Original Article

Journal of Oncology Pharmacy Practice

J Oncol Pharm Practice
0(0) 1–10

DOI: 10.1177/1078155212473001
opp.sagepub.com
SAGE

A retrospective study of patients' out-of-pocket costs for granulocyte colony-stimulating factors

Karen Tomic*
Oxford PharmaGenesis, Newtown, PA, USA

Stacey Long
Truven Health Analytics, Cambridge, MA, USA

Xiaoyan Li
Amgen Inc., Thousand Oaks, CA, USA

An-Chen Fu
HealthCore, Wilmington, DE, USA

Tzy-Chyi Yu
HealthCore, Wilmington, DE, USA

Richard Barron
Amgen Inc., Thousand Oaks, CA, USA

Abstract

Objective: With rising healthcare costs, there is an increasing concern with the burden of out-of-pocket costs on cancer patients. This study examined patients' out-of-pocket expenditures for granulocyte colony-stimulating factors, pegfilgrastim and filgrastim, which are given to cancer patients receiving myelosuppressive chemotherapy and have been shown to decrease the incidence of febrile neutropenia.

Methods: Adult patients who received chemotherapy and granulocyte colony-stimulating factors in the outpatient setting in the United States between January 2007 and June 2010 were evaluated using medical and pharmacy claims data from two healthcare data sources, the MarketScan® Commercial and Medicare Supplemental Databases and the HealthCore Integrated Research Database℠. The distribution of out-of-pocket costs for granulocyte colony-stimulating factors per patient and per administration was described for each quarter. Longitudinal analyses of out-of-pocket costs for granulocyte colony-stimulating factors were also performed for patients with continuous health plan eligibility during each calendar year from 2007 to 2009.

Results: The pattern of out-of-pocket expenditures for pegfilgrastim and filgrastim was generally consistent between the databases and over time. On average, about 65%–75% of patients had zero quarterly out-of-pocket costs for granulocyte colony-stimulating factors. Across the years, the mean quarterly out-of-pocket costs per patient were $100–$150 and $50–$80 for pegfilgrastim and filgrastim, respectively. The mean quarterly out-of-pocket costs for granulocyte colony-stimulating factors per administration were $40–$70 and $8–$10, respectively.

*At the time of the study analysis, Karen Smoyer Tomic was an employee of HealthCore and then Thomson Reuters (presently Truven Health Analytics).

Corresponding author:
Karen Smoyer Tomic, US Practice Lead, Value Demonstration/Market Access, Oxford PharmaGenesis Inc., 503 E. Washington Avenue, Newton, PA 18940, USA.
Email: Karen.Tomic@pharmagenesis.com

Conclusion: In this retrospective analysis of medical and pharmacy claims data, most patients who received chemotherapy and granulocyte colony-stimulating factors in 2007 to 2010 had incurred no quarterly out-of-pocket costs associated with G-CSF use.

Keywords
Out-of-pocket costs, granulocyte colony-stimulating factors, pegfilgrastim, filgrastim, claims database

Introduction

As the costs of cancer care continue to rise, there is growing concern with the increasing out-of-pocket burden on patients with cancer, especially those in need of chemotherapy. Out-of-pocket costs may have several consequences, including limiting patient access to care and decreasing patient compliance with prescribed treatment, which may negatively impact health outcomes; patient financial well-being may also be adversely affected.[1–5] Several studies have evaluated out-of-pocket expenditures on patients receiving cancer care. In a survey of patients with breast cancer who had private, Medicare, or Medicaid insurance, the average out-of-pocket costs per month were $597 overall, $487 within 6 months of diagnosis, $912 from 6 to 12 months after diagnosis, and $390 after 12 months of diagnosis (all estimates were reported in 2004 dollars).[6] In another study, the incidence of patients with high out-of-pocket burdens (defined as out-of-pocket shares greater than 20% of pre-tax family income) was higher for patients with cancer (13%) than patients with other chronic conditions (10%) and those without chronic conditions (4%).[7] As patients are becoming more involved in medical decision-making, these high economic burdens may affect treatment choices for patients with cancer and may also affect the decisions of physicians and/or patients to use recommended treatments.

Febrile neutropenia (FN) is a common complication of myelosuppressive chemotherapy and is associated with morbidity and mortality, with estimates of mortality risk ranging from 7% to 20% among patients with FN-related hospitalization.[8] Treatment with granulocyte colony-stimulating factors (G-CSF) reduces the incidence of FN in patients with cancer receiving myelotoxic chemotherapy and helps keep patients on the scheduled dose and regimen to facilitate optimal chemotherapy outcomes.[9–12] Clinical guidelines recommend primary prophylaxis of a G-CSF when the risk for FN is at least 20%.[13–15] The risk assessment involves several factors, including disease type, chemotherapy regimen, treatment intent, and patient risk factors (older age, poor performance status, comorbidities including liver or renal dysfunction, pre-existing conditions [e.g., neutropenia and infection/open wounds], recent surgery, and prior chemo- or radiotherapy).[13] Filgrastim, a recombinant human G-CSF, is administered as multiple daily doses throughout the chemotherapy cycle, with the average number of administrations varying in clinical practice but generally fewer than those found effective in randomized clinical trials.[10,16–20] Pegfilgrastim, a pegylated form of filgrastim, is administered as a single dose per chemotherapy cycle.[11,21]

Given the growing concern regarding the costs of cancer care, we conducted a study to examine patients' out-of-pocket expenditures for G-CSF in an outpatient setting. Data were collected from two healthcare claims databases to evaluate quarterly out-of-pocket costs associated with G-CSF use for adult patients who received chemotherapy and pegfilgrastim or filgrastim.

