug ratio for the pediatric and women's populations in a tertiary pediatric-women's healthcare facility.

Results: The DDDs/100 Occupied Bed Days were calculated for the 5 year time period. The total Women DDDs/ 100 Occupied Bed Days increased from 0.9 in 1997/8 to 2.2 in 2001/2. The total Pediatric DDDs/ 100 Occupied Bed Days increased from 0.41 in 1997/8 to 0.87 in 2001/2. The mean formulation ratio of IV/Total in the pediatric population was 0.08 in 1997/8 and 0.2 in 2001/2. Forty-five percent of the Total DDDs had no indication specified in the system.

Conclusions: The WHO ATC/DDD System can be applied to hospital information data to provide prescribing indicators for specific drug therapy. Drug utilization trends and the impact of pharmacy interventions can be monitored utilizing this methodology. This information must be combined with information on patient outcomes to provide a measure of performance within a system.

THE DEVELOPMENT OF PERIOPERATIVE MEDICATION GUIDELINES FOR THE PRE-ADMISSION UNIT

May Musing, BScPhm; Lt Liz McMahon, BScPharm; Lisa Burry, PharmD, FCCP; Chris Fan-Lun, BScPhm; Pavin Gill, BScPharm; Stacie Harley, BScPhm; Holly Leung, BPharm; Yasmin Rajmohamed, BScPhm, MSc; Ioanna Tzianetas, BScPhm; Yun Wong, BSNRN, BScPhm; Cristina Zanchetta, BScPhm, Mount Sinai Hospital, Toronto, ON.

Pharmacists at our institution have recently joined the multidisciplinary Pre-Admission Unit (PAU) team. It was found that a lack of consensus existed in the literature and amongst health care professionals on the time for perioperative medication discontinuation. As well other medications must be replaced or transiently administered by another route during the perioperative period. Consequently information passed onto patients was often confusing and inconsistent.

The purpose of this project was to develop standards to be used by the team in the PAU. On a rotational basis, 7 pharmacist, 7 nurses and 3 physician specialties interview patients within the PAU. These standards would: 1) identify medications that should be stopped preoperatively; 2) standardize the time of discontinuation prior to surgery and their re-institution postoperatively.

MEDLINE, EMBASE and the Cochrane Database (1966 – February 2003) were used to conduct a literature search for each class of drug and their safety during the perioperative period. After reviewing the literature, guidelines were standardized and tabulated. The table was categorized alphabetically by drug class. Information contained on the table include time for preoperative discontinuation, pharmaceutical effects, recommendations for drug levels, monitoring parameters, alternate routes of administration and time for postoperative re-institution. The table was reviewed by the department of Anesthesia, Surgery and Medicine and then submitted to the Pharmacy & Therapeutic Committee for approval. Once reviewed, the table will be used 1) by the multidisciplinary team in the PAU for screening preoperative medications 2) by the Surgery and Intensive Care Units to re-institute medications postoperatively. Standardization of information will help health care professionals give clear consistent instructions thus eliminate ambiguity and benefit patient compliance and outcomes.

Submitting author's name: May Musing

TREATMENT OF ECTOPIC PREGNANCY USING PRE-FILLED SYRINGES OF METHOTREXATE SIGNIFICANTLY REDUCES LENGTH OF STAY IN THE EMERGENCY DEPARTMENT AND RESULTS IN OVERALL COST SAVINGS

Michael Ritchie B.Sc.Phm., Frank Brommecker B.Sc.Phm., Sunnybrook and Women's College Health Sciences Centre - Women College Campus, Toronto

Methotrexate, a folic acid antagonist, is commonly used intramuscularly to treat ectopic pregnancy in selected patients. These patients are seen in the emergency department (ER) where the diagnosis and decision to treat medically may not occur within the usual hours of pharmacy operation. In the past, this has meant calling back a pharmacist to prepare the dose. Unfortunately, this is an inefficient and expensive method of providing a single dose of medication. In 2002, 36 patients treated in the ER waited an average of 4.94(±2.49) hours. Call back premiums for pharmacists totaled $4532.37.

A procedure utilizing pre-filled methotrexate syringes was instituted for 2003 to see if waiting times and ER length of stay could be reduced and call back premiums reduced by eliminating the need for Pharmacy staff to prepare doses on demand during the day or after hours via call back.

A sealed kit containing a selection of pre-filled syringes of methotrexate was created and placed in the ER refrigerator where it would be immediately available. Physicians are instructed to round the 50mg/m2 dose to the nearest 5mg. The usual precautions for handling and disposal of chemotherapy agents are followed.

To date in 2003, 11 patients treated in the ER waited an average of 3.94(±1.32) hours. Cost avoidance of call back premiums for pharmacists to date total $1866.27.

This procedural change has resulted in decreased lengths of stay for patients and reduced pharmacy premium costs and could easily be adopted by other institutions that treat such patients.

IMPLEMENTATION OF THE CANADIAN FORCES DRUG EXCEPTION CENTRE

LCol Régis Vaillancourt, BPharm, Pharm.D., Alan Gervais BSP Deputy Chief of Staff Medical Policy, Pharmacy Policies and Standards, Canadian Forces Health Services, Ottawa, ON

Rationale: The Canadian Forces (CF) no longer provides 24-hour pharmacy services on military bases; this has resulted in increased dependence on non-military health care providers. The Canadian Forces Drug Exception Centre was developed to enable consistent provision of care through both military and non-military sites.

Description: This program aims to achieve good patient outcomes. Clinical literature, published in peer-reviewed journals, forms the basis for assessment of drugs for coverage by the drug benefit provider. Following literature review, recommendations for drug use are made by the Federal Pharmacy and Therapeutics Committee (P&T), an advisory body of medical professionals providing impartial and practical advice to federally funded departments. The CF P&T then weighs these recommendations against the established Spectrum of Care and operational requirements for drug use. All requests for drugs which are not listed as CF benefit items are reviewed individually by a clinical pharmacist, using an evidence-based medicine (EBM) approach.

Results: Patient care is optimized through the application of EBM. Drug utilization evaluations completed to date have confirmed good adherence to clinical practice guidelines. This has resulted in overall reductions in drug expenditures for the CF, in contrast to the increase in drug costs observed by other private and government agencies.

Importance: Under this program, approximately 60,000 members of the CF receive equitable drug benefits through military and civilian pharmacies across Canada.

PROVISION OF NON-PRESCRIPTION MEDICATIONS TO CANADIAN FORCES MEMBERS WITHOUT ACCESS TO A BASE PHARMACY: A PHARMACOECONOMIC ANALYSIS

LCol Régis Vaillancourt, BPharm, PharmD. Michel Trottier, BScPhm. Alan Gervais, BSP. Deputy Chief of Staff Medical Policy Pharmacy Policy and Standards, Canadian Forces, Ottawa, ON. Rosemin Kassam, BScPharm, PharmD,University of British Columbia, Vancouver, BC.

