PCN345

Uptake of Filgrastim 'Biosimilars' in the United States: Analysis of a Medical Transcription Database of Patient Office Visits

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Objective

- The objective of this study was to assess the uptake of 'biosimilar' filgrastim by identifying physician documentation referencing use of tbo-filgrastim and filgrastim-sndz in the USA during patient office visits.

Background

- Filgrastim is a short-acting, recombinant granulocyte colony-stimulating factor (G-CSF) used to treat neutropenia (abnormally low neutrophil levels that can leave a patient susceptible to infections) in patients receiving chemotherapy.
  - Filgrastim was originally developed by Amgen and marketed under the trade name Neupogen®.
  - Pegfilgrastim (Neulasta®, Amgen), a long-acting G-CSF is also available.
- Biosimilars of filgrastim have been available in Europe since 2008.
- As of November 2015, 2 additional filgrastim products, tbo-filgrastim and filgrastim-sndz, are available in the USA.[1-3]
  - A timeline (Figure 1) and summary (Table 1) of these approvals are adjacent.
- Amgen, the manufacturer of Neupogen, initiated litigation against the manufacturers of both tbo-filgrastim and filgrastim-sndz.
  - This litigation delayed the launch of filgrastim-sndz until September 2015.
- Based on average wholesale price (AWP), pricing for both tbo-filgrastim and filgrastim-sndz is discounted approximately 15% versus Neupogen in US markets.[4,5]
  - In European markets, discounting of filgrastim biosimilars has ranged from 10–30%.[6]

Methods

- Physician records were extracted from RealHealthData (RHD), a US medical transcription database (Figure 2).
  - Data are available within 72 hours of each visit to a participating provider, enabling uptake of newly launched products to be observed with a limited lag time.
  - Records are in the form of physician-reported notes for office visits that document real-time data, without concern for recall or bias.
  - The data provide context about the physician's intent-to-treat at the time of the visit.
- Data were scanned over the study period from 1 November 2013 to 13 October 2015 and compared with online market reports.
- Records were searched, with counts tabulated, for mention of filgrastim agents as follows:
  - Tbo-filgrastim: "tbo-filgrastim," "Granix," or "Neutroval"
  - Filgrastim-sndz: "filgrastim-sndz," "Zarxio" or "Zarzio"
  - Filgrastim: "filgrastim" or "Neupogen"
  - Pegfilgrastim: pegfilgrastim" or "Neulasta."

Figure 1. Timeline of Filgrastim Approval and Launch

To view an animated, descriptive timeline, scan the QR Code here ›

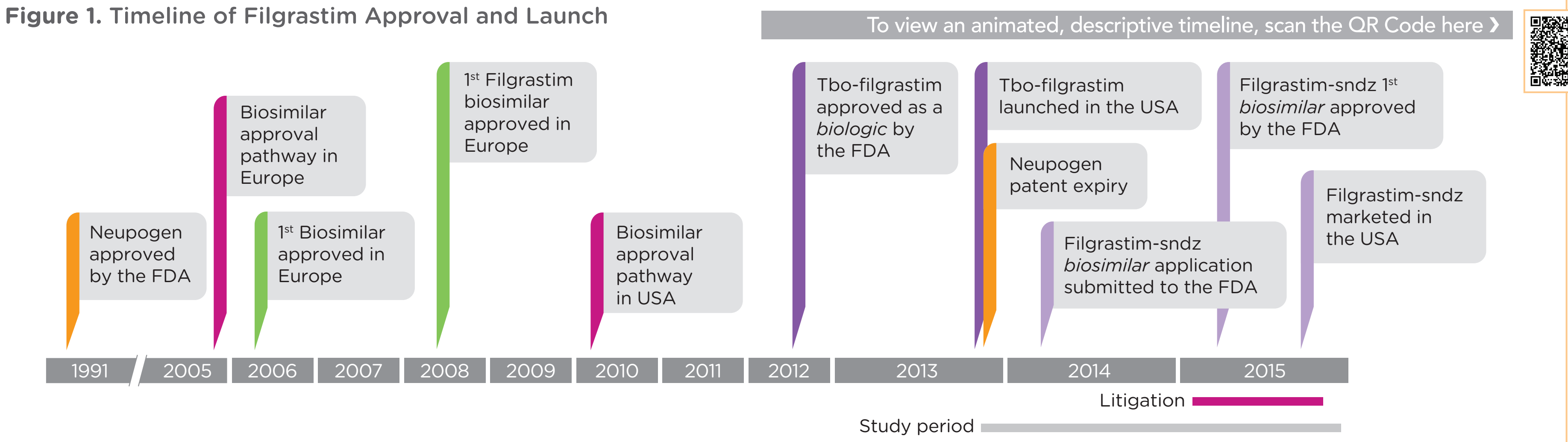
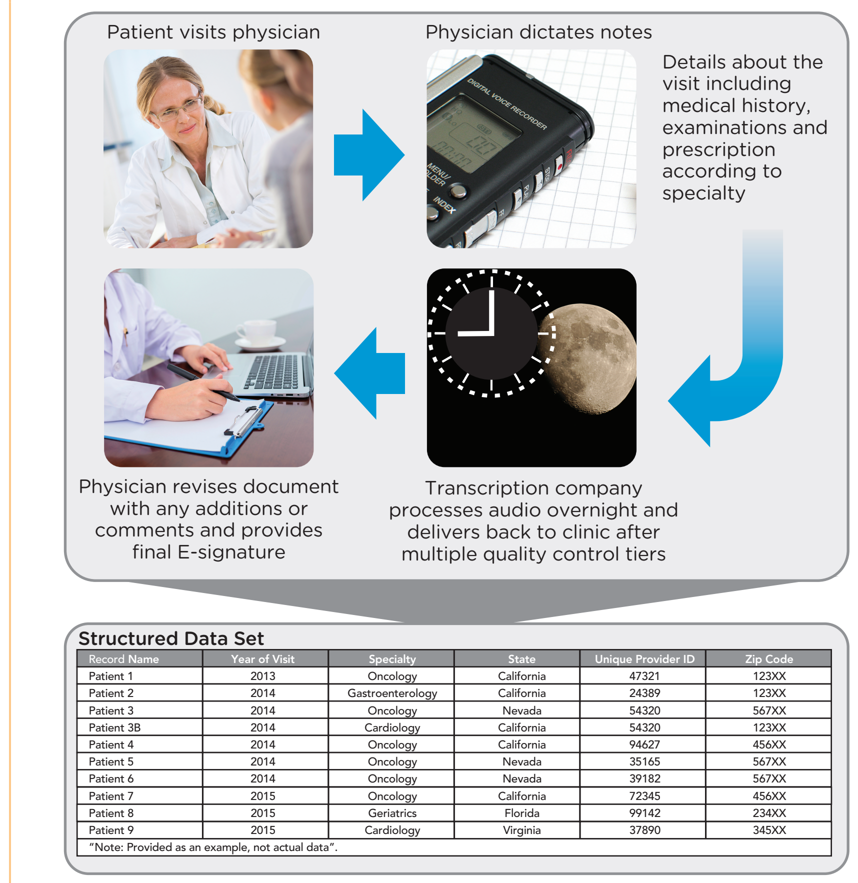


