# G-CSF: Follow-up and Use in a French University Hospital

Isabelle Furet, Violaine Closson, Isabelle Madelaine and Pierre Faure

**ABSTRACT**

*Granulocyte Colony-Stimulating Factor or G-CSF (NEUPOGEN®) was approved for use in France in November 1991 for prevention of chemotherapy-induced neutropenia. This retrospective study was conducted at Saint-Louis Hospital, Paris, France, from November 1991 to March 1993 with a more detailed analysis of patient profiles for courses ordered between November 1991 and December 1992. Data were collected on standardized G-CSF-treatment summary forms. The purpose of the study was to define, in clinical terms, the patients treated by G-CSF to determine the average cost per course of therapy and its impact on the hospital pharmacy budget.*

*From November 1991 to December 1992 data from 307 patient profiles were collected and analyzed. The subcutaneous route was the preferred route and only 16.6% of courses were administered intravenously. 45.6% of patients received a single course, 24.3% received two courses, and 30.1% received more than two courses. Each patient completed an average of 2.3 courses at an average cost per course of $2,000.00 (Canadian dollars). During March 1993, 50% of vials dispensed were administered to outpatients.*

*During the 14-month period, an average of 613.8 vials were dispensed per month corresponding to an average monthly expenditure of $104,000.00 (Canadian dollars). In the first 12 months following the commercial availability of G-CSF, G-CSF expenditures accounted for 8% of the pharmacy budget.*

**Key Words:** *chemotherapy, cost, DUE, G-CSF, neutropenia.*

**Can J Hosp Pharm 1995; 48:90-97**

**RÉSUMÉ**

*Le facteur de stimulation des colonies -granulocytes ou G-CSF (NEUPOGEN®) a été approuvé en France en novembre 1991, pour la prévention de la neutropénie d'origine chimiothérapeutique. L'étude rétrospective qui a été menée à l'hôpital Saint-Louis de Paris, en France, de novembre 1991 à mars 1993 a permis d'analyser plus en détail les profils des patients pour les traitements prescrits entre novembre 1991 et décembre 1992. Les données ont été recueillies sur des formulaires standardisés de résumé des traitements au G-CSF. Le but de l'étude était de définir, en termes, cliniques le type de patients traités au G-CSF, de déterminer le coût moyen par traitement et son impact sur le budget de la pharmacie d'hôpital.*

*De novembre 1991 à décembre 1992, les chercheurs ont recueilli des données sur le profil de 307 patients, et les ont analysées. La voie d'administration privilégiée était la voie sous-cutanée; seulement 16,6 % des traitements ont été administrés par voie intraveineuse. En tout, 45,6 % des patients n'ont reçu qu'un seul traitement, 24,3 % deux traitements et 30,1 % plus de deux traitements. Chaque patient a reçu en moyenne 2,3 traitements pour un coût moyen de 2 000 $ canadiens par traitement. En mars 1993, 50 % des flacons utilisés ont été administrés en clinique externe.*

*Au cours de la période d'étude de 14 mois, on a administré en moyenne 613,8 flacons par mois, pour une facture moyenne mensuelle de 104 000 $ canadiens. Dans les 12 mois qui ont suivi la mise en marché du G-CSF, ce dernier comptait pour 8 % du budget de la pharmacie.*

**Mots Clés :** *chimiothérapie, coût, G-CSF, neutropénie, RUM*

## INTRODUCTION

Recombinant methionyl human Granulocyte-Colony Stimulating Factor or G-CSF (NEUPOGEN®, Amgen, USA) is a hematopoietic growth factor.[1] G-CSF distinguishes itself from other growth factors by its specificity for neutrophils and its effects which are limited to the human myeloid lineage.[2,3] Its administration produces a rapid and substantial increase in mature peripheral blood neutrophils[4] which possess normal function. To elicit this activity, G-CSF must bind to a specific receptor located on the surface of the hematopoietic progenitor cell.[5-7]

G-CSF was approved for use in France in November 1991 for chemotherapy-induced neutropenia in non-myeloid malignancies. It was the first hematopoietic growth factor registered in France. The marketing approval was based on criteria of pharmaceutical quality, efficacy, and safety. However, due to its high purchase price and since its activity was far from being well known at the time, the French Health Ministry restricted the use of G-CSF. French