Background: Although some non-prescription (OTC) medications are approved for all Canadian Forces (CF) members, access is compromised for members without access to a base pharmacy. As the CF endeavors to provide equitable access to both medication and pharmacy services, an alternative method of providing OTC medications from community pharmacies was designed and evaluated in a pilot project.

Description: A pharmacoeconomic analysis of three different options of providing OTC medication to CF members from Canadian Forces Health Services (direct costs) and from the CF (indirect costs) perspective

Evaluation: Three options were incorporated into the pharmacoeconomic model: 1) members consult a community pharmacist for all OTC medication needs; 2) If all CF members consult a physician for all OTC medication needs; 3) members obtain a prescription and present to a community pharmacy (status quo).

Results: Direct costs of providing all OTC medications to members directly from a community pharmacist were $17.95 while indirect costs were $13.48 for a total of $31.43 per transaction. Direct costs of providing all OTC medications in consultation with a physician were $46.10 while indirect costs were $55.69, for a total of $101.79 per

transaction. The current costs of providing OTC medications to members (status quo) totals $57.34 per transaction (direct costs = $23.69, indirect costs = $33.65). Compared to the status quo, the option of providing OTC medications to members directly from a pharmacist could result in a savings of $25.91 per transaction.

Impact: Allowing CF members direct access to the community pharmacist for the provision of OTC medications is the most cost-effective option. Members are very satisfied initiating contact with a pharmacist to obtain OTC medications.

PROVISION OF NON-PRESCRIPTION MEDICATIONS BY PHARMACISTS IN THE CANADIAN ARMED FORCES

Régis Vaillancourt, BPharm, PharmD. Michel Trottier, BScPhm. Alan Gervais, BSP. Mélanie St-Hilaire, BPharm. Deputy Chief of Staff Medical Policy Pharmacy Policy and Standards, Canadian Forces, Ottawa, ON.

Background: In consultation with a base pharmacist, non-prescription, over-the-counter (OTC) medications are made available to Canadian Forces (CF) members.

Description: Treatment outcomes and patient satisfaction with pharmacist interventions were assessed.

Implementation: Members consulted with the base pharmacist for the treatment of minor ailments. OTC medication recommendations were documented on the member's electronic profile. Electronic records of recommendations were tabulated to identify members. These members were contacted to participate in a telephone survey.

Evaluation: Evaluation involved documenting health outcomes and assessing member satisfaction resulting from pharmacist consultations.

Results: One hundred and sixty members, accessing 203 OTC medications, were included in the analysis. Most members (88%) were "very satisfied" with the process. The majority of interactions (82%) were perceived to be 1 to 3 minutes duration. Practically all members (98%) interacted with the pharmacist, 69% recalled being asked about relevant medical history, and 39% reported being counseled to see a physician if symptoms did not resolve. About half of members (48%) likely would have consulted a physician to obtain a prescription to treat their ailment. Overall, symptoms completely resolved in 82% of cases. Most recommendations were for analgesics (32%), antihistamines (29%) and cough and cold preparations (20%). Complete symptom control was reported in 91%, 69% and 80% of cases, respectively.

Impact: Members are satisfied initiating contact with pharmacists to treat minor ailments with OTC medications. As reported by members, interventions by pharmacists successfully treated the majority of their ailments.

PRE-TESTING OF PICTOGRAMS USED IN MEDICINES DISPENSED IN MISSIONS OF HUMANITARIAN RELIEF

LCol Régis Vaillancourt, BPharm, Pharm D; Kath Ryan PhD; Gordon Becket, Sulakshi de Silva

Rationale: The Canadian Forces Disaster Assistance Response Team (DART) provides health services during humanitarian relief missions. The recipients of health care during these deployments often do not speak English, French, or Spanish; many are also illiterate. This presents serious problems for communicating medication use.

Objective: To assess the effectiveness and comprehensibility of medication label pictograms among non-English speaking people. To determine the cultural appropriateness of the images used in such pictograms.

Study Design: For each of three different ethnic populations, a focus group was convened. Each focus group consisted of 6-8 participants with a diverse range of education, literacy, and occupations. Discussion was facilitated by and interpreter, and individual interviews were used to determine responses to each pictogram.

Results: Some pictograms were understood by all ethnic groups. Other must be redesigned either to address cultural values or allow greater comprehension.

Importance: The findings will help to create pictograms which are suitable for general use in non-English populations. These universal pictograms will help to enhance the provision of health care during humanitarian missions.

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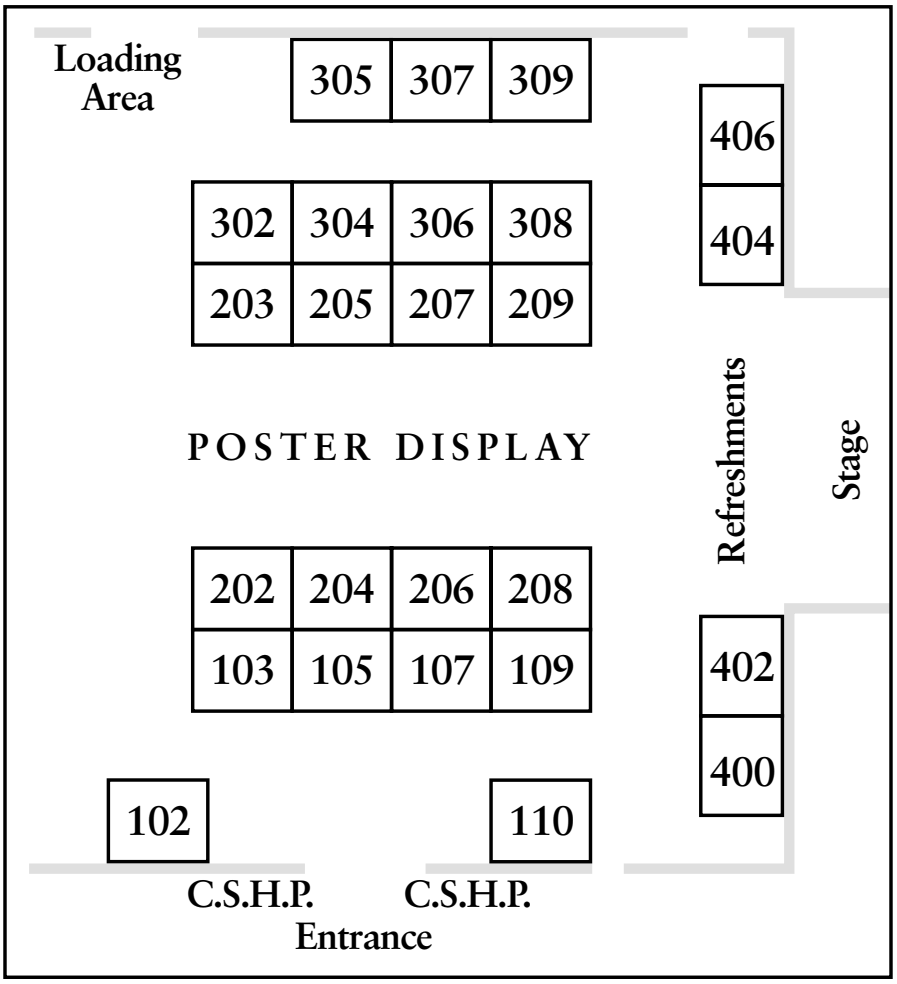