Table 1. Approval and Launch of Additional Filgrastim Products in the USA

	Tbo-filgrastim (Granix®, Teva)	Filgrastim-sndz (Zarxio®, Sandoz)
FDA approval pathway[1]	351(a) Biologic License Application (BLA) *Considered a biologic; biosimilars pathway did not exist at time of application*	351(k) Biosimilar application, BPCIA *First biosimilar in the USA; submitted under the biosimilars pathway*
Indications	Only 1 of the Neupogen® indications: *reduction in the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia*	All 5 approved Neupogen® indications as of March 2015 *(including neutropenia treatment and prophylaxis but excluding the newest Neupogen® indication for acute radiation exposure, approved March 2015)*
FDA approval date[1]	August 2012	March 2015
US launch date	November 2013[2]	September 2015[3]
AWP Discounting	Approximately 15% from Neupogen® [4]	Approximately 15% from Neupogen® [5]

Abbreviations: AWP, average wholesale price; BPCIA, Biologics Price Competition and Innovation Act.

Figure 2. Data Capture Process



Results

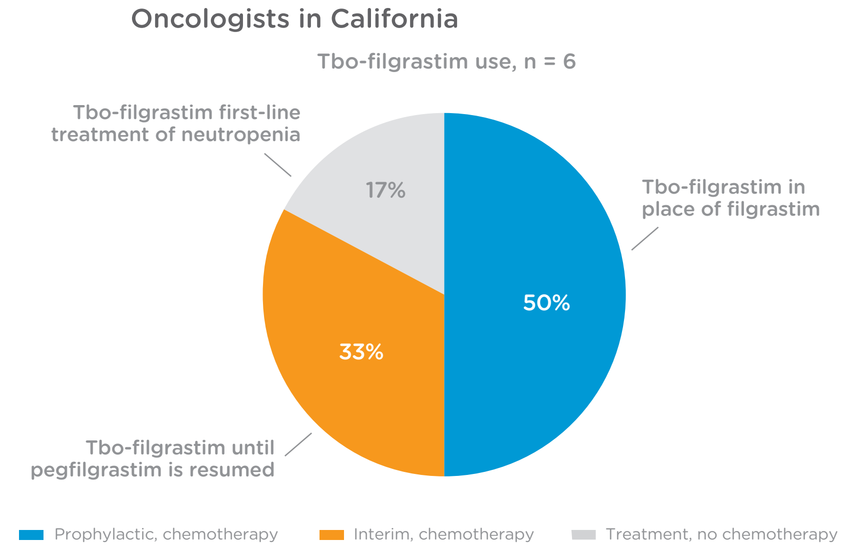
- Although RHD includes provider-reported data from all 50 states, approximately 86% of the available reports mentioning use of a G-CSF were from oncologists in California.
- Counts of mentions of G-CSF by product name and by number of unique patients and prescribers are presented in Table 2.
- Tbo-filgrastim was reported 6 times, for 5 unique patients, with all mentions referred to as "Granix".
- 59 Providers reported use of filgrastim, while only 4 reported use of tbo-filgrastim.
  - The 4 tbo-filgrastim providers were all located in the North of California.
- Based on physician reports, tbo-filgrastim was utilised as follows (Figure 3):
  - Tbo-filgrastim, a short-acting G-CSF, was prescribed as an interim treatment for 2 patients undergoing chemotherapy who normally received pegfilgrastim, a long-acting G-CSF.
    - An example of patient chart notes showing this use is provided in a supplemental figure (Exhibit 2).
  - 1 Patient, who had no evidence of receiving chemotherapy, reported taking tbo-filgrastim, as needed, for neutropenia symptoms
  - Prophylactic tbo-filgrastim was prescribed in 3 visits for 2 chemotherapy patients
  - Only 2 of the 4 patients undergoing chemotherapy received tbo-filgrastim as their primary G-CSF therapy.
- No mentions of filgrastim-sndz were identified.