Methods

Study design

This retrospective study evaluated patients who received chemotherapy and G-CSF in the outpatient setting in the United States between January 1, 2007 and June 30, 2010. The objective was to examine patients' out-of-pocket expenditures for pegfilgrastim and filgrastim. Medical and pharmacy claims data were collected from two healthcare databases, the MarketScan® database and the HealthCore Integrated Research Database^{SM} (HIRD^{SM}), to provide a representative sample of private health plans in the United States.

The MarketScan® Database used combined information from the MarketScan® Commercial Claims and Encounters Database and the MarketScan® Medicare Supplemental and Coordination of Benefits Database. These databases provide information on individuals covered by a variety of employer-sponsored private health insurance plans and employer-paid Medicare supplemental insurance. In the most recent full data year, the MarketScan® database contained information on approximately 56 million insured individuals. The database is considered to be nationally representative of persons with employer-sponsored health insurance with respect to geography, age, and gender. We used the MarketScan® Database to identify patients who received chemotherapy and G-CSF between January 1, 2008 and June 30, 2010. The MarketScan® data were first analyzed using medical claims for pegfilgrastim from 2008 only. In a subsequent analysis, MarketScan® data were analyzed

using medical and pharmacy claims for pegfilgrastim and filgrastim from January 1, 2009 to June 30, 2010.

The second database, the HIRD^{SM}, is assembled by WellPoint and provides information on over 40 million insured individuals covered by 14 geographically dispersed United States commercial health plans. We used the HIRD^{SM} to identify patients who received chemotherapy and G-CSF between January 1, 2007 and June 30, 2009. The HIRD^{SM} data were analyzed using medical and pharmacy claims for pegfilgrastim and filgrastim during this time period.

Eligibility criteria

Patients 18 years or older were included in the study if they had at least one claim for chemotherapy and at least one medical or pharmacy claim for pegfilgrastim or filgrastim in the outpatient setting between January 1, 2007 and June 30, 2010. The outpatient setting included both office and non-office (e.g., hospital outpatient) visits, as well as prescriptions filled at an outpatient pharmacy, and did not include emergency room visits. Patients were excluded if they had at least one medical claim for a bone marrow or stem cell transplant or had at least one medical claim indicating that services were provided in a skilled nursing facility or hospice during the study period.

Statistical analysis

The out-of-pocket costs for G-CSF per patient were calculated for each quarter of the calendar year from January 1, 2007 to June 30, 2010. Analyses were performed per quarter because a course of chemotherapy generally takes about 12–24 weeks (i.e., 1–2 quarters) to complete. The quarters were defined as follows: first quarter (Q1) includes January 1 to March 31; second quarter (Q2) includes April 1 to June 30; third quarter (Q3) includes July 1 to September 30; and fourth quarter (Q4) includes October 1 to December 31. The out-of-pocket costs for G-CSF per administration were also calculated for each quarter and were analyzed using medical claims data only; pharmacy claims were not included in the per administration analysis because the number of injections could not be determined from the available data (i.e., different number of injections filled with each prescription and inability to determine when injections were given). The out-of-pocket costs for pegfilgrastim per chemotherapy cycle were equivalent to out-of-pocket costs per administration because one pegfilgrastim injection was administered per cycle. The out-of-pocket costs for filgrastim per chemotherapy cycle were not analyzed due to possible variations in the number of filgrastim injections per cycle. All costs were adjusted to and reported as June 2010 dollars using the medical care component of the Consumer Price Index.

Analyses were further stratified by claim type (medical or pharmacy), outpatient setting (office or non-office) as recorded on the medical claim, and payment type (co-payment, co-insurance, or deductible). Longitudinal analyses of patients with continuous health plan eligibility during each calendar year from 2007 to 2009 were performed for the entire annual timeframe on the following four cohorts: (1) HIRD^{SM} 2007, (2) HIRD^{SM} 2008, (3) MarketScan® 2008, and (4) MarketScan® 2009.

Descriptive statistics on the out-of-pocket costs associated with G-CSF use, including means and standard deviations, are provided. Categorical data were summarized by frequency counts and/or percentages. Data for pegfilgrastim and filgrastim are presented separately.

Results

A total of 45,400 and 17,048 patients overall were analyzed in the MarketScan® and HIRD^{SM} databases, respectively. Table 1 presents the characteristics of patients (n = 28,979) from MarketScan® who received chemotherapy and G-CSF between January 1, 2009 and June 30, 2010. Approximately 71% of these patients were female, 29% were 65 years or older, and 26% had Medicare insurance. Furthermore, 23,704 and 8582 patients had at least one pegfilgrastim or filgrastim claim, respectively. The characteristics of patients from MarketScan® who received treatment in 2008 and patients from the HIRD^{SM} were similar to those shown in Table 1.