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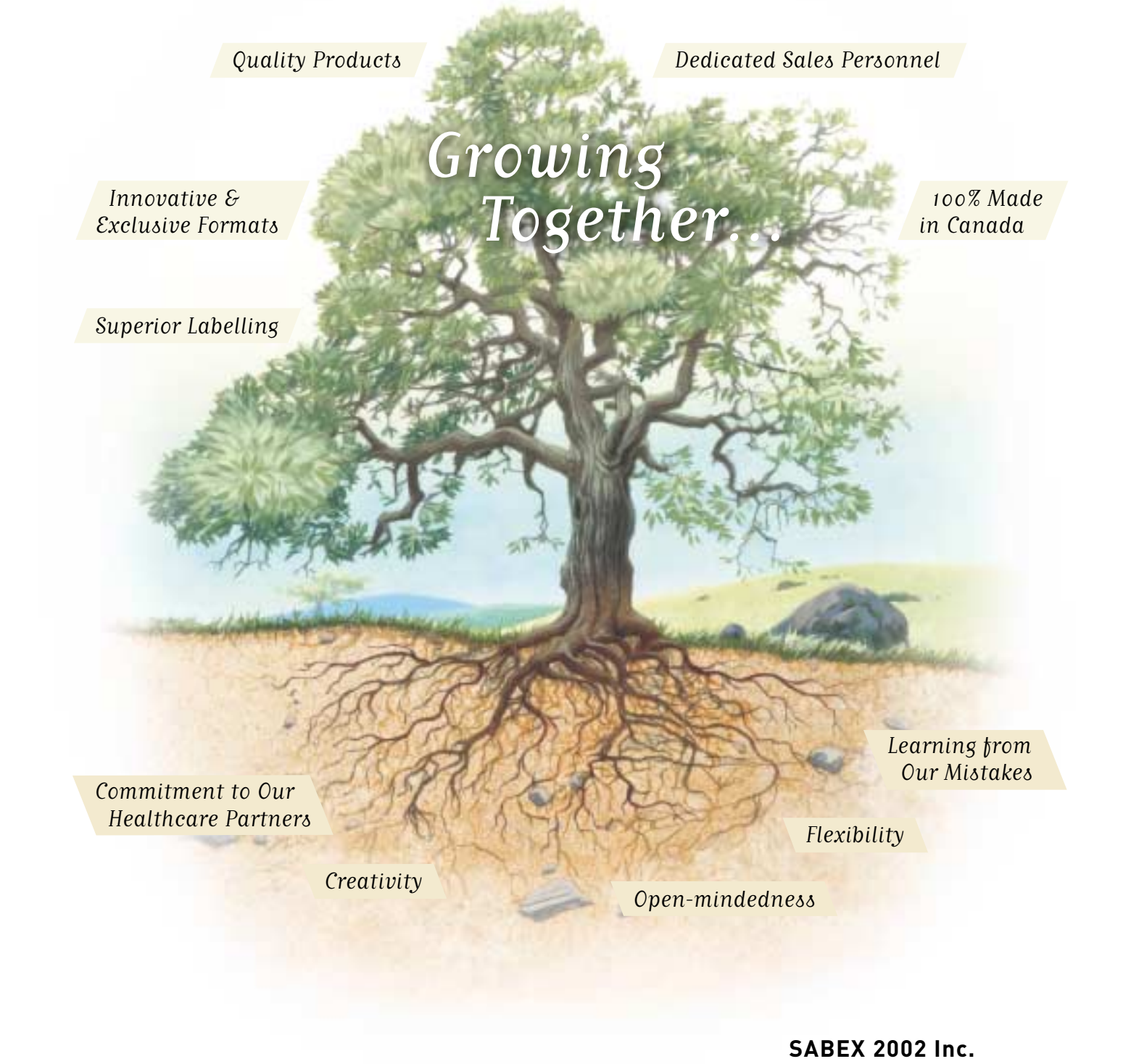

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LIPITOR (atorvastatin calcium) is a synthetic lipid-lowering agent. It is a selective, competitive inhibitor of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, which is an early and rate-limiting step in the biosynthesis of cholesterol.

LIPITOR lowers plasma cholesterol and lipoprotein levels by inhibiting HMG-CoA reductase and cholesterol synthesis in the liver and by increasing the number of hepatic Low Density Lipoprotein (LDL) receptors on the cell surface for enhanced uptake and catabolism of Low Density Lipoprotein (LDL).

LIPITOR reduces LDL-Cholesterol (LDL-C) and the number of LDL particles. LIPITOR also reduces Very Low Density Lipoprotein-Cholesterol (VLDL-C), serum triglycerides (TG) and Intermediate Density Lipoproteins (IDL), as well as the number of apolipoprotein B (apo B)-containing particles, but increases High Density Lipoprotein-Cholesterol (HDL-C). Elevated serum cholesterol due to elevated LDL-C is a major risk factor for the development of cardiovascular disease. Low serum concentration of HDL-C is also an independent risk factor. Elevated plasma TG is also a risk factor for cardiovascular disease, particularly if due to increased IDL, or associated with decreased HDL-C or increased LDL-C.

Atorvastatin is rapidly absorbed after oral administration; maximum plasma concentrations occur within 1 to 2 hours. Atorvastatin tablets are 95% to 99% bioavailable compared to solutions.

Mean distribution of atorvastatin is approximately 381 litres. Atorvastatin is ≥98% bound to plasma proteins. Atorvastatin is extensively metabolized by cytochrome P-450 3A4 to ortho- and para-hydroxylated derivatives and to various beta-oxidation products. Approximately 70% of circulating inhibitory activity for HMG-CoA reductase is attributed to active metabolites.

Atorvastatin and its metabolites are eliminated by biliary excretion. Less than 2% of a dose of atorvastatin is recovered in urine following oral administration. Mean plasma elimination half-life of atorvastatin in humans is approximately 14 hours, but the half-life of inhibitory activity for HMG-CoA reductase is 20 to 30 hours due to the contribution of longer-lived active metabolites.

INDICATIONS AND CLINICAL USE

LIPITOR (atorvastatin calcium) is indicated as an adjunct to lifestyle changes, including diet, for the reduction of elevated total cholesterol, total-Cholesterol, LDL-C, TG and apolipoprotein B (apo B) in hypercholesterolemic 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. These changes in HDL-C with HMG-CoA reductase inhibitors should be considered as modest when compared to those observed in LDL-C and do not play a primary role in the lowering of LDL-C/HDL-C and total-C/HDL-C ratios.

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 (25-66%) 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 (40-51%), TG (40-56%) and IDL-C + VLDL-C levels (34-59%).

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 15% in receptor negative patients (see PHARMACOLOGY, Clinical Studies).