**Isabelle Furet,** Ph.D., is a pharmacist, Department of Pharmacy, Saint-Louis Hospital, Paris, France.
**Violaine Closson,** Ph.D., is a pharmacist, Department of Pharmacy, Saint-Louis Hospital.
**Isabelle Madelaine,** Ph.D., is a pharmacist, Department of Pharmacy, Saint-Louis Hospital.
**Pierre Faure,** Ph.D., is a pharmacist, Department of Pharmacy, Saint-Louis Hospital.
**Address Correspondence to:** Isabelle Furet, Ph.D., Department of Pharmacy, Saint-Louis Hospital, 1 Avenue Claude Vellefaux, 75010 Paris, France.

authorities recommended that G-CSF prescribing be restricted to qualified oncologists for defined cytotoxic chemotherapy regimens. G-CSF use was restricted to hospitals and required that the chemotherapy had to be composed of at least two drugs at doses above those indicated in Table I. As a result of these restrictions, an "Inclusion Report Form" (Appendix A) or a "Follow-up Report Form" (Appendix B) had to be completed. Each hospital pharmacy department ensured completion of these forms to prevent non-authorized use. This restricted approval was specific for France.

In July 1992, following the completion of additional clinical trials, G-CSF became available to all patients with severe chemotherapy-induced neutropenia, defined as an absolute neutrophil count below 0.5 x $10^9$ per litre, and to patients receiving autologous or allogenic bone marrow transplantation. Chemotherapy-induced myelosuppression often results in treatment delays and/or dose reductions which might affect the outcome in chemosensitive malignancies.[8-10] When given after myelosuppressive cytotoxic chemotherapy, G-CSF is effective in preventing and correcting chemotherapy-induced neutropenia.[11-14] This benefit is also observed in patients receiving high-dose chemotherapy followed by bone marrow transplantation.[15-17]

**Table I. Required Combination Chemotherapy Doses for G-CSF Qualification**

| DRUGS | COMBINATION THERAPY 2 Agents Dose per Cycle (mg/m²) | COMBINATION THERAPY More than 2 Agents Dose per Cycle (mg/m²) |
|---|---|---|
| Aclarubicin | >80 | >80 |
| Amsacrin | >300 | >300 |
| Busulfan | >400 | >400 |
| Carboplatin | >400 | >300 |
| Carmustine | - | - |
| Chlorambucil | - | >30 |
| Chlormethine | >12 | >12 |
| Cisplatin | - | >80 |
| Cyclophosphamide | >1000 | >1000 |
| Cytosine arabinoside | >500 | >500 |
| Dacarbazine | - | >400 |
| Daunorubicin | >200 | >200 |
| Doxorubicin | >50 | >50 |
| Elliptinium | >240 | >240 |
| Epirubicin | >75 | >75 |
| Etoposide | >360 | >360 |
| Fluorouracil | - | >2000 |
| Fotemostine | - | - |
| Ifosfamide | >4500 | >3000 |
| Lomustine | - | - |
| Melphalan | - | >30 |
| Mercaptopurine | - | - |
| Methotrexate | - | - |
| Mitomycin | - | - |
| Mitoxantrone | >12 | >12 |
| Pirarubicin | >50 | >40 |
| Procarbazine | - | >700 |
| Teniposide | >200 | >200 |
| Thiotepa | >40 | >30 |
| Vinblastine | >12 | >10 |
| Vincristin | - | - |
| Vindesine | - | >6 |
| Vinorelbine | >60 | >50 |
| Zorubicin | >600 | >400 |

This retrospective study was carried out at Saint-Louis University Hospital, Paris, France. This 800-bed hospital treats many oncology/hematology patients. It has six oncology/hematology medical services with a total of 170 beds. This retrospective evaluation follows the evolution of G-CSF use and was performed in order to define, in clinical terms, the patients treated by G-CSF, determine the average cost per course of therapy, and evaluate the impact of G-CSF on the hospital pharmacy budget. This study was limited to the assessment of the patients treated by G-CSF in which a prescription report form was completed. The impact of G-CSF on health care cost, evaluating cost savings, was considered to be beyond the scope of this study.

## METHODS

Information about patients was collected on standardized prescription report forms kept by the pharmacy. For each patient, prescribers were required to complete the "Inclusion Report Form" (Appendix A) when G-CSF was ordered for the first time for a patient. For each subsequent prescription, prescribers were required to complete the "Follow-up Report Form" (Appendix B). If the information was not complete the pharmacy would not dispense G-CSF.