‹ Scan the QR Code here to view an example of tbo-filgrastim use in patient chart notes (Exhibit 2)

Table 2. Counts of Mentions and Number of Unique Providers for G-CSFs, 1 November 2013 to 13 October 2015

G-CSF	Unique mentions	Unique patients	Unique providers
Pegfilgrastim	2400	960	44
Filgrastim	566	351	59
Tbo-filgrastim	6	5	4
Filgrastim-sndz	0	0	0

Figure 3. Tbo-filgrastim Utilisation in RHD Sample Comprising Oncologists in California



- Additional biosimilars are expected to enter the US market within the next 1–2 years.
  - These include biosimilars of pegfilgrastim (Neulasta®), the pegylated, long-acting version of filgrastim, for which the US patent expired in October 2015.
  - Apotex submitted biosimilar applications under the 351(k) pathway for both pegfilgrastim (December 2014) and filgrastim (February 2015).[8]
- US Payers will likely take advantage of new, lower priced biosimilars, accelerating uptake.

Discussion

- Data from this small sample show that tbo-filgrastim is mentioned in slightly more than 1% of provider records that report a short-acting G-CSF.
  - In comparison, tbo-filgrastim is reported to have captured approximately 15–16% of the overall market for short-acting G-CSF in the USA based on IMS sales data.[7]
- There may be several reasons why uptake of tbo-filgrastim in the study sample was much lower than the reported market share:
  - The sample was small and highly localised, and therefore is not representative of US prescribing patterns
  - Differences between sales data and utilisation data
  - Providers may have had service contracts in place for filgrastim that could delay adoption of competing agents.

Study Limitations

- The underlying data from which the sample was drawn are not static and represent patient records from prescribers currently participating in the transcription service. New prescribers may join or leave the service at any time during the study period.
- Filgrastim-sndz was available for less than 2 months of the study period, thus limiting the observation timeframe.
  - Next year's follow-up data will be more revealing of uptake.
- It is not clear how the 6-month delay to launch after FDA approval has affected market uptake of filgrastim-sndz.
- Anticipation of the impending availability of filgrastim-sndz, the first official biosimilar in the USA, may have dampened prescriptions for tbo-filgrastim.
- Payer coverage and formulary policy in California, both in commercial plans and in Medicare, entailed additional reauthorisation requirements for use of tbo-filgrastim not needed for filgrastim.[9,10]
  - These policies may have dampened provider use of tbo-filgrastim.
  - It is unknown to what extent such drug coverage policy may have affected provider reimbursement as well as patient costs, and how these might have influenced physicians' tbo-filgrastim prescribing patterns.

Conclusions

- Among nearly 3000 records reporting a G-CSF in this snapshot of primarily Californian oncologists, uptake of subsequent filgrastim agents was limited and highly concentrated in 1 region in the North of California.
  - Only 6 mentions of tbo-filgrastim were noted in the 18 months since launch.
  - No mentions of filgrastim-sndz were identified in the more than 2 months since launch.
- As educational initiatives increase physician awareness of alternate G-CSFs, existing supply contracts with originator manufacturers expire, and the length of time on the market increases, uptake of new filgrastim agents in the USA is expected to accelerate.

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Disclosures

The authors are employees of Envision Pharma Group and developed the data extraction criteria. RealHealthData provided the data for this study at the authors' request and without compensation.

Acknowledgements

The authors would like to thank Philip Howell of RealHealthData for his assistance in providing the patient counts. We also would like to thank our graphics and editorial divisions for their assistance in poster production.

This study was funded by Envision Market Access Solutions, part of the Envision Pharma Group.

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Presented at the 18th Annual European Congress of the International Society for Pharmacoeconomics and Outcomes Research, 7–11 November 2015, Milan, Italy