For more details on efficacy results by pre-defined classification and pooled data by Fredrickson types, 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:

LDL-C (mmol/L) = total-C - [(0.37 x (TG) + HDL-C)]
LDL-C (mg/dL) = total-C - [(0.2 x (TG) + 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), under SELECTED BIBLIOGRAPHY in product monograph).

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

The Atorvastatin Versus Revascularization Treatments (AVERT) study examined the effect of intensive lipid-lowering on 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 randomized 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 (see SELECTED BIBLIOGRAPHY in product monograph).

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

The effects of atorvastatin-induced changes in lipoprotein levels, including reduction of serum cholesterol on cardiovascular morbidity or mortality or total mortality have not been established.

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 (see SELECTED BIBLIOGRAPHY in product monograph).

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 (see SELECTED BIBLIOGRAPHY in product monograph).

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 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 6 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 (see PHARMACOLOGY, Human Pharmacokinetics; SELECTED BIBLIOGRAPHY in product monograph).

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 inhibition interferes 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

1. Friedewald WT, *et al. Clin Chem* 1972;18(6):499-502.

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 (-43%) than when either drug was administered alone (-35% for LIPITOR and -22% for colestipol).

Patients with severe hypercholesterolemia: LDL-C reduction was similar (-53%) 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 (see PHARMACOLOGY, Clinical Studies).

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 and SELECTED BIBLIOGRAPHY in product monograph).

Coumarin Anticoagulants: LIPITOR had no clinically significant effect on prothrombin time when administered to patients receiving chronic warfarin therapy (see SELECTED BIBLIOGRAPHY in product monograph).

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 (see Human Pharmacokinetics). 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 (see Human Pharmacokinetics).

(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) (see Human Pharmacokinetics).

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 (see SELECTED BIBLIOGRAPHY in product monograph). 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; SELECTED BIBLIOGRAPHY in product monograph).

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; Human Pharmacokinetics).

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	†
Diarrhea	1	†
Dyspepsia	2	†
Flatulence	2	†
Nausea	0	†
NERVOUS SYSTEM		
Headache	2	†
MISCELLANEOUS		
Pain	<1	†
Myalgia	1	†
Asthenia	<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).

SYMPTOMS AND TREATMENT OF OVERDOSAGE

There is no specific treatment for atorvastatin overdosage. Should an overdose occur, the patient should be treated symptomatically and supportive measures instituted as required. Due to extensive drug binding to plasma proteins, hemodialysis is not expected to significantly enhance atorvastatin clearance.

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) Hyperlipidemia, Including Familial Combined Hyperlipidemia: The recommended dose of LIPITOR is 10 mg once a day. The majority of patients achieve and maintain target cholesterol levels with LIPITOR 10 mg/day. 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. 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 baseline LDL-C and/or TG levels, the desired LDL-C and/or TG 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. Adjustments of dosage, if necessary, should be made at intervals of 4 weeks or more. The recommended dose range for most patients is 10 to 40 mg/day. The maximum dose is 80 mg/day, which may be required in a minority of patients (see section below).

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[a] (273 mg/dL)[b]	-29	-33	-37	-45
LDL-C: 4.9 mmol/L[a] (190 mg/dL)[b]	-39	-43	-50	-60

a. Results are pooled from 2 dose-response studies.
b. 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.

PHARMACEUTICAL INFORMATION

Drug Substance

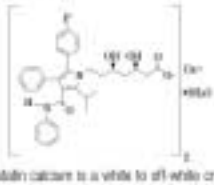
Proper Name: Atorvastatin calcium

Chemical Name: [R-(R*,R*)]-2-(4-fluorophenyl)-β, δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino) carbonyl]-1H-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate

Empirical Formula: $(C_{33}H_{34}FN_2O_5)_2Ca \cdot 3H_2O$

Molecular Weight: 1209.42

Structural Formula:



Description: Atorvastatin calcium is a white to off-white crystalline powder that is practically insoluble in aqueous solutions of pH 4 and below. Atorvastatin calcium is very slightly soluble in distilled water; pH 7.4 phosphate buffer and acetonitrile; slightly soluble in ethanol; and freely soluble in methanol.

Tablet Composition:

Each tablet contains either 10 mg, 20 mg, 40 mg or 80 mg atorvastatin as the active ingredient. Each tablet also contains the following non-medicinal ingredients: calcium carbonate, candelilla wax, croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, hydroxypropyl methylcellulose, polyethylene glycol, talc, titanium dioxide, polysorbate 80 and simethicone emulsion.

Stability and Storage Recommendations:

Store at controlled room temperature 15 to 30°C.

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. Blisters of 30 tablets (3 strips x 10).

References:

1. LIPITOR (atorvastatin calcium) Product Monograph, Pfizer Canada Inc., February 2002. **2.** IMS Global Services; March 1997 – September 2002. **3.** Pitt B, *et al.* Aggressive lipid-lowering therapy compared with angioplasty in stable coronary artery disease. *N Engl J Med* 1999;341:70-76. **4.** Data on File, Pfizer Canada Inc. **5.** Simon Day. Dictionary for Clinical Trials. 1999. John Wiley & Sons Ltd. 137-38.

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

Pfizer

Life is our life's work

Pr IFOSFAMIDE for Injection, USP

1 g/vial and 3 g/vial

Antineoplastic

CAUTION: IFOSFAMIDE FOR INJECTION IS A POTENT DRUG AND SHOULD BE USED ONLY BY PHYSICIANS EXPERIENCED WITH CANCER CHEMOTHERAPEUTIC DRUGS (SEE WARNINGS AND PRECAUTIONS). IN THOSE PATIENTS WHO DEVELOP BACTERIAL, FUNGAL OR VIRAL INFECTIONS, INTERRUPTION OR MODIFICATION OF DOSAGE SHOULD BE CONSIDERED. BLOOD COUNTS SHOULD BE TAKEN AT REGULAR INTERVALS. DUE TO THE UROTOXIC EFFECT OF OXAZAPHOSPHORINES, IFOSFAMIDE FOR INJECTION SHOULD NOT BE ADMINISTERED WITHOUT THE USE OF A UROPROTECTIVE AGENT SUCH AS MESNA (SEE MESNA FOR INJECTION PRODUCT MONOGRAPH FOR DOSAGE AND ADMINISTRATION).

ACTION AND CLINICAL PHARMACOLOGY

Ifosfamide for Injection is activated by metabolism in the liver by the mixed function oxidase system of the smooth endoplasmic reticulum. The activation is induced by hydroxylation at the ring carbon atom 4. Opening of the ring results in the formation of aldo-ifosfamide, the tautomer of 4-hydroxy-ifosfamide. Two stable metabolites, 4-keto-ifosfamide and 4-carboxyifosfamide, appear in the urine. However, they have no cytotoxic activity. N,N'-bis(2-chloroethyl)-phosphoric acid diamide and acrolein are also found. The enzymatic oxidation of the chloroethyl side chains and subsequent dealkylation may produce further metabolites.