G-CSF is administered once daily according to patient weight. The recommended dose in France is 5 mg per kilogram body weight per day for conventional chemotherapy regimens, and 10 mg per kilogram per day for

bone marrow transplantation (autologous or allogenic transplantation). G-CSF should be administered at least 24 hours after the last anticancer agent is administered. The recommended duration of G-CSF treatment is 10 to 14 days for each cycle given after conventional chemotherapy regimen. At the Saint-Louis Hospital the pharmacy dispensed either 300 or 480 mg vials directly to the patient ward.

The Inclusion Report Form (Appendix A) for each patient provided the pharmacist with information on the diagnosis, previous and current chemotherapy regimens, current blood counts, the dose and duration of G-CSF treatment, and the intent of treatment. Only the Inclusion Report Forms (Appendix A) provided information as to whether G-CSF was used for prevention or treatment of chemotherapy-induced neutropenia. Follow-up Report Forms (Appendix B), necessary for subsequent courses, provided information about intercurrent infectious diseases and the effectiveness of the previous course. These forms also provided information on the period between two consecutive courses of G-CSF, indicating if cycles of chemotherapeutic agents had been delayed and/or the dosage reduced. The G-CSF treatment, number of courses, interval between courses, duration of G-CSF treatment, method of administration, the dose, and number of vials used were recorded for each G-CSF course for each patient. Reasons for chemotherapy dose reduction and/or an increase and the duration between courses were not analyzed due to the lack of explicit explanations contained in the Report Forms. Severe chemotherapy-induced neutropenia plus leucopheresis were included as indications for G-CSF beginning in July 1992. However, since the Report Forms (Appendix A and B) were developed prior to this and did not require entry of this information, it is difficult to determine the number of courses which were prescribed for cytopheresis. When a course was prolonged, the order to prolong the therapy was counted as an additional prescription. Consequently, the number of prescriptions exceeded the number of courses.

During one month (March 1993), the number of G-CSF vials dispensed to outpatients was tabulated to estimate the proportion of vials that were being used by outpatients.

## RESULTS

During the first 17 months of commercial availability of G-CSF in France (from November 1991 to March 1993), a total of 393 cancer patients admitted to Saint-Louis Hospital were treated with G-CSF. Over this 17-month period this corresponds to an average of 23.1 new patients per month. However, this number progressively increased from three in November 1991 to 37 in March 1993, with some month-to-month fluctuations. The number of new patients and prescriptions per month is illustrated in Figure 1. The number of vials dispensed also accelerated steadily from November 1991, paralleling the number of prescriptions written. During this period, on average, 428.1 - 300 mg vials and 185.7 - 480 mg vials were dispensed per month. Overall, 69.7% of vials used were 300 mg vials. The usage of the 480 mg vials fluctuated during the study, decreasing transiently from 357 vials in October 1992 to 71 vials in January 1993, but then rebounded to 257 vials within two months. It is possible that some cost saving initiatives induced the transient drop. Figure 2 illustrates the number of 300 mg and 480 mg vials of G-CSF used per month.

In accordance with the authorized indications, 94.8% of patients were prescribed G-CSF by either an oncologist or hematologist. Cancer chemotherapy was indicated for both hematologic malignancies and solid tumours and 78% of these were hematologic malignancies. The single most prevalent malignancy was non-Hodgkin's lymphoma (52.8% of patients) (Table II). The interval between the end of chemotherapy

