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

Smoyer KE1, Jones CA2, Lane P3
1Envision Pharma Group, Philadelphia, PA, USA; 2Envision Pharma Group, Hammersmith, UK; 3Envision Pharma Group, Horsham, UK

Objective
• The objective of this study was to assess the uptake of biosimilar filgrastim by identifying physician documentation referencing use of bio-filgrastim and filgrastim-ndz in the USA during patient office visits.

Background
• Filgrastim, a short-acting, recombinant granulocyte colony-stimulating factor (G-CSF) used to treat neutropenia (abnormally low neutrophil counts 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 biosimilar products, bio-filgrastim and filgrastim-ndz, are available in the USA.1
• A timeline (Figure 1) and summary (Table 1) of these 3 approaches are adjacent.
• Amgen, the manufacturer of Neupogen, initiated litigation against the manufacturers of both bio-filgrastim and filgrastim-ndz.
• This litigation delayed the launch of filgrastim-ndz until September 2015. Based on average wholesale price (AWP), pricing for both bio-filgrastim and filgrastim-ndz is discounted approximately 15% versus Neupogen in US markets.1,2
• In European markets, discounting of filgrastim biosimilars has ranged from 10–30%.3

Methods
• Physician records were extracted from RealHealthData (RHD), a US medical transcription database (Figure 2).
• Data were available within 72 hours of each visit to a participating provider, enabling a real-time snapshot 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 present 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 tabulated, with counts tallied, for mention of filgrastim agents as follows:
  - Bio-filgrastim: “bio-filgrastim,” “Granix,” or “Neutroval” (Tbo-filgrastim)
  - Filgrastim-ndz (“filgrastim-sndz”) or “Zarzio”
  - Filgrastim: “filgrastim” or “Neupogen”
  - Pegfilgrastim: “pegfilgrastim” or “Neulasta.”

Results
• Although RHD includes provider-reported data from all 50 states, approximately 61% of the available reports mentioning use of a G-CSF were from oncologists in California.
• Counts of mentions of bio-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 Neupogen.
• 59 Providers reported use of filgrastim, while only 4 reported use of bio-filgrastim.
  - The 4 bio-filgrastim providers were all located in the North of California.
• Based on physician reports, bio-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.
  - 1 Patient, who had no evidence of receiving chemotherapy, reported taking bio-filgrastim, as needed, for neutropenia symptoms.
  - Prophylactic bio-filgrastim was prescribed in 3 vials for 2 chemotherapy patients.
• Only 2 of the 4 patients undergoing chemotherapy received bio-filgrastim as their primary G-CSF therapy.
• No mentions of filgrastim were identified in this data set.

Discussion
• Data from this small sample show that bio-filgrastim is mentioned in slightly more than 1% of provider records that report a short-acting G-CSF.
• In comparison, bio-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.
• There may be several reasons why uptake of bio-filgrastim in the study sample was much lower than the reported market share.
  - The sample was small and highly localized, and therefore is not representative of US prescribing patterns.
  - Differences between sales data and utilization data.
  - Providers may have had service contracts in place for filgrastim that could delay adoption of competing agents.

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

<table>
<thead>
<tr>
<th>G-CSF</th>
<th>Unique mentions</th>
<th>Unique patients</th>
<th>Unique providers</th>
<th>Pegfilgrastim</th>
<th>Bio-filgrastim</th>
<th>Filgrastim-ndz</th>
<th>Filgrastim</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bio-filgrastim</td>
<td>245</td>
<td>301</td>
<td>51</td>
<td>48</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filgrastim-ndz</td>
<td>556</td>
<td>301</td>
<td>59</td>
<td></td>
<td>48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filgrastim</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pegfilgrastim</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

References
  1st biosimilar in united states. & http://www.realhealthdata.com/publications/ft illustrating-
5. http://www.biosimilars.org/articles/2013/03/biosimilar-filgrastim
  1st biosimilar.pdf
  1st biosimilar.pdf

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 data used in this study. The authors also would like to thank our graphical and editorial producers for their assistance in paper production.

To see an animated, descriptive timeline, scan the QR Code here 2

Figure 1. Timeline of Filgrastim Approval and Launch

Figure 2. Data Capture Process

Figure 3. Tbo-filgrastim Utilisation in RHD Sample Completing Oncology visits in California

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

<table>
<thead>
<tr>
<th>G-CSF Product</th>
<th>FDA Approval Date</th>
<th>US Launch Date</th>
<th>Approval Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tbo-filgrastim (Granix®, Teva)</td>
<td>May 2005</td>
<td>November 2013, 2015</td>
<td>351(k) license</td>
</tr>
<tr>
<td>Filgrastim-ndz (Zarzio®, Sandimmune)</td>
<td>January 2015</td>
<td>September 2015</td>
<td>351(k) license</td>
</tr>
</tbody>
</table>

Timeline of Filgrastim Approval and Launch

1. Tbo-filgrastim was approved as a biosimilar by the FDA in May 2005
2. Filgrastim-ndz was approved as a biosimilar by the FDA in January 2015
3. Filgrastim-ndz was launched in the USA in February 2015
4. Filgrastim-ndz was approved by the FDA
5. Filgrastim-ndz was approved by the FDA

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

Objective
• The objective of this study was to assess the uptake of biosimilar filgrastim by identifying physician documentation referencing use of bio-filgrastim and filgrastim-ndz in the USA during patient office visits.