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

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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 biosimilar products, tbo-filgrastim and filgrastim-sndz, are available in the USA.
• A timeline (Figure 1) and 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.1

In European markets, discounting of filgrastim biosimilars has ranged from 10–30%.2

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 data to be observed at a time of newly learning chemotherapy – Records are in the form of physician-reported notes for office visits that document real-time data, without concern for recall 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 “Neutrophil Accelerator”
  • Filgrastim-sndz: “filgrastim-sndz”, “Zarxio” or “Zarzio”
  • Filgrastim: “filgrastim” or “Neupogen”
  • Pegfilgrastim: pegfilgrastim or “Neulasta”.

Results
• Although RHD includes provider-reported data from all 50 states, approximately 8 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 providers and patients are presented in Table 2. Tbo-filgrastim was reported 6 times, for 5 unique patients, with all mentions referred to 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 utilized as follows (Figure 3): – Tbo-filgrastim, a short-acting G-CSF, was prescribed as an intermittent treatment for 2 patients undergoing chemotherapy who normally received pegfilgrastim, a long-acting G-CSF. – An example of patient chart notes showing how this is used in a supplemental figure 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 mention of filgrastim-sndz was identified in the more than 2 months since launch.

Discussion
• From the small sample size that both 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 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.

Conclusions
• Among nearly 3000 records reporting a G-CSF in this snapshot of primarily California oncologists, uptake of subsequent biosimilar 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.
• An educational initiative 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.

Table 2. Counts of Mentions and Number of Unique Providers for G-CSF, 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>
</tr>
</thead>
<tbody>
<tr>
<td>Pegfilgrastim</td>
<td>345</td>
<td>196</td>
<td>46</td>
</tr>
<tr>
<td>Filgrastim</td>
<td>566</td>
<td>301</td>
<td>59</td>
</tr>
<tr>
<td>Tbo-filgrastim</td>
<td>6</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Filgrastim-end</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Products in the USA</th>
<th>Approval and Launch of Additional Filgrastim Products in the USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tbo-filgrastim (Granix, Teva)</td>
<td>FDA approval pathway</td>
</tr>
<tr>
<td>Filgrastim-sndz (Zarxio, Sandzand)</td>
<td>FDA approval pathway</td>
</tr>
<tr>
<td>Neupogen (Neupogen, Amgen)</td>
<td>FDA approval pathway</td>
</tr>
<tr>
<td>Filgrastim-end</td>
<td>FDA approval pathway</td>
</tr>
</tbody>
</table>

References
2. http://www.nej.org/content/378/12/1513.full.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.

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