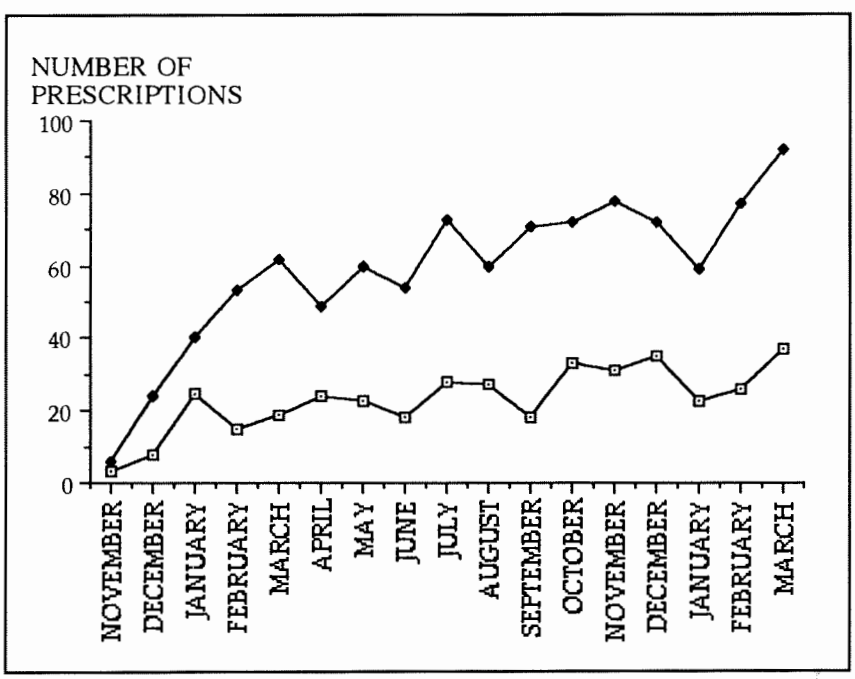


**Figure 1. Number of new patients and prescriptions per month between November 1991 to March 1993. Closed diamonds represent new prescriptions and open squares represent new patients.**

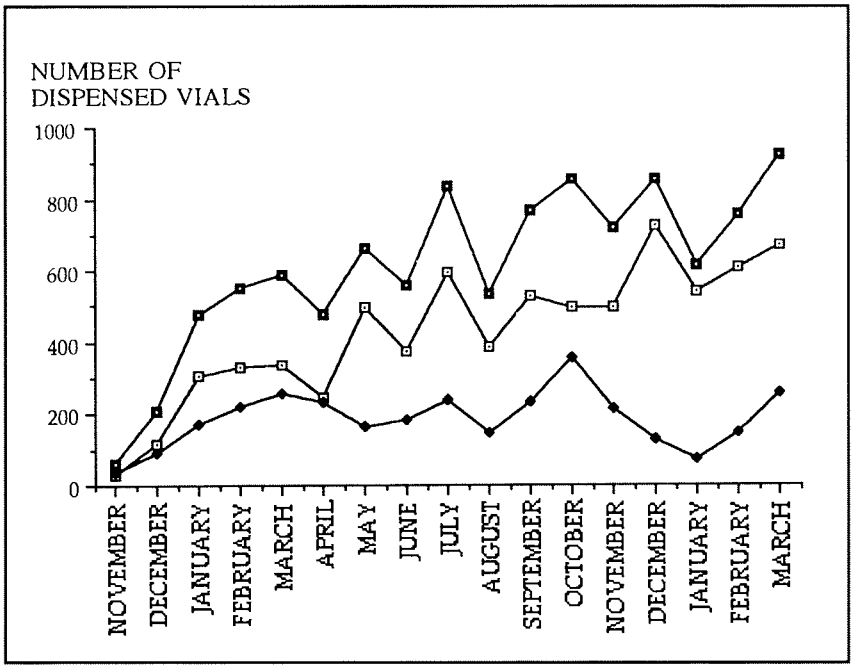


**Figure 2.** **Number of 480 mg vials (closed diamonds), 300 mg vials (open squares), and total number of vials (closed squares) dispensed per month between November 1991 and March 1993.**

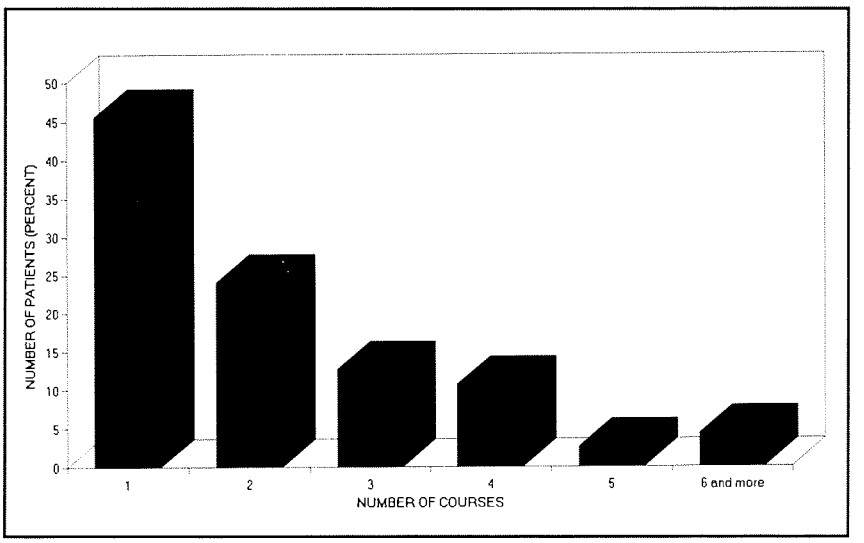


**Figure 3.** **Percentage of patients receiving one or more courses of G-CSF between November 1991 and December 1992.**

and administration of G-CSF was left to the assessment of the physician and ranged from one to seven days. A further 20.2% of patients were prescribed G-CSF related to bone marrow transplantation.