The pattern of patients' out-of-pocket costs associated with G-CSF use was generally similar between MarketScan® and the HIRD^{SM} and was consistent over time (Figures 1, 2, and 3). On average, 65%–75% of patients across databases who received chemotherapy and G-CSF between January 1, 2007 and June 30, 2010 incurred zero out-of-pocket costs for G-CSF in a quarter (Figure 1). Higher out-of-pocket costs associated with G-CSF use were observed in the first quarter compared with subsequent quarters of a calendar year. Across the years, the mean out-of-pocket costs per patient were \$100–\$150 and \$50–\$80 for pegfilgrastim and filgrastim, respectively, per quarter (Figure 2). In the 2008 MarketScan® analysis, the mean out-of-pocket costs per patient for pegfilgrastim were \$116 for those with commercial benefits and \$95 for those with Medicare supplemental benefits per quarter. The mean out-of-pocket costs for G-CSF per administration were \$40–\$70 and \$8–\$10 for pegfilgrastim and filgrastim, respectively, per quarter (Figure 3).

Table 1. Characteristics of patients included in MarketScan® 2009–Q2 2010 analysis.

Patient characteristics	Entire cohort N = 28,979
Sex, n (%)	
Male	8411 (29)
Female	20,568 (71)
Mean age, years (SD)	59 (12)
Age group, n (%)	
18–49 years	6328 (22)
50–64 years	14,170 (49)
65–74 years	5275 (18)
75 + years	3206 (11)
Payer, n (%)	
Commercial	21,575 (74)
Medicare	7404 (26)
Health plan type, n (%)	
Preferred provider organization	16,545 (57)
Comprehensive	4117 (14)
Health maintenance organization	3947 (14)
Point of service	2499 (9)
Other	1871 (6)
Capitated, n (%)	
Capitated	1811 (6)
Non-capitated	27,168 (94)
Geographic region, n (%)	
Northeast	4186 (14)
Midwest	8414 (29)
South	11,348 (39)
West	4914 (17)
Unknown	117 (0)
Urban/Rural, n (%)	
Urban	24,171 (83)
Rural	4703 (16)
Unknown	105 (0)
≥1 claim for a G-CSF during 2009–Q2 2010, n (%)	
Any pegfilgrastim	23,704 (82)
Any filgrastim	8582 (30)
Only pegfilgrastim	20,397 (70)
Only filgrastim	5275 (18)
Pegfilgrastim and filgrastim	3307 (11)

G-CSF: granulocyte colony-stimulating factors; SD: standard deviation.

Findings from the longitudinal analysis were similar across the four cohorts of patients with continuous health plan eligibility in a calendar year. Results of the MarketScan® 2009 cohort are shown as a representative sample of our findings. An average of 69% and 64% of patients who received pegfilgrastim and filgrastim, respectively, had zero out-of-pocket costs for G-CSF in a quarter (Figure 4 and Table 2). Furthermore, few patients who received pegfilgrastim and filgrastim (<6% and <3%, respectively, on average) had quarterly out-of-pocket costs for G-CSF reaching $500 or above (Figure 4). In patients who incurred non-zero quarterly out-of-pocket costs associated with G-CSF use, the mean out-of-pocket costs per patient were $324 and $146 for pegfilgrastim and filgrastim, respectively, per quarter. Moreover, in patients who received pegfilgrastim, the distribution of out-of-pocket expenditures for G-CSF by payment type was 81% for co-insurance, 14% for co-payment, and 5% for deductible. In patients who received filgrastim, the distribution of out-of-pocket expenditures for G-CSF was 36% for co-insurance, 60% for co-payment, and 5% for deductible.

The longitudinal analysis of the MarketScan® 2009 cohort stratified by claim type and outpatient setting is presented in Table 3. Most patients had medical claims for pegfilgrastim and filgrastim in an office setting. Pharmacy claims accounted for a smaller share of a patient's out-of-pocket burden for G-CSF (8% and 27% for pegfilgrastim and filgrastim, respectively) than medical claims in an office setting (78% and 64%, respectively). In patients who incurred non-zero quarterly out-of-pocket costs associated with G-CSF use in the medical office setting, the average number of administrations per quarter was 2.4 for pegfilgrastim and 5.5 for filgrastim. The mean out-of-pocket costs for G-CSF per administration were $137 and $26 for pegfilgrastim and filgrastim, respectively. Few patients received pegfilgrastim or filgrastim in a pharmacy setting. Most patients with pharmacy claims incurred non-zero out-of-pocket costs for pegfilgrastim (93%) and filgrastim (91%).

