Do market withdrawals impact patient access to treatment in Germany?  
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Introduction

- Under the AMNOG legislation introduced in 2011, the G-BA determines the extent and certainty of additional benefit (AB) of new therapies relative to the appropriate comparator therapy (ACT) through its early benefit assessment.
- Products are re-assessed at least once every 4 years, and the G-BA may decide to remove an AB determination.
- If both parties cannot agree on a price, one will be determined within 3 months through arbitration.

Methods

- We analyzed all G-BA assessments conducted before 13 May 2019 for products that were withdrawn.
- The current status on Laser Taze® was reviewed on 15 May 2019. A product was no longer listed on Laser Taze®, it was assumed to have been withdrawn.
- The reasons for withdrawal were identified from the GKV-Spitzenverband status and additional publications.

Results

- We identified 40 products that had been withdrawn from the German market since 2011 (Figure 1).

Figure 1: Number of products withdrawn from the German market per year

- Across the 40 products withdrawn, 15 were within 4 weeks of the AB determination (stop-out), and 2 during price negotiations (Figure 2). Omitting all at this point prevents publication of a negotiated price that could be referenced by other countries.

Figure 2: Time point of product withdrawal

- A further 3 products were withdrawn after price negotiations; 14 were withdrawn after a price was determined through arbitration.

In addition, 6 products are no longer available because their license was withdrawn or had expired.

Table 1: Details of identified product withdrawals

<table>
<thead>
<tr>
<th>Active substance</th>
<th>Manufacturer</th>
<th>Indication</th>
<th>AB determination</th>
<th>G-BA resolution</th>
<th>Year of withdrawal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ospemifene, Santen®</td>
<td>Santen</td>
<td>Breast cancer</td>
<td>AB not proven</td>
<td>2017</td>
<td>2013</td>
</tr>
<tr>
<td>Osimertinib, Tagrisso®</td>
<td>AstraZeneca</td>
<td>Non-small cell lung cancer</td>
<td>AB not proven</td>
<td>2018</td>
<td>2017</td>
</tr>
<tr>
<td>Lurasidone, Latuda®</td>
<td>Janssen-Cilag</td>
<td>Schizophrenia</td>
<td>AB not proven</td>
<td>2018</td>
<td>2017</td>
</tr>
<tr>
<td>Empagliflozin + metformin, Vokanamet®</td>
<td>Boehringer Ingelheim</td>
<td>Type 2 Diabetes mellitus</td>
<td>AB not proven</td>
<td>2019</td>
<td>2016</td>
</tr>
<tr>
<td>Regorafenib, Stivarga®</td>
<td>Bayer</td>
<td>Colorectal cancer/GIST</td>
<td>AB not proven</td>
<td>2019</td>
<td>2017</td>
</tr>
<tr>
<td>Simeprevir, Olysio®</td>
<td>Janssen-Cilag</td>
<td>Hepatitis C</td>
<td>AB not proven</td>
<td>2019</td>
<td>2016</td>
</tr>
<tr>
<td>Alipogene tiparvovec, BioBag®</td>
<td>Alnylam</td>
<td>Duchenne muscular dystrophy</td>
<td>AB not proven</td>
<td>2019</td>
<td>2015</td>
</tr>
</tbody>
</table>

Conclusions

- Product withdrawals restrict access and lead to treatment disruption for patients.
- Several pathways exist for continuing supply to German patients; however, treatment withdrawal can lead to delayed price agreements. Introductions are still likely.

- While statutory health insurance funds argue that withdrawals from the market following a re-assessment is a reason to delay price agreements, introductions are still likely.

- In 8 cases, a price was agreed after the withdrawal, and the product was re-introduced.

- Overall, 12 of the 40 withdrawn products were subsequently re-introduced and are available in Germany for the same indications and cost settings.

- In 7 cases, a price was agreed after the withdrawal, and the product was re-introduced. For 2 products (Alipogene, BioBag), the manufacturer initiated a re-assessment with new data. Although for insulin degludec the re-assessment still resulted in no AB, the product was re-introduced.

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