The recommended dose for bone marrow transplantation is 10 mg/kg, although clinicians were found to administer G-CSF at a dose of 5 mg/kg for all indications. 96% of G-CSF courses were dispensed at the dose of 5 mg/kg per day even though 20.2% of patients received bone marrow transplantation. Only 0.8% of G-CSF courses were administered at the recommended dose for transplantation of 10 mg/kg of body weight per day. This percentage included patients getting leucopheresis.

**Table II.**

| MALIGNANCIES | PERCENT |
|---|---|
| non-Hodgkin's lymphoma | 52.8 |
| Hodgkin's disease | 6.2 |
| myeloma | 4.2 |
| acute leukaemia | 7.5 |
| chronic leukaemia | 4.6 |
| aplasia | 1.3 |
| myelodysplasia | 1.4 |
| breast cancer | 5.2 |
| ovarian cancer | 4.6 |
| lung cancer | 3.6 |
| testicular cancer | 1.6 |
| various cancers | 7.0 |

Patients prescribed G-CSF with curative intent accounted for 24.4%, and 77.3% of these patients had aplasia associated with clinical signs of infection, and 14.7% had neutropenia (without aplasia) associated with infection. The remaining 8% of patients had neither infection nor neutropenia. This indicates that aplasia associated with infectious episodes occurred in more than 75% of cases, and 92% of the patients prescribed G-CSF with a curative intent were found to have infection.

## Analysis of Patient Profiles

The analysis of G-CSF patient profiles was restricted to a 14-month period (from November 1991 to December 1992) in which 721 G-CSF courses were documented for 307 patients. During this period only two prescription Report Forms were not interpretable through lack of information.

The mean age of patients treated with G-CSF was 43 years (range; 3 to 80 years). The majority (57%) of these patients were male. Each patient completed a mean of 2.3 cycles with 45.6% of patients (140 of 307) completing one cycle of G-CSF, 24.3% (74) completing two cycles and 30.1% (93) completing more than two cycles (see Figure 3). Both subcutaneous and intravenous routes of

administration were used. Intravenous route of administration was only used for 16.6% (120 out of 721) of the courses. The duration of G-CSF treatment was not always sufficient to obtain a satisfactory neutrophil recovery and ranged from two to 57 days. However, duration of treatment did not exceed 14 days in 89.8% of courses. In 35.3% of courses G-CSF was administered for 10 days, and in a further 13.2% of courses G-CSF was administered for 14 days. The average duration of therapy was 11 days. When the course was prolonged, the order to prolong the therapy was counted as an additional prescription. Consequently, the number of prescriptions (774) was greater than the number of courses as 8.4% of courses (61) were prolonged by a new prescription.

Complete data were not available for the final course in any patient. Therefore, complete data were only available for 414 courses (721 less 307). During the 14-month study period, the dose of chemotherapy was reduced or there was a delay in dosing prior to the next cycle in 8.5% of courses (35 out of 414). In seven courses there was a reduction in the dose and prolonged delay between cycles, in 18 courses there was a prolonged duration between cycles without reduction in the dose, and in an additional 10 courses the dose was reduced without an increase in the interval between cycles. The reasons for reducing the dose or modifying the frequency of repeated chemotherapy cycles included neutropenia (five courses), infection (two courses), neutropenia associated with infection (17 courses), and an unknown reason (11 courses). Cases of neutropenia associated with infection were represented in almost 50% of cycles (17 out of 35).

### Cost

The unit price of 300 mg vials is 750.66 French Francs (approximately $150.00 Canadian per vial) and 480 mg vials is 1197.27 French Francs (approximately $240.00 Canadian). The average monthly expenditure for G-CSF at Saint-Louis Hospital was approximately 520,000 French Francs ($104,000.00 Canadian). Over the 14-month study period, total G-CSF expenditures reached 7.30 million French Francs ($1.46 million Canadian). These expenditures come entirely from the hospital budget and represent approximately 8% of the hospital pharmacy's drug expenditures. Given that there were 774 prescriptions filled during the study period, the average cost of a G-CSF prescription is 9,720 French Francs (about $2,000.00 Canadian). This estimate includes only G-CSF acquisition cost and does not include the cost of laboratory monitoring, adverse effects, hospital hotel costs, nursing time, or treatment of failures.