DNA is one of the main target sites of Ifosfamide for Injection. In vitro, incubation of DNA with activated Ifosfamide for Injection produces phosphotriesters as the predominant reaction products. The treatment of intact cell nuclei may also result in the formation of DNA-DNA crosslinks. DNA repair occurs in G-1 and G-2 stage cells. Repair capacity is more marked in less sensitive tumours. An accumulation of cells in the G-1 phase is found in tumours that respond well.

INDICATIONS AND CLINICAL USE

Ifosfamide for Injection is indicated as follows:

Soft Tissue Sarcoma

– first-line single agent therapy
– second-line single agent therapy in patients who have failed to respond or who have relapsed on other chemotherapeutic regimens.

Pancreatic Carcinoma

– second-line single agent therapy in patients who have failed to respond or who have relapsed on other chemotherapeutic regimens.

Cervical Carcinoma

– as a single agent or in combination with Cisplatin and Bleomycin in advanced or recurrent disease.

CONTRAINDICATIONS

Ifosfamide for Injection is contraindicated in individuals with a known hypersensitivity to it. It is also contraindicated in patients having severe leukopenia, thrombocytopenia and severe renal and/or hepatic impairment. Ifosfamide for Injection should not be administered to patients with advanced cerebral arteriosclerosis.

WARNINGS

UROTOXIC SIDE EFFECTS, ESPECIALLY HEMORRHAGIC CYSTITIS, HAVE BEEN FREQUENTLY ASSOCIATED WITH THE USE OF IFOSFAMIDE. UNTIL RECENTLY THESE EFFECTS RESULTED IN CESSATION OF THERAPY. THE THERAPEUTIC BENEFIT OF MESNA AS A UROPROTECTIVE AGENT HAS BEEN DEMONSTRATED IN THAT THE INCIDENCE OF URINARY TRACT COMPLICATIONS WAS REDUCED FROM 40% TO 3.5%. THUS IFOSFAMIDE FOR INJECTION SHOULD ALWAYS BE ACCOMPANIED BY UROPROTECTIVE TREATMENT WITH MESNA (SEE MESNA FOR INJECTION PRODUCT MONOGRAPH FOR DOSAGE AND ADMINISTRATION).

PATIENTS, MALE OR FEMALE, DURING THE REPRODUCTIVE PERIOD OF LIFE, SHOULD BE ADVISED OF THE MUTAGENIC POTENTIAL OF IFOSFAMIDE. ADEQUATE METHODS OF CONTRACEPTION ARE RECOMMENDED FOR SUCH PATIENTS (SEE ADVERSE REACTIONS).

USE IN PREGNANCY: IFOSFAMIDE FOR INJECTION CAN BE TERATOGENIC OR CAUSE FETAL RESORPTION IN EXPERIMENTAL ANIMALS. IT SHOULD NOT BE USED IN PREGNANCY, PARTICULARLY IN EARLY PREGNANCY, UNLESS IN THE JUDGEMENT OF THE PHYSICIAN THE POTENTIAL BENEFITS OUTWEIGH THE POSSIBLE RISKS. AS IS THE CASE WITH THE OXAZAPHOSPHORINE CLASS OF ALKYLATING AGENTS, IFOSFAMIDE FOR INJECTION IS EXCRETED IN BREAST MILK AND BREAST FEEDING SHOULD BE TERMINATED PRIOR TO INSTITUTION OF IFOSFAMIDE FOR INJECTION THERAPY.

SINCE THE POSSIBILITY OF INTERFERENCE WITH NORMAL WOUND HEALING HAS BEEN REPORTED WITH OTHER OXAZAPHOSPHORINES, IFOSFAMIDE FOR INJECTION THERAPY SHOULD NOT BE INITIATED FOR AT LEAST 10 TO 14 DAYS AFTER SURGERY.

IFOSFAMIDE FOR INJECTION, LIKE OTHER ALKYLATING AGENTS, HAS BEEN REPORTED TO HAVE ONCOGENIC ACTIVITY IN ANIMALS. THUS THE POSSIBILITY THAT IT MAY HAVE ONCOGENIC POTENTIAL IN HUMANS SHOULD BE CONSIDERED.

PRECAUTIONS

IFOSFAMIDE FOR INJECTION SHOULD BE GIVEN CAUTIOUSLY TO PATIENTS WITH ANY OF THE FOLLOWING CONDITIONS:

1. Leukopenia
2. Thrombocytopenia
3. Tumour-cell infiltration of the bone marrow
4. Prior radiotherapy
5. Prior treatment with other antineoplastic agents
6. Brain metastases and advanced cerebral arteriosclerosis
7. Impaired renal function
8. Impaired hepatic function
9. In the presence of known infections
10. Abnormal serum creatinine and serum albumin levels

Because Ifosfamide for Injection may exert a suppressive action in immune mechanisms, the interruption or modification of dosage should be considered for patients who develop bacterial, fungal or viral infections. This is especially true for patients receiving concomitant steroid therapy, since infections in some of these patients have been fatal.

Ifosfamide may cause significant neurologic, renal and hematologic toxicities which may prove fatal despite careful monitoring prior to and during therapy.

Urinary sediment should be examined at regular intervals. Extra care is required in unilaterally nephrectomised patients, who obviously tolerate high-doses of Ifosfamide for Injection less well. Ifosfamide for Injection should not be given until three months after the nephrectomy.

Careful monitoring is also required for patients with cerebral metastases, as ifosfamide has been associated with several CNS symptoms.

Leukocyte, erythrocyte and platelet counts should be carried out at regular intervals. There is normally a reduction in the leukocyte count beginning on approximately day 5. The nadir, depending on dosage and baseline count, tends to be reached after 8-10 days. Recovery occurs after 10-14 days and is usually complete after 2-3 weeks.

Neurologic manifestations consisting of somnolence, confusion, hallucinations and in some instances, coma have been reported following ifosfamide therapy. The occurrence of these symptoms requires discontinuing ifosfamide therapy. These symptoms have usually been reversible and supporting therapy should be maintained until their resolution.

ADVERSE REACTIONS

Urinary System

Hemorrhagic cystitis, manifested by the occurrence of hematuria, dysuria, urinary frequency and occasionally urinary incontinence or retention, develops frequently in patients treated with Ifosfamide for Injection. The incidence, severity and persistence of Ifosfamide-induced hemorrhagic cystitis increase as the dose of the drug increases. In most instances, the hematuria resolves spontaneously upon cessation of Ifosfamide for Injection therapy.

Granular casts in the urinary sediment have occurred mainly after high doses of Ifosfamide for Injection. The cylinduria generally resolves spontaneously a few days after the last Ifosfamide for Injection injection.

Renal parenchymal and tubular necrosis, which could lead to death, have been reported. Renal tubular acidosis, Fanconi Syndrome and renal rickets have also been reported. Close clinical monitoring of serum and urine chemistries including phosphorus, potassium, alkaline phosphatase and other appropriate laboratory studies is recommended. Appropriate replacement therapy should be administered as indicated.

Metabolic acidosis was reported in 31% of patients in one study when ifosfamide was administered at doses of 2.0-2.5 g/m^2/d for four days.

Increases and decreases in creatinine clearance are usually reversible.