Discussion

This retrospective study showed that the majority of patients who received chemotherapy and G-CSF from 2007 to 2010 did not incur any incremental out-of-pocket costs associated with their G-CSF use during a quarter. Our findings from MarketScan® and the HIRD℠ were similar, and the results were consistent across years. Out-of-pocket costs for G-CSF in the first quarter were higher compared with subsequent quarters of a calendar year, which reflect the unmet deductibles and annual caps for out-of-pocket expenditures early in the year. Differences in costs were observed among the three settings (office, non-office, and pharmacy) and were attributed to the different insurance pay structures associated with each place of service. Approximately one-third of patients incurred non-zero out-of-pocket costs associated with

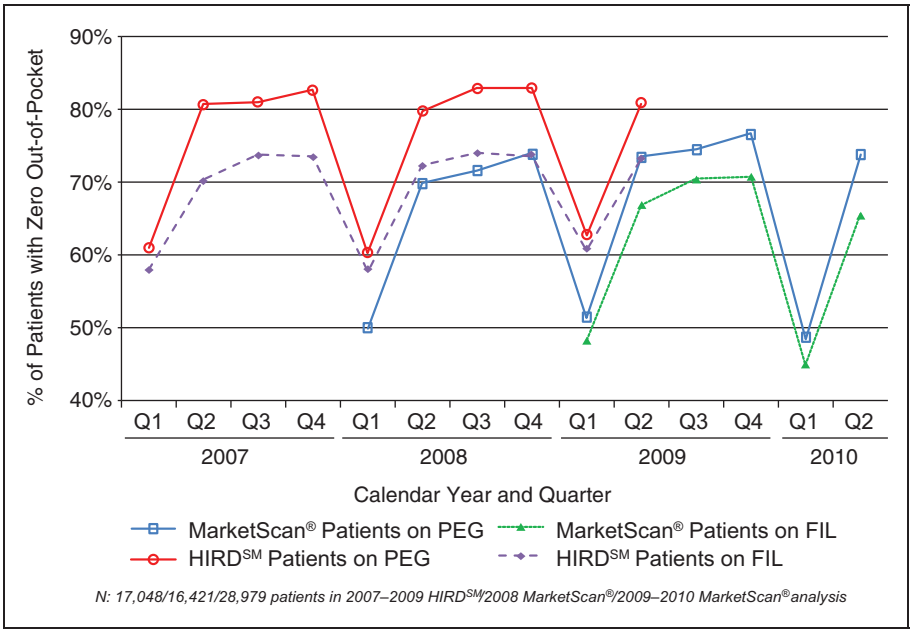

Figure 1. Percentage of patients with zero out-of-pocket costs for G-CSF.
G-CSF, granulocyte colony-stimulating factors; FIL, filgrastim; PEG, pegfilgrastim.

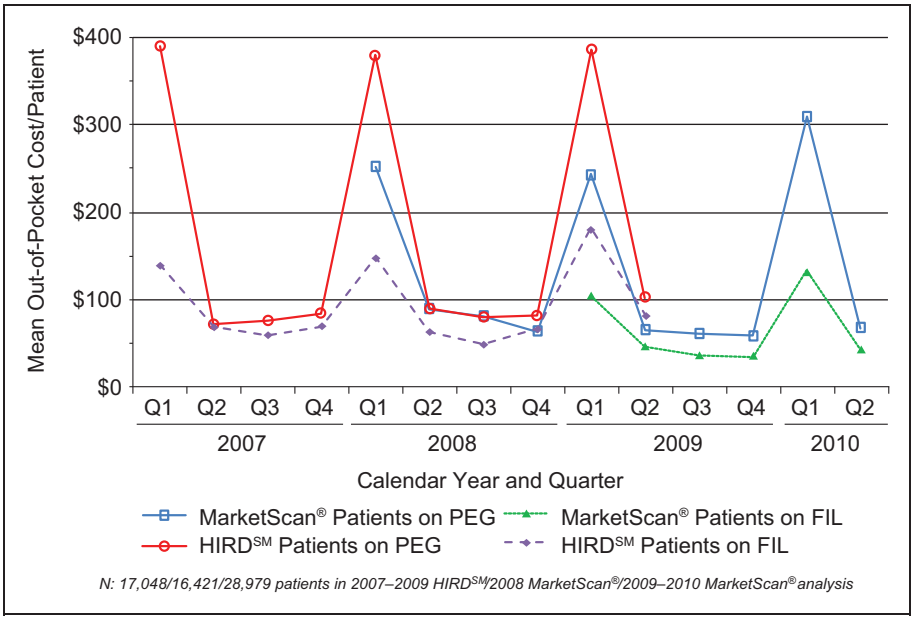

Figure 2. Mean out-of-pocket costs for G-CSF per patient. The analysis included patients with zero out-of-pocket costs.
G-CSF, granulocyte colony-stimulating factors; FIL, filgrastim; PEG, pegfilgrastim.

G-CSF use, which were partly due to co-payments in the pharmacy setting, which are typically independent of the deductible. This out-of-pocket burden may affect a patient's decision to use recommended treatments, such as pegfilgrastim and filgrastim.