## DISCUSSION

The funding of public hospitals is similar in Canada and France. In France, the government finances public hospitals entirely and annual budgets are determined by the Social Affairs and Health Ministry. The total cost of both inpatient and outpatient treatment is borne by the hospital. This is why an evaluation of the outpatient prescription volume was considered important. Although the subcutaneous route of therapy is likely to be less expensive than intravenous therapy due to the savings in nursing time, since it is well tolerated, it permits the continuation of therapy in the home setting. We observed that approximately 50% of vials dispensed from the pharmacy in March 1993 were administered on an outpatient basis. This was definitely unexpected and since this amount was not included in the hospital budget, it permitted us to obtain a substantial budgetary increase for outpatient delivery.

Approximately 50% of patients completed only one course of G-CSF. This is largely due to the short duration of the study and because approximately 20% of patients received G-CSF for bone marrow transplantation. The intervals between courses varied widely (15 days to more than one month) due to the dependence on the chemotherapy regimen. When chemotherapy induced-neutropenia occurred between cycles of G-CSF, patients were hospitalized and received intravenous antibiotic therapy. Approximately 50% of these G-CSF courses were associated with both neutropenia and an infection.

Although infusion of autologous peripheral blood progenitor cells (harvested by leucopheresis followed by G-CSF) has been investigated as an adjunct to autologous bone marrow transplantation in patients receiving high-dose chemotherapy[15,16] it was not initially an authorized indication by the French authorities. Since our Report Forms were designed based on the initial indications, the forms did not include cytopheresis as an indication. Therefore, even when cytopheresis became an approved indication, we were unable to obtain this information for our standardized forms.

Nevertheless, due to its high purchase cost (about $2,000.00 Canadian per course on average), cost considerations have limited the indications of G-CSF to specifically-defined risk situations.[8] The system established jointly by pharmacy and prescribers at Saint-Louis Hospital, included a table which specified doses of severely myelosuppressive chemotherapy regimens (Table I) and ensured delivery of G-CSF to appropriate patients. If the information was not complete, the pharmacists would not dispense the G-CSF.

After more than one year of G-CSF use, interesting and promising outcomes have been observed at Saint-Louis Hospital. The greatest challenge will be to continue to identify the areas where the G-CSF is most beneficial. Further work remains to be done to determine the effects of G-CSF on survival and

mortality by a reduction in deaths due to infections.