The urinary tract toxicity of Ifosfamide for Injection can be minimized by administering a uroprotective agent such as MESNA (SEE MESNA FOR INJECTION PRODUCT MONOGRAPH FOR DOSAGE ADMINISTRATION).

Hematopoietic System

Leukopenia is an expected effect and ordinarily is used as a guide to therapy. Thrombocytopenia and anemia have been known to occur in a few patients. These effects are almost always reversible when therapy is interrupted. Episodes of petechial bleeding due to severe thrombocytopenia have been reported.

Gastrointestinal System

Nausea and vomiting are dose-related and also depend on individual sensitivity.

Effects on Gonads

Gonadal suppression, resulting in amenorrhea or azoospermia, has been reported with other oxazaphosphorines and thus may occur with Ifosfamide for Injection.

Integumentary System

It is ordinarily advisable to inform patients in advance of possible alopecia, a frequent complication of Ifosfamide for Injection therapy. Regrowth of hair can be expected although occasionally the new hair may be of a different colour or texture. Non-specific dermatitis has been reported to occur with Ifosfamide for Injection.

Central Nervous System

Cerebral side effects consist mainly of somnolence, confusion, hallucinations and depressive psychosis. Other less frequent symptoms included dizziness, disorientation and cranial nerve dysfunction. Seizures of the tonic-clonic type have been reported occasionally. Isolated cases of encephalitis, generalized seizure and seizures resulting in coma have also been observed.

It is possible that the severity and incidence of cerebral effects increase with the administration of high doses, the presence of brain metastases, or advanced cerebral arteriosclerosis. The incidence and extent of cerebral effects due to Ifosfamide for Injection may also be affected by the age of the patient, and by impaired renal clearance.

Cardiotoxicity

Although cardiotoxicity is rarely encountered, there have been reported cases of arrhythmia at high doses of Ifosfamide for Injection.

Respiratory System

Interstitial pulmonary fibrosis has been reported in patients treated with large doses of alkylating agents for prolonged periods. Although not reported in patients treated with Ifosfamide for Injection, physicians should be aware of its possible occurrence.

Adverse reactions in addition to those mentioned above have been noted with Ifosfamide for Injection. They include infection with or without fever, diarrhea, anorexia, hematemesis, asthenia, thrombophlebitis, increase in liver enzymes and/or bilirubin, allergic reactions, stomatitis and polyneuropathy.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

No specific antidote for Ifosfamide for Injection is known. Management of overdosage would include general supportive measures to sustain the patient through any period of toxicity that might occur.

DOSAGE AND ADMINISTRATION

Chemotherapy with Ifosfamide for Injection, as with other drugs used in cancer chemotherapy, is potentially hazardous and fatal complications can occur. It is recommended that it be administered only by physicians aware of the associated risks. Total dosage of 250-300 mg/kg per cycle is the usual standard. As a rule, 50-60 mg/kg are administered intravenously each day for 5 consecutive days. If the calculation of the dosage is based on body surface area, the recommended dosage is 2000-2400 mg/m² daily on 5 consecutive days. If a lower daily dosage or the total dosage over a longer period is indicated, Ifosfamide for Injection can be given every other day (days 1, 3, 5, 7 and 9) or on 10 consecutive days in lower doses.

A treatment series should be repeated after an interval of not less than 3-4 weeks. The therapeutic administration of Ifosfamide for Injection should invariably be accompanied by uroprotective treatment with Mesna for Injection. Alternately, the administration of high single dose infusions is now feasible up to 5 to 8 g/m²/24 h under protection of continuous mesna-infusion. The optimal use of ifosfamide in combination with other myelosuppressive agents requires dosage adjustments according to the regimen and schedule to be adopted.

Prevention of Cystitis

The concomitant administration of Mesna for Injection helps to prevent the urotoxic side effects of Ifosfamide for Injection which had previously limited the drug's therapeutic use. Every Ifosfamide for Injection regimen should be accompanied by uroprotective treatment with mesna.

Mesna for Injection is usually given by intravenous injection concurrently with Ifosfamide for Injection and 4 and 8 hours afterwards, each dose being 20% of the Ifosfamide for Injection dose. (See Mesna for Injection Product Monograph for Dosage and Administration.)

Even with the administration of the uroprotector mesna, the daily fluid intake should be at least 2 liters. If urinary excretion appears insufficient, a fast-acting diuretic such as furosemide may be administered.

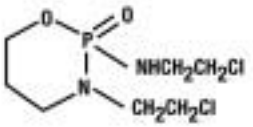
PHARMACEUTICAL INFORMATION

Drug Substance

Common Name: Ifosfamide

Chemical Name: 3-(2-chloroethyl)-2-[(2-chloroethyl) amino]tetrahydro-2H-1,3, 2-oxazaphosphorine-2-oxide

Structural Formula:



Molecular Formula: $C_7H_{15}Cl_2N_2O_2P$

Molecular Weight: 261.09

Description: Ifosfamide belongs to the family of oxazaphosphorine nitrogen mustards. It is white crystalline powder, soluble in water or saline. pH of 10% solution (w/v) is 4.5 – 7.0. Melting Range: 48.0 – 51.0°C.

Composition: Ifosfamide for Injection vials contain ifosfamide sterile powder. The pH of freshly reconstituted 5% w/v solutions usually range from 4 to 7.

Stability and Storage Recommendations

Store Ifosfamide for Injection vials at room temperature (15°C to 25°C). Protect from temperatures above 30°C.

Parenteral Products

Preparation for Intravenous Use:

Reconstitute with Sterile Water for Injection as follows:

Vial Size	Volume to be Added	Approximate Available Volume	Approximate Average Concentration
1 gram	20 mL	20 mL	50 mg/mL
3 gram	60 mL	60 mL	50 mg/mL

Shake well until dissolved. The prepared solution may be further diluted to achieve concentrations of 0.6 to 20 mg/mL with any of the solutions for I.V. infusion listed below in PVC bags.

Solution for I.V. Infusion

5% Dextrose Injection U.S.P.
0.9% Sodium Chloride U.S.P.
Lactated Ringer's Injection U.S.P.

Stability of Solutions

Reconstituted solutions should be used within 24 hours if stored at room temperature, or within 72 hours if refrigerated. Use further diluted solutions immediately.

Note: 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. Solution showing haziness, particulate matter, precipitate, discolouration or leakage should not be used. Discard unused portion.

AVAILABILITY OF DOSAGE FORMS

Ifosfamide for Injection is available as sterile lyophilized powder supplied in 1 g. and 3 g vials.

Vial stoppers do not contain natural rubber latex.

C104210 1 g single-dose vial in 30-mL vial, packaged individually
C104300 3 g single -dose vial in 100-mL vial, packaged individually

Handling and Disposal

Preparation of Ifosfamide for Injection should be done in a vertical laminar flow hood (Biological Safety Cabinet – Class II). Personnel preparing Ifosfamide for Injection should wear PVC gloves, safety glasses, disposable gowns and masks.