Previous literature has shown that the average number of filgrastim injections per chemotherapy cycle used in clinical practice is lower than that administered in randomized clinical trials.[16–18,22–25] According to its package label, filgrastim should be administered daily for up to 2 weeks, until the absolute neutrophil count (ANC) has reached 10,000/mm^3 following the expected chemotherapy-induced neutrophil nadir.[10] The average daily doses of filgrastim required

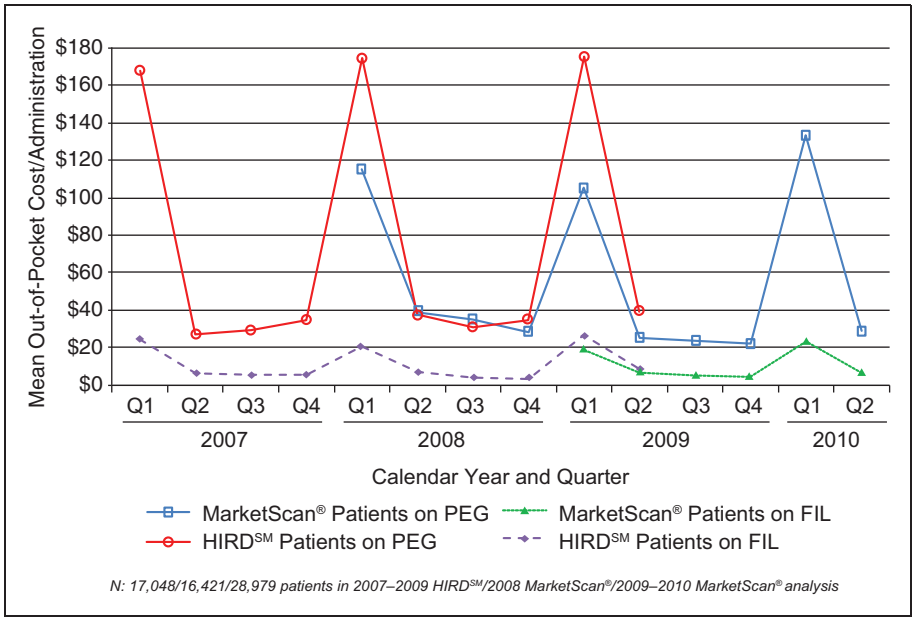

Figure 3. Mean out-of-pocket costs for G-CSF per administration. The analysis included patients with zero out-of-pocket costs and included medical claims only.
G-CSF, granulocyte colony-stimulating factors; FIL, filgrastim; PEG, pegfilgrastim.

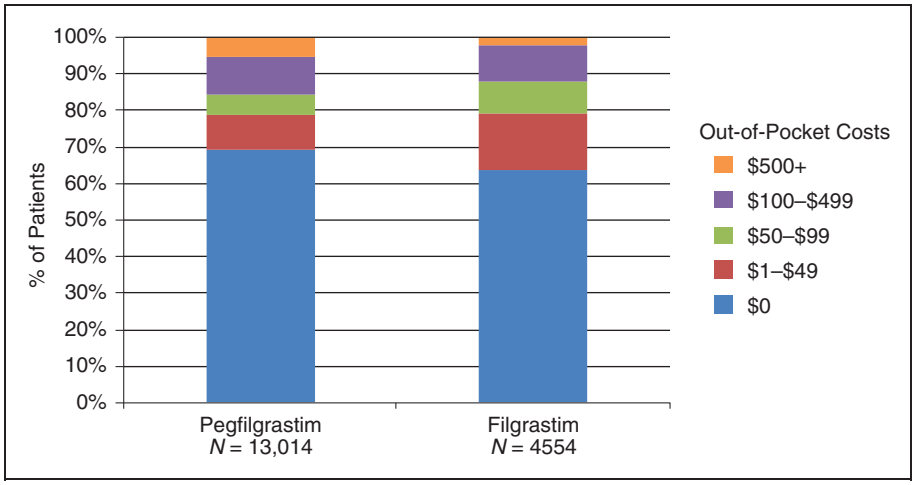

Figure 4. Distribution of patients by quarterly out-of-pocket costs for G-CSF (MarketScan® 2009 longitudinal cohort).
G-CSF, granulocyte colony-stimulating factors.

for post-nadir ANC recovery were 10–11 in registrational trials in patients with breast cancer receiving docetaxel and doxorubicin[19,20] and in a phase 3 trial in patients with small-cell lung cancer receiving cyclophosphamide, doxorubicin, and etoposide.[26] In addition, registrational trials have demonstrated that once per cycle pegfilgrastim and daily filgrastim (10–11 day administration) have similar efficacy in reducing the incidence of chemotherapy-induced neutropenia.[19,20] In clinical practice, however, filgrastim is often administered for fewer days (e.g. 4–6 days), which has been associated with decreased effectiveness (in terms of higher FN risk and increased incidences of neutropenia-related and all-cause hospitalizations compared with pegfilgrastim prophylaxis).[16–18,22–25] Concerns about the out-of-pocket costs for filgrastim may be a possible reason for the shorter duration of filgrastim in clinical practice. In the study reported here, we did not identify the number of filgrastim doses received per cycle. Previous studies with MarketScan® data have shown that the average number of days of filgrastim prophylaxis was 4–5 days per chemotherapy cycle.[23,24]

Table 2. Quarterly out-of-pocket costs for G-CSF (MarketScan® 2009 longitudinal cohort).

