CRA Charles River Associates

Part 1

Impact of EU orphan designation on generic and biosimilar entry

Orphan designation (OD) status was introduced to encourage development of therapies for rare diseases. Products that fulfil the OD criteria benefit from a 10-12-year market exclusivity period from market authorisation (MA), which can extend protection from generic (Gx) or biosimilar (Bx) competition beyond patent expiry. In this study, we explore the impact of OD market exclusivity on the likelihood of Gx and Bx entry. Factors which may influence the attractiveness of Gx entry are also analysed.

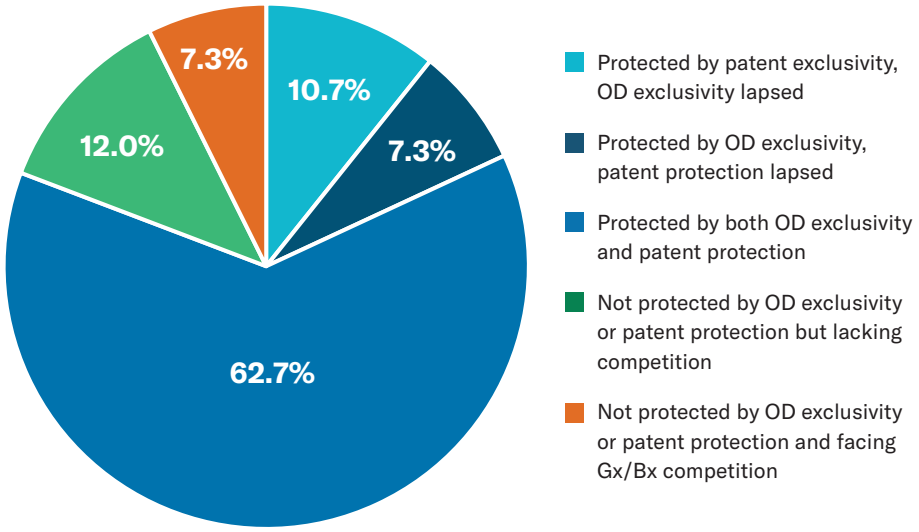
Methodology

A database containing all products with an OD, which were granted MA from 2000-2020 was compiled by supplementing data from the European Medicines Agency (EMA) community register. Orphan medicinal products (OMPs) withdrawn from the register for reasons other than OD expiry were not included in the analysis. The database was curated to distinguish oncologic vs. non-oncologic, paediatric vs. non-paediatric and small molecule vs. biologic OMPs. Patent expiry dates were collected using GlobalData, Evaluate Pharma and other publicly available sources. The EMA's European public assessment report (EPAR) database was used to identify the earliest date of centralised MA for Gx and Bx, and the numbers of these competitors that were centrally approved.[1]

Results and discussion

Of the 177 OMPs granted MA from 2000-2020, three quarters are still patent protected (as of July 2021). Of the products that have lost patent protection, ~28% still benefit from OD market exclusivity, thereby confirming that an OD can extend protection from Gx/Bx competition beyond patent expiry. On average, the OD has extended the exclusivity of these OMPs by approximately 4.5 years beyond that conferred by their patents. Approximately 19% of OMPs have no protection from competitive entry. At the time of analysis, Gx or Bx entry had only occurred in 38% of these non-protected OMPs.

Market exclusivity status of OMPs granted a European market authorisation from 2000-2020



Conclusions

This study provides evidence that the OD status can afford OMPs formal protection from Gx/Bx competition beyond that conferred by patent protection by extending the market exclusivity period, with ~28% of off-patent OMPs still benefiting from OD market exclusivity. In addition to this legal protection, analysis indicates that the OD status provides another layer of defence, through diminishing the attractiveness of Gx/Bx entry compared to non-OMPs. A combination of factors likely contribute to this diminished attractiveness, including population size, therapy area and brand loyalty.

[1] European public assessment reports (EPAR) database. EMA. (July 2021) Available at: https://www.ema.europa.eu/sites/default/files/Medicines_output_european_public_assessment_reports.xlsx

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Part 2

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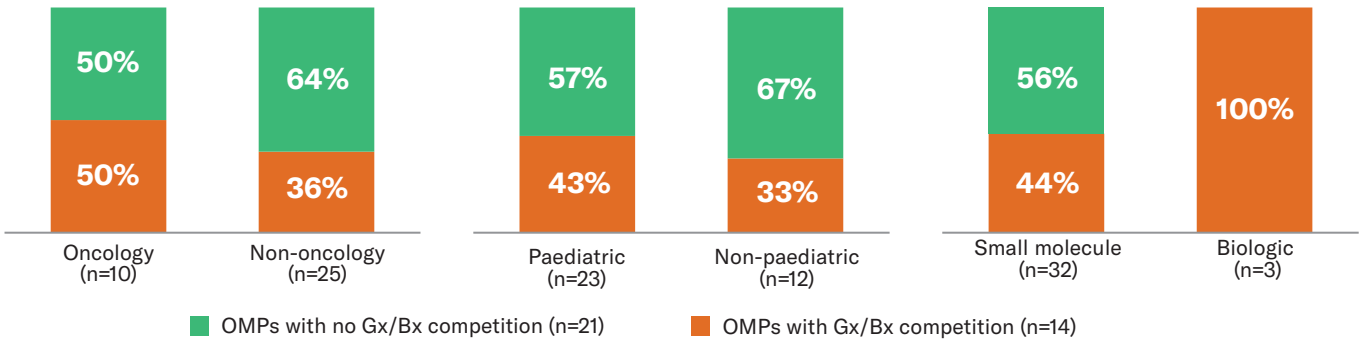
Results and discussion

Characteristics of non-protected OMPs



To understand the drivers or barriers for Gx/Bx competition for non-protected OMPs, several product characteristics were analysed. The analysis demonstrated that competition for non-protected OMPs is higher for oncology products compared to non-oncology and for those with paediatric indications vs. adult-only indications. This finding indicates that oncology and paediatric indications may represent a more attractive opportunity for Gx/Bx manufacturers. Focusing specifically on the non-oncology OMPs, again there is a small trend for greater Gx competition in paediatric indications, supporting the findings from the full sample. Within the non-protected OMPs, there are considerably more small molecules (n=32) vs. biologics (n=3), which in turn makes it difficult to draw conclusive insights on how this characteristic influences competitive entry