All needles, syringes, vials and other materials which have come in contact with Ifosfamide for Injection should be segregated and incinerated at 1000°C or more. Sealed containers may explode while still sealed. Intact vials should be returned to the Manufacturer for destruction. Proper precautions should be taken in packaging these materials for transport. Personnel regularly involved in the preparation and handling of Ifosfamide for Injection should have bi-annual blood examinations.

Product Monograph available upon request.

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9050 Yonge Street, Suite 306, Richmond Hill, Ontario, Canada L4C 9S6
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PAAB

Pr

MESNA for Injection

Uroprotector

ACTION

Mesna is rapidly and easily converted by autooxidation to its only metabolite disodium 2,2-dithio-bis ethane sulfonate (mesna disulfide, dimesna), forming a disulphide link. Following intravenous injection, only a small portion of the administered dose is detected in the blood as a reactive thiol compound (mesna). Mesna disulphide remains in the intravascular space and is rapidly forwarded to the kidney. In the renal tubular epithelium a considerable proportion of mesna disulphide is again reduced to a free thiol compound, presumably by mediation of glutathione reductase. It is then capable of chemically reacting with acrolein or other urotoxic oxazaphosphorine metabolites in the urine, thereby developing its detoxifying activity.

The first and most important step towards detoxification is the addition of mesna to the double bond of acrolein, resulting in the formation of a stable thio ether which could be detected in the urine by chromatography. In the second step, mesna reduces the speed of degradation of the 4-hydroxy metabolite in the urine. A relatively stable, non-urotoxic condensation product from 4-hydroxy cyclophosphamide or 4-hydroxy ifosfamide and mesna is formed. By such stabilization mesna inhibits the degradation of 4-hydroxy cyclophosphamide or 4-hydroxy ifosfamide and hence the formation of acrolein. This intermediate deactivated product could also be detected by chromatographic urinalysis.

INDICATIONS

Mesna is indicated for the reduction and prevention of urinary tract toxicity (hemorrhagic cystitis) of oxazaphosphorines. (SEE **ADVERSE REACTION** SECTIONS OF THE CYTOXAN AND IFEX PRODUCT MONOGRAPHS.)

CONTRAINDICATIONS

Mesna is contraindicated in individuals with a known hypersensitivity to it.

WARNINGS

The protective effect of Mesna applies only to the urotoxic effects of oxazaphosphorines. Additional prophylactic or accompanying measures recommended during treatment with oxazaphosphorines are thus not affected and should not be discontinued.

IN VITRO, MESNA IS INCOMPATIBLE WITH CISPLATIN.

The combination of an oxazaphosphorine cytostatic agent with Mesna and cisplatin in the same infusion solution is not stable and is not to be used.

PRECAUTIONS

Mesna treatment may cause false positive reactions in tests for ketone bodies in the urine. The colour reaction is reddish purple rather than purple. The reddish purple colour is less stable, and fades immediately by adding glacial acetic acid.

Use in Children

Mesna has been administered to patients as young as 13 years of age. Due to the presence of benzyl alcohol, the product should not be used in neonates or infants.

Use in Pregnancy

Although the use of Mesna in pregnant women has not been established, animal studies have not revealed any embryotoxic or mutagenic effects. However, in view of the fact that oxazaphosphorines are not recommended during pregnancy, this would eliminate the need for Mesna.

ADVERSE REACTIONS

At recommended doses, side effects are not usually observed.

The following adverse reactions have been reported in a phase I trial in healthy volunteers:

1) Diarrhea
2) Abdominal pain
3) Headache
4) Pain in limbs and joints
5) Transient drop in blood pressure
6) Increase in pulse rate

These reactions occurred at doses of 60 mg/kg or more, given as a single bolus. Venous irritation may occur in rare instances. This reaction may be attributed to the physical properties of Mesna (i.e., pH 6, and hypertonic solution).

No venous complications were observed when the solution was given diluted with Sterile Water for Injection USP (one part Mesna solution to three parts water).

SYMPTOMS AND TREATMENT OF OVERDOSAGE

No specific antidote for Mesna is known. Overdosage should be managed with supportive measures to sustain the patient through any period of toxicity. Mesna has been administered at doses from 70 to 100 mg/kg without any toxic effect on hematopoiesis, hepatic and renal function or the central nervous system.

DOSAGE AND ADMINISTRATION

Mesna should be administered by intravenous injection, usually at 20% of the respective oxazaphosphorine dose at times 0 (= administration of the cytostatic agent), 4 hours and 8 hours. In the case of IFEX (ifosfamide), the usual dose of Mesna is 10 -12 mg/kg i.v. at 0, 4 and 8 hours after the IFEX dose.(SEE **DOSAGE AND ADMINISTRATION** SECTIONS OF CYTOXAN AND IFEX PRODUCT MONOGRAPHS.)

In the treatment of children, and particularly when administering very high doses – such as required when conditioning patients for bone marrow transplantations – the Mesna doses should be given at 0, 1, 3, 6, 9 and 12 hours or dosage increased to 30% of the respective oxazaphosphorine dose.

Oral administration of Mesna – e.g., in patients with poor veins – is also feasible. Mesna is then given either at doses of 20% of the oxazaphosphorine dose at time 0 hours by the parenteral route, followed by oral doses of 40% of the oxazaphosphorine dose after 4 and 8 hours, taken in juice or cola, or in 3 oral doses of 40% of the oxazaphosphorine dose at time 0, 4 and 8 hours.

PHARMACEUTICAL INFORMATION

Drug Substance

Proper Name: Mesna

Chemical Name: Sodium 2-mercaptoethanesulfonate

Structural Formula: $HS\text{-}CH_2\text{-}CH_2\text{-}SO_3^-Na^+$

Molecular Formula: $C_2H_5O_3S_2Na$

Molecular Weight: 164.18

Description

Mesna is a white to slightly cream coloured crystaline or microcrystalline powder with a characteristic odour. It is freely soluble in water, sparingly soluble in methanol and practically insoluble in the usual organic solvents.

Composition

Each mL of Mesna for Injection contains: 100 mg Mesna, 10.4 mg Benzyl Alcohol, Edetate Disodium, Water for Injection, and Sodium Hydroxide for pH adjustment.

Stability and Storage Recommendations

Store the vials at 15°C - 30°C. Vials must be discarded within 28 days after initial puncture.

Solution for I.V. Infusion

5% Dextrose Injection USP
0.9% Sodium Chloride Injection USP
Solutions for infusion should be made up at
a concentration of 1 mg/mL or greater.

Stability of Solution

Storage: Solutions for infusion should be used within 24 hours, if stored below 25°C, or 48 hours if stored refrigerated (2 - 8°C), from the time of preparation.

As with all parenteral drug products, intravenous admixtures should be inspected visually for clarity, particulate matter, precipitate, discoloration and leakage prior to administration. The unused portion should be discarded.

AVAILABILITY

Mesna for Injection is available as 100 mg/mL in 10 mL multi dose vials as follows: C730310 10 mL vials in packages of 10 vials.

Product Monograph available upon request.