	Q1 2009	Q2 2009	Q3 2009	Q4 2009	Mean
Patients receiving pegfilgrastim					
Patients with ≥1 claim, n (%)	4684 (100)	5030 (100)	5386 (100)	5707 (100)	5202 (100)
Patients with quarterly out-of-pocket >$0, n (%)	2307 (49)	1381 (28)	1377 (26)	1347 (24)	1603 (31)
Patients with quarterly out-of-pocket = $0, n (%)	2377 (51)	3649 (73)	4009 (74)	4360 (76)	3599 (69)
Out-of-pocket cost/patient among all patients, mean (SD)	$233 ($552)	$69 ($276)	$59 ($261)	$57 ($273)	$100 ($173)
Out-of-pocket cost/patient among patients with quarterly out-of-pocket >$0, mean (SD)	$474 ($710)	$251 ($482)	$230 ($476)	$240 ($522)	$324 ($314)
Patients receiving filgrastim					
Patients with ≥1 claim, n (%)	1404 (100)	1643 (100)	1822 (100)	1877 (100)	1687 (100)
Patients with quarterly out-of-pocket >$0, n (%)	740 (53)	558 (34)	565 (31)	574 (31)	609 (36)
Patients with quarterly out-of-pocket = $0, n (%)	664 (47)	1085 (66)	1257 (69)	1303 (69)	1077 (64)
Out-of-pocket cost/patient among all patients, mean (SD)	$100 ($221)	$47 ($168)	$38 ($126)	$37 ($112)	$53 ($77)
Out-of-pocket cost/patient among patients with quarterly out-of-pocket >$0, mean (SD)	$189 ($276)	$139 ($266)	$122 ($203)	$120 ($177)	$146 ($121)

G-CSF: granulocyte colony-stimulating factors; N = 13,014 (pegfilgrastim); N = 4554 (filgrastim); SD: standard deviation.

In a study with HIRD[SM] data, filgrastim prophylaxis was administered for 6 days or less in 74% of chemotherapy cycles and 9 days or more in only 18% of cycles.[25]

There has been a shift toward increased focus on patient preferences in the clinical setting, and physicians are encouraging patients to be more involved in their treatment decisions. In a simplified conceptual framework of decision-making, a patient compares his/her perceived benefit of a particular treatment option (often measured as a monetary willingness-to-pay value) against the sum of the out-of-pocket cost and other indirect costs associated with the treatment. This evaluation may impact whether the patient decides to undergo the treatment and may even affect patient compliance and adherence, which in turn may have consequences to clinical outcomes.

Out-of-pocket costs, willingness to pay, and indirect costs are key factors that affect a patient's medical decision-making. In a French willingness-to-pay survey, Tan Sean et al. reported that healthy subjects would prefer a single injection of pegfilgrastim over multiple injections of filgrastim.[27] According to a survey on cancer patients in the United States, the mean time required for a single visit for neutropenia management was about 2 h for patients and 1 h for their caregivers.[28] The once-per-cycle dosing of pegfilgrastim simplifies the management of neutropenia as it requires fewer injections, reduces time spent at each visit, eliminates the need for multiple visits for injections, and minimizes other indirect costs (e.g. traveling cost to the clinic, lost time from work, and time spent by caregivers) that are associated with filgrastim administrations.[29,30]

Co-payment is the bulk of the out-of-pocket expenditures for filgrastim due to the higher number of administrations needed and the higher percentage of filgrastim claims in the pharmacy setting. Co-insurance is the bulk of the out-of-pocket expenditures for pegfilgrastim due to the higher per administration costs. This different distribution of the out-of-pocket payment types may impact patient compliance and adherence.[31] However, the evaluation of those impacts is beyond the scope of this study.

Several limitations of the current study are noted. First, the study included patients with commercial and Medicare supplemental insurance coverage, so out-of-pocket costs for G-CSF incurred by patients with Medicaid, Medicare alone, and other types of insurance may not be comprehensively captured; patients without insurance coverage were also not analyzed. Second, the study did not directly exclude patients without cancer; however, there is no non-cancer indication for pegfilgrastim and while filgrastim is indicated for severe chronic neutropenia, this condition is rare and not treated with chemotherapy. Third, as the objective of the study was to perform a high-level evaluation in patients receiving chemotherapy and G-CSF, comprehensive analyses of out-of-pocket costs for G-CSF by tumor type, disease stage, chemotherapy regimen, payer type, and geographic region were not conducted. Fourth, we were unable to distinguish patients who received G-CSF for prophylaxis or for the treatment of FN. As aforementioned, we also were unable to identify patients who received a shorter duration of filgrastim. Furthermore, the two databases did not have detailed information on the benefit

Table 3. Quarterly average out-of-pocket costs for G-CSF by claim type and setting (MarketScan® 2009 longitudinal cohort).