## REFERENCES


1. Metcalf D. The colony stimulating factors : discovery, development, and clinical applications. *Cancer* 1990; 65: 2185-95.
2. Shigetaka A. Human granulocyte colony stimulating factor : Its basic aspects and clinical applications. *Am J Pediatr Hematol Oncol* 1991; 13: 400-13.
3. Bussolino H, Wang JM, Defilippi F, et al. Granulocyte- and granulocyte-macrophage colony-stimulating factors induce human endothelial cells to migrate and proliferate. *Nature* 1989; 337: 471-3.
4. Sheridan WP, Begley CG, Juttner CA, et al. Effects of peripheral blood progenitor cells mobilised by Filgrastim (G-CSF) on platelet recovery after high-dose chemotherapy. *Lancet* 1992; 339: 640-4.
5. Hanzono Y, Hosoi T, Kuwaki T, et al. Structural analysis of the receptors for granulocyte colony-stimulating factor on neutrophils. *Exp Hematol* 1990; 18: 1097-103.
6. Demetri GD, Griffin JD. Granulocyte colony-stimulating factor and its receptor. *Blood* 1991; 78: 2791-808.
7. Gordon MY. Hematopoietic growth factors and receptors : bound and free. *Cancer cells* 1991; 3: 127-32.
8. Faulds D, Lewis JW, Milne RJ. Recombinant Granulocyte Colony-Stimulating Factor (r G-CSF) : pharmacoeconomic considerations in chemotherapy-induced neutropenia. *Pharmacoeconomics* 1992; 1: 231- 49.
9. Meyer RM, Hryniuk WM, Goodyear MDE. The role of dose intensity in determining the outcome of intermediate-grade non-Hodgkin's lymphoma. *J Clin Oncol* 1991; 9: 339-47.
10. Kwak LW, Halpern J, Olshen RA, et al. Prognostic significance of actual dose intensity in diffuse large cell lymphoma : Results of a tree-structured survival analysis. *J Clin Oncol* 1990; 8: 963-77.
11. Morstyn G, Campbell L, Souza LM, et al. Effects of granulocyte colony stimulating factor on neutropenia induced by cytotoxic chemotherapy. *Lancet* 1988; 1: 667-72.
12. Trillet-Lenoir V, Green J, Manegold C, et al. Recombinant granulocyte colony stimulating factor reduces the infectious complications of cytotoxic chemotherapy. *Eur J Cancer* 1993; 29: 319-24.
13. Yoshida T, Nakamura S, Ohtake S, et al. Effect of granulocyte colony-stimulating factor on neutropenia due to chemotherapy for non-Hodgkin's lymphoma. *Cancer* 1990; 66: 1904-9.
14. Crawford J, Hozer H, Stoller R, et al. Reduction by granulocyte colony-stimulating factor of fever and neutropenia induced by chemotherapy in patients with small-cell lung cancer. *N Eng J Med* 1991; 315: 164-70.
15. Sheridan WP, Morstyn G, Wolf M, et al. Granulocyte colony-stimulating factor and neutrophil recovery after high-dose chemotherapy and autologous bone marrow transplantation. *Lancet* 1989; 2: 891-4.
16. Taylor K, Jagannath S, Spitzer G, et al. Recombinant human granulocyte colony-stimulating factor hastens granulocyte recovery after high-dose chemotherapy and autologous bone marrow transplantation in Hodgkin's disease. *J Clin Oncol* 1989; 7: 1791-9.
17. Masaoka T, Takaku F, Kato S, et al. Recombinant human granulocyte colony stimulating factor in allogeneic bone marrow transplant. *Exp Hematol* 1989; 17: 1047-50.
18. Coiffier B, Gisselbrecht C, Herbrecht R, et al. LNH-84 Regimen : a multicenter study of intensive chemotherapy in 737 patients with aggressive malignant lymphoma. *J Clin Oncol* 1989; 7: 1018-26.
19. Coiffier B, Gisselbrecht C, Vose JM, et al. Prognostic factors in aggressive malignant lymphomas : description and validation of a prognostic index that could identify patients requiring a more intensive therapy. *J Clin Oncol* 1991; 9: 211-9.
20. Biron P, Goldstone A, Colombat Ph, et al. A new cytoreductive conditioning regimen before ABMT for lymphomas : the BEAM protocol - A phase II study - in autologous marrow transplantation. In Dicke KA, Spitzer G, Zander AR. eds 1987; Proceedings of the third international symposium, USA University of Texas MD Anderson Hospital and Tumor Institute): 593-600.
21. Shriber JR, Negrin RS. Use and toxicity of the colony-stimulating factors. *Drug Safety* 1993; 8: 457-68.

## Appendix A

*To return to pharmacist*

INCLUSION REPORT FORM/NEUPOGEN° PRESCRIPTION

NAME ❑❑❑ Date of birth /_ _/_ _/_ _/
Firstname_____ sexe : F /M_____ N° of inclusion : 17138

1) Hospital_____ Medical service_____
Pharmacist_____ Prescriber _____
Signature

2) Anamesis
Diagnosis _____ Evolution duration : /_ _/years /_ _/months
Actual stage ❑ localized-stage ❑ metastatic
❑ extensive-stage ❑ no clinical sign
*Previous radiotherapy : Y /N_____
1- Territory _____ End date /_ _/_ _/_ _/
2- Territory_____ End date /_ _/_ _/_ _/
*Previous chemotherapy : Y /N____ Number of regimens /_ _/

*Previous regimens:* *Toxicity grade* WBC ❑ 3 ❑ 4 PLA ❑ 3 ❑ 4
1- Regimen_____ End date /_ _/_ _/_ _/ ❑ 3 ❑ 4 ❑ 3 ❑ 4
Number of cycles _____
2- Regimen_____ End date /_ _/_ _/_ _/ ❑ 3 ❑ 4 ❑ 3 ❑ 4
Number of cycles _____
*Previous cytokin : Y / N_____ ❑Interferon ❑ IL2 ❑ IL3
❑ HGF Name of HGF :_____