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PAAB

75 mg ONCE DAILY

Plavix*

75 mg clopidogrel tablets

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 antagonists, lipid-lowering drugs, calcium channel blockers, nitrates, beta blockers, ACE-inhibitors, percutaneous coronary intervention (with or without stent) or CABG (coronary artery bypass graft), 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). 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 20% relative risk reduction (95% CI of 10%, 28%; 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 1035 (16.54%) in the PLAVIX-treated group and 1187 (18.83%) in the placebo-treated group; an absolute risk reduction of 2.29% and a 14% relative risk reduction (95% CI of 6%, 21%, 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 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.

Outcome	PLAVIX* (n=6259)	Placebo* (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%)	0.33%	0.89 (0.74, 1.07)
Stroke	75 (1.20%)	87 (1.38%)	0.18%	0.86 (0.63, 1.18)
Refractory ischemia†	544 (8.68%)	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 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 enzymes/cardiac marker changes);

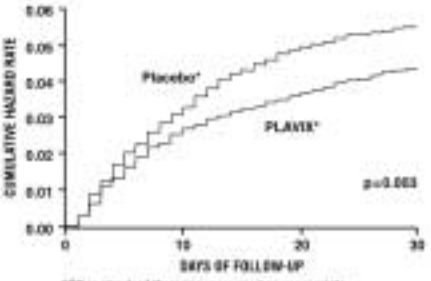
Stroke: neurological deficit ≥24 hours (CT/MRI encouraged);

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 (Fig. 1) and continued to diverge (Fig. 2). The benefits of PLAVIX were maintained throughout the course of the trial (up to 12 months).

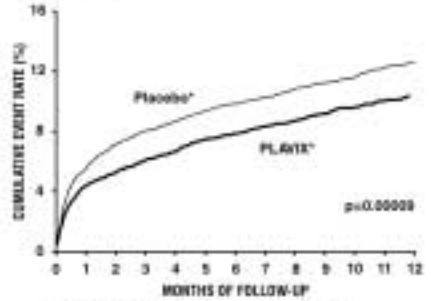
Figure 1: Cumulative Hazard Ratio for First Primary Outcome (death from cardiovascular causes, non-fatal myocardial infarction or stroke) During the First 30 days after Randomization.



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

The results demonstrate the early effects of clopidogrel.

Figure 2: Cardiovascular Death, Myocardial Infarction or Stroke in the CURE Study.



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

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

	PLAVIX* (n=6259)	Placebo* (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.

INDICATIONS AND CLINICAL USE

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.

PLAVIX is also indicated for the reduction of atherothrombotic events (myocardial infarction, ischemic stroke, cardiovascular death and/or refractory ischemia) in patients with acute coronary syndromes, unstable angina or non-Q-wave myocardial infarction, without ST segment elevation. 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.

The safety of the coadministration of PLAVIX with warfarin has not been established. Consequently, concomitant administration of these two agents 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 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	The safety of the coadministration of PLAVIX with warfarin has not been established. Consequently, concomitant administration of these two agents 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 inhibitors, calcium antagonists, lipid-lowering agents, coronary vasodilators, antidiabetic agents (including insulin), antiepileptic agents, hormone replacement therapy, unfractionated and/or LMW heparin, and glycoprotein IIb/IIIa antagonists. Patients on HMG CoA reductase inhibitors and clopidogrel experienced a higher incidence of bleeding events (primarily epistaxis). There is no known pathophysiological or pharmacological explanation for this observation. Patients on HMG CoA reductase inhibitors and ASA experienced a higher incidence of intracranial hemorrhage.

At high concentrations *in vitro*, clopidogrel inhibits isoenzyme CYP 2C9 of the cytochrome system P450 (2C9). 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 9000 patients treated for 1 year or more.

CAPRIE:

PLAVIX was well tolerated compared to ASA in a large controlled clinical trial (CAPRIE). The overall tolerability of PLAVIX was similar regardless of age, gender 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 (<12000/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 9599 patients who received PLAVIX had neutrophil counts of zero. None of the 8586 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=8586)
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[1]	0.3	0.2
– with sequelae[1]	0.1	0.1
Platelet disorders:		
– severe thrombocytopenia (0 ≤ x < 80,000/mm³)	0.2	0.1
– thrombocytopenia (0 ≤ x < 100,000/mm³)	0.1	0.2
Skin disorders:		
– rash	4.2*	3.5
– severe[1]	0.1	0.1
– leading to discontinuation[1]	0.5	0.2
– pruritus	3.3*	1.8
Gastrointestinal disorders:		
– peptic, gastric, duodenal ulcer	0.7	1.2
– diarrhea	4.5*	3.4
– severe[1]	0.2	0.1
– leading to discontinuation[1]	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	7.0	7.5
– fatigue	3.3	3.4
– pain	6.4	6.3
– headache	7.6	7.2
– coughing	2.1	2.7

*: Statistically significant difference between treatments (p ≤ 0.05)
[1]: Patients may be included in more than one category

CURE:

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

In CURE, PLAVIX when given with ASA, 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* (n=6259)	Placebo* (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%
[1] 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 trial was 68 in the clopidogrel group and 73 in the placebo group (relative risk, 0.94; 95 percent confidence interval, 0.68 and 1.30; 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 trial was 78 in the clopidogrel group and 70 in the placebo group (relative risk, 1.12; 95 percent confidence interval, 0.81 and 1.55; 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 (LMW) 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.

Allergic Disorders: Hypersensitivity reactions have been reported: these mainly include skin reactions (maculopapular or erythematous rash, urticaria) and/or pruritus. Very rare cases of bronchospasm, angioedema or anaphylactoid reactions have been observed.

Platelet, Bleeding and Clotting Disorders: Very rare cases of thrombotic thrombocytopenic purpura (TTP) have been reported (see **WARNINGS**).

DOSAGE AND ADMINISTRATION

The recommended dose of PLAVIX is 75 mg once daily long term with or without food.

For patients with an 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 (75 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.

Product Monograph available upon request.

References: **1.** PLAVIX Product Monograph. Sanofi-Synthelabo Canada Inc., April 9, 2002. **2.** Harker LA, *et al.* Comparative safety and tolerability of clopidogrel and aspirin. *Drug Safety* 1999;21(4):325 – 35. **3.** Hankey GJ. Current oral antiplatelet agents to prevent atherothrombosis. *Cerebrovasc Dis* 2001; 11 (Suppl 2):11 – 7. **4.** CAPRIE Steering Committee. A randomised, blinded trial of clopidogrel versus aspirin in patients at risk of ischemic events (CAPRIE). *Lancet* 1996;348:1329 – 39. **5.** 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. **6.** Bhatt DL, *et al.* Amplified benefit of clopidogrel versus aspirin in patients with diabetes mellitus. *Am J Cardiol* 2002;90:625 – 8. **7.** Mehta SR, *et al.* Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. *Lancet* 2001;358: 527 – 33. **8.** Alberts MJ. Secondary prevention of stroke and the expanding role of the neurologist. *Cerebrovasc Dis* 2002;13(Suppl 1):12 – 6.

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