	Medical claims in office setting[a]	Medical claims in non-office setting[b]	Pharmacy claims[c]
Patients receiving pegfilgrastim			
Patients with ≥1 claim, n (%)	4065 (100)	850 (100)	407 (100)
Patients with quarterly out-of-pocket >$0, n (%)	1135 (28)	107 (13)	378 (93)
Patients with quarterly out-of-pocket = $0, n (%)	2930 (72)	744 (87)	29 (7)
Out-of-pocket cost/patient among all patients, mean (SD)	$99 ($155)	$87 ($242)	$105 ($132)
Out-of-pocket cost/patient among patients with quarterly out-of-pocket >$0, mean (SD)	$356 ($286)	$689 ($779)	$114 ($136)
Number of administrations/patient among all patients, mean (SD)	2.6 (0.7)	2.4 (0.7)	–
Number of administrations/patient among patients with quarterly out-of-pocket >$0, mean (SD)	2.4 (0.7)	2.2 (0.7)	–
Out-of-pocket cost/administration among all patients, mean (SD)	$40 ($76)	$38 ($146)	–
Out-of-pocket cost/administration among patients with quarterly out-of-pocket >$0, mean (SD)	$137 ($149)	$288 ($497)	–
% of all patients who received pegfilgrastim and had pegfilgrastim claims within this claim type and setting[d]	78	16	8
% of total out-of-pocket burden on pegfilgrastim within this claim type and setting	78	14	8
Patients receiving filgrastim			
Patients with ≥1 claim, n (%)	1323 (100)	210 (100)	273 (100)
Patients with quarterly out-of-pocket >$0, n (%)	352 (27)	28 (13)	248 (91)
Patients with quarterly out-of-pocket = $0, n (%)	971 (73)	183 (87)	25 (9)
Out-of-pocket cost/patient among all patients, mean (SD)	$43 ($69)	$38 ($92)	$87 ($82)
Out-of-pocket cost/patient among patients with quarterly out-of-pocket >$0, mean (SD)	$163 ($124)	$287 ($259)	$96 ($85)
Number of administrations/patient among all patients, mean (SD)	6.3 (3.3)	4.8 (2.6)	–
Number of administrations/patient among patients with quarterly out-of-pocket >$0, mean (SD)	5.5 (3.0)	4.2 (2.8)	–
Out-of-pocket cost/administration among all patients, mean (SD)	$7 ($12)	$8 ($25)	–
Out-of-pocket cost/administration among patients with quarterly out-of-pocket >$0, mean (SD)	$26 ($21)	$60 ($68)	–
% of all patients who received filgrastim and had filgrastim claims within this claim type and setting[d]	78	13	16
% of total out-of-pocket burden on filgrastim within this claim type and setting	64	9	27

G-CSF: granulocyte colony-stimulating factors; SD: standard deviation; N = 13,014 (pegfilgrastim); N = 4554 (filgrastim).
[a]Patients were administered the injection in the physician's office.
[b]Most patients (>96%) were administered the injection in an outpatient hospital.
[c]Patients picked up the G-CSF in a pharmacy and self-administered or received the injection from a caregiver.
[d]A patient may have claims within various claim types and/or settings during a quarter.

structures of individual health plans, so the out-of-pocket costs associated with G-CSF use in individual health plans could not be determined. Moreover, potential crossover may exist as some patients may have been captured in both of the two large databases. Furthermore, the study was based on fully adjudicated claims associated with G-CSF, so it is unlikely that reverse charges were included; however, we were not able to identify whether patients did not receive G-CSF because the perceived out-of-pocket burden was too high. Use of patient assistance programs could not be identified with claims data. We expect that if patient assistance programs were used, the actual out-of-pocket costs would be lower than reported herein due to patient reimbursements that were not captured in claims data. Lastly, patient costs outside of out-of-pocket expenses for G-CSF were not evaluated.

Conclusion

From January 2007 to June 2010, the majority of patients receiving chemotherapy and a G-CSF had zero out-of-pocket costs for G-CSF in an office or other outpatient setting. Most patients received G-CSF in an office setting, and although fewer patients received G-CSF in a pharmacy setting, most patients with pharmacy claims incurred non-zero out-of-pocket expenses associated with G-CSF use. Additional research is needed to better understand the impact of out-of-pocket costs on patients' medical decision-making and compliance and adherence to recommended treatments, as well as its clinical and economic implications. Further studies on patients' willingness to pay for G-CSF support are also warranted.

Funding

This research was supported by Amgen Inc.

Acknowledgements

The authors would like to thank Jingbo Yu and Stacey Yager of HealthCore and Lynn Jurss, Dana Hurley, and Robert Deeter of Amgen Inc. for their contributions to this study, and Michelle Zakson and Jenilyn Virrey of Amgen Inc. for providing writing assistance.

