A comparison of approved indications between regulatory agencies

INTRODUCTION

Medicinal products are allowed on the market following approval by autonomous regulatory agencies which are tasked with their evaluation. Differences in evaluation practices during the registration of medicinal products are found in Europe and the United States of America which may lead to discrepancies in clinical guidelines, pricing policies, and drug use.

AIMS

To compare the differences in the indications of medicinal products authorised by the European Medicines Agency (EMA) and the US Food & Drug Administration (FDA) using new molecular entity cardiology-related medicinal products as examples.

METHOD

1. A list of all medicinal products evaluated by the EMA between 1995-2016 was extracted.
2. Cardiology-related medicinal products were identified using the Anatomical Therapeutic & Chemical (ATC) code.
3. The European Public Assessment Reports were extracted for the identified products.
4. The FDA counterparts were identified using the branded name, active ingredient & authorisation holder details.
5. The FDA reviews were extracted for the matched products.
6. Approved product information (PI) from the EMA and the FDA were obtained.
7. A tool was developed and validated using 6 experts in the regulatory field to compare indications between the two regulatory agencies.

RESULTS

- Twenty-six products have been identified.
- Fourteen products were determined to have different indications when comparing PI.
- Differences in the indications have been categorised as follows (Table 1):
  - restriction based on diseased states (n=5),
  - restrictions related to patient characteristics (n=4),
  - different clinical scenario (n=3),
  - restrictions based on severity of the condition (n=3),
  - combination restrictions (n=3),
  - restriction based on previous therapy failure (n=1),
  - restriction of use when alternative therapies are inappropriate (n=1).

- Pharmaceutical companies submitted different clinical studies for the different clinical scenario category.
- Reasons for restrictions have been attributed to alignment with the conducted clinical trials.
- Both agencies have been found to restrict indications.

CONCLUSION

Differences in approved indications exist between the EMA and the FDA. Pharmaceutical companies also contribute to discrepancies based on marketing strategies employed during submission of applications. Regulatory collaboration between agencies is deemed essential to ensure a harmonised approach to the use of medications.

Table 1: Differences in indications

<table>
<thead>
<tr>
<th>Differences</th>
<th>No. of products</th>
<th>Active ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous Therapy Failure</td>
<td>1</td>
<td>Guanfacine</td>
</tr>
<tr>
<td>Alternative therapies inappropriate</td>
<td>1</td>
<td>Guanfacine</td>
</tr>
<tr>
<td>Different clinical scenario</td>
<td>3</td>
<td>Apixaban, Dabigatran, Ibavradine</td>
</tr>
<tr>
<td>Severity of condition restriction</td>
<td>3</td>
<td>Bosentan, Iloprost, Selexipag</td>
</tr>
<tr>
<td>Combination restriction</td>
<td>3</td>
<td>Bivalirudin, Cangrelor, Prasugrel</td>
</tr>
<tr>
<td>Patient characteristic restriction</td>
<td>4</td>
<td>Dronedarone, Edoxaban, Regadenoson, Tolvaptan</td>
</tr>
<tr>
<td>Disease state restriction</td>
<td>5</td>
<td>Bivalirudin, Bosentan, Dronedarone, Edoxaban, Tolvaptan</td>
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</tbody>
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