3) Inclusion parameters
*Regimen Number of cycles_____
❑ Adjuvant ❑ Tumoral reduction with curative intent ❑ Palliative tumoral reduction

*For each cycle*
Agent 1 :_____ Dose (mg/m2)_____ Number of days /_ _/
Agent 2 :_____ Dose (mg/m2)_____ Number of days /_ _/
Agent 3 :_____ Dose (mg/m2)_____ Number of days /_ _/
Agent 4 :_____ Dose (mg/m2)_____ Number of days /_ _/
Agent 5 :_____ Dose (mg/m2)_____ Number of days /_ _/

*HGF treatment : ❑ Preventive intent ❑ Curative intent
Date of beginning/_ _/_ _/_ _/
If curative intent, justification
1) Undocumented fever ❑ Date : /_ _/_ _/_ _/
2) Minor infection ❑ Date : /_ _/_ _/_ _/
3) Documented septicemia ❑ Date : /_ _/_ _/_ _/
4) Others_____ ❑ Date : /_ _/_ _/_ _/

*Blood counts :
WBC ($10^9$/l) /__/__/__/./__/__/ Neutrophils ($10^9$/l)/__/__/__/./__/__/
Monocytes ($10^9$/l) /__/__/./__/ Platelets ($10^9$/l) /__/__/__/./__/__/
Hemoglobin (g/dl) /__/__/./__/

4) Neupogen° treatment
Date of beginning/_ _/_ _/_ _/ Expected duration /_ _/ days
Dose (µg/m2/j) / _ / _ / _ /or (µg/kg/j)/ _ / _ / Daily total dose (µg) / _ / _ / _ /
Route : ❑ Subcutaneous ❑ Intravenous
Height /__/__/__/cm Body weight /__/__/__/./__/kg Body surface/__/./__/__/ $m^2$

Date of dispensation /_ _/_ _/_ _/
Pharmacist_____
Signature

**Appendix B**

*To return to pharmacist*

FOLLOW UP REPORT FORM/NEUPOGEN° PRESCRIPTION

NAME ❑❑❑ Date of birth /_ _/_ _/_ _/
Firstname_____ sexe : F /M_____ N° of inclusion : 17138

## Follow up of the last Neupogen°cycle

Date of beginning /_ _/_ _/_ _/ Date of the end /_ _/_ _/_ _/
Total dose /__/__/__/__/µg Route ❑SC ❑ IV

1)Did the patient present fever or infection under Neupogen° treatment ?
(only if preventive intent) ❑Yes ❑No

If yes
❑ Febrile neutropenia (Neutrophils < 1 $10^9$/l and temperature level >38,2°C, the same day)
❑ Clinical infection :
❑ Microbiologically documented infection
- microbial agent _____
- isolation site _____
❑ Antibiotherapy IV Number of days/_ _/_ _/
❑ Hospitalisation Number of days/_ _/_ _/

2) Neutropenia episode, grade 4 ❑Yes ❑No
Thrombopenia episode, grade 3/4 ❑Yes ❑No
Platelets transfusion ❑Yes ❑No If yes, number of units /_ _/_ _/

3) Blood count at the end of Neupogen°treatment Date /_ _/_ _/_ _/
WBC ($10^9$/l) /__/__/__/./__/__/ Neutrophils ($10^9$/l) /__/__/__/./__/__/
Platelets ($10^9$/l) /__/__/__/./__/__/

## Informations about the new cycle Cycle N°/__/

1) Chemotherapy Was period between the two cycles prolonged ? ❑Yes ❑No
Were doses reduced ? ❑Yes ❑No

2) Blood count between new Neupogen°treatment Date /_ _/_ _/_ _/
WBC ($10^9$/l)/__/__/__/./__/__/ Neutrophils ($10^9$/l)/__/__/__/./__/__/
Platelets ($10^9$/l) /__/__/__/./__/__/

3) New prescription of Neupogen°

Date of beginning/_ _/_ _/_ _/ Expected duration /_ _/ days
Dose (µg/m2/j) / _ / _ / _ /or (µg/kg/j)/ _ / _ / Daily total dose (µg) / _ / _ / _ /
Route : ❑ Subcutaneous ❑ Intravenous
Height /__/__/__/cm Weight/__/__/__/./__/kg Body surface/__/./__/__/$m^2$

Name of prescriber Signature of prescriber

_____

Date of dispensation /_ _/_ _/_ _/
Pharmacist_____
Signature