References

1. Bradley CJ. Financial hardship: a consequence of survivorship? *J Clin Oncol* 2012; 30: 1579–1580.
2. Macready N. The climbing costs of cancer care. *J Natl Cancer Inst* 2011; 103: 1433–1435.
3. Streeter SB, Schwartzberg L, Husain N, et al. Patient and plan characteristics affecting abandonment of oral oncolytic prescriptions. *J Oncol Pract* 2011; 7: 46s–51s.
4. Meropol NJ and Schulman KA. Cost of cancer care: issues and implications. *J Clin Oncol* 2007; 25: 180–186.
5. Pisu M, Azuero A, McNees P, et al. The out of pocket cost of breast cancer survivors: A review. *J Cancer Survivor* 2010; 4: 202–209.
6. Arozullah AM, Calhoun EA, Wolf M, et al. The financial burden of cancer: estimates from a study of insured women With breast cancer. *J Support Oncol* 2004; 2: 271–278.
7. Bernard DS, Farr SL and Fang Z. National estimates of out-of-pocket health care expenditure burdens among nonelderly adults with cancer: 2001 to 2008. *J Clin Oncol* 2011; 29: 2821–2826.
8. Kuderer NM, Dale DC, Crawford J, et al. Mortality, morbidity, and cost associated with febrile neutropenia in adult cancer patients. *Cancer* 2006; 106: 2258–2266.
9. Kuderer NM, Dale DC, Crawford J, et al. Impact of primary prophylaxis with granulocyte colony-stimulating factor on febrile neutropenia and mortality in adult cancer patients receiving chemotherapy: a systematic review. *J Clin Oncol* 2007; 25: 3158–3167.
10. NEUPOGEN® (Filgrastim) prescribing information, Amgen.
11. Neulasta® (pegfilgrastim) prescribing information, Amgen.
12. Hecht JR, Pillai M, Gollard R, et al. A randomized, placebo-controlled phase ii study evaluating the reduction of neutropenia and febrile neutropenia in patients with colorectal cancer receiving pegfilgrastim with every-2-week chemotherapy. *Clin Colorectal Cancer* 2010; 9: 95–101.
13. NCCN. National Comprehensive Cancer Network: NCCN Clinical Guidelines in Oncology. Myeloid Growth Factors. NCCN v1.2012.
14. Smith TJ, Khatcheressian J, Lyman GH, et al. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. *J Clin Oncol* 2006; 24: 3187–3205.
15. Aapro MS, Bohlius J, Cameron DA, et al. 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumours. *Eur J Cancer* 2011; 47: 8–32.
16. Morrison VA, Wong M, Hershman D, et al. Observational study of the prevalence of febrile neutropenia in patients who received filgrastim or pegfilgrastim associated with 3–4 week chemotherapy regimens in community oncology practices. *J Manag Care Pharm* 2007; 13: 337–348.
17. Scott SD, Chrischilles EA, Link BK, et al. Days of prophylactic filgrastim use to reduce febrile neutropenia in patients with non-Hodgkin's lymphoma treated with chemotherapy. *J Manag Care Pharm* 2003; 9: 15–21.
18. von Minckwitz G, Kummel S, du Bois A, et al. Pegfilgrastim +/− ciprofloxacin for primary prophylaxis with TAC (docetaxel/doxorubicin/cyclophosphamide) chemotherapy for breast cancer. Results from the GEPARTRIO study. *Ann Oncol* 2008; 19: 292–298.
19. Holmes FA, O'Shaughnessy JA, Vukelja S, et al. Blinded, randomized, multicenter study to evaluate single administration pegfilgrastim once per cycle versus daily

filgrastim as an adjunct to chemotherapy in patients with high-risk stage II or stage III/IV breast cancer. *J Clin Oncol* 2002; 20: 727–731.
20. Green MD, Koelbl H, Baselga J, et al. A randomized double-blind multicenter phase III study of fixed-dose single-administration pegfilgrastim versus daily filgrastim in patients receiving myelosuppressive chemotherapy. *Ann Oncol* 2003; 14: 29–35.
21. Lyman GH. Pegfilgrastim: a granulocyte colony-stimulating factor with sustained duration of action. *Expert Opin Biol Ther* 2005; 5: 1635–1646.
22. Weycker D, Hackett J, Edelsberg JS, et al. Are shorter courses of filgrastim prophylaxis associated with increased risk of hospitalization? *Ann Pharmacother* 2006; 40: 402–407.
23. Weycker D, Malin J, Kim J, et al. Risk of hospitalization for neutropenic complications of chemotherapy in patients with primary solid tumors receiving pegfilgrastim or filgrastim prophylaxis: a retrospective cohort study. *Clin Ther* 2009; 31: 1069–1081.
24. Weycker D, Malin J, Barron R, et al. Comparative effectiveness of filgrastim, pegfilgrastim, and sargramostim as prophylaxis against hospitalization for neutropenic complications in patients with cancer receiving chemotherapy. *Am J Clin Oncol* 2012; 35: 267–274.
25. Tan H, Tomic K, Hurley D, et al. Comparative effectiveness of colony-stimulating factors for febrile neutropenia: a retrospective study. *Curr Med Res Opin* 2011; 27: 79–86.
26. Crawford J, Glaspy JA, Stoller RG, et al. Final results of a placebo-controlled study of filgrastim in small-cell lung cancer: exploration of risk factors for febrile neutropenia. *Support Cancer Ther* 2005; 3: 36–46.
27. Tan Sean P, Chouaid C, Hettler D, et al. Economic implications of using pegfilgrastim rather than conventional G-CSF to prevent neutropenia during small-cell lung cancer chemotherapy. *Curr Med Res Opin* 2009; 25: 1455–1460.
28. Fortner BV, Tauer KT, Zhu L, et al. The impact of anemia and neutropenia treatment visits on patients and their caregivers. Poster presented at: *27th Annual San Antonio Breast Cancer Symposium*, San Antonio, TX, 8–11 December 2004, Abstract 6031.
29. Fortner BV, Tauer K, Zhu L, et al. Medical visits for chemotherapy and chemotherapy-induced neutropenia: a survey of the impact on patient time and activities. *BMC Cancer* 2004; 4: 22.
30. Haithcox SR, Ramnes C, Lee H, et al. The impact of frequent injections for hematopoietic growth factor support on patients receiving chemotherapy: an observational study. *BMC Nurs* 2003; 2: 2.
31. Dor A, Lage MJ, Tarrants ML, et al. Cost sharing, benefit design, and adherence: the case of multiple sclerosis. *Adv Health Econ Health Serv Res* 2010; 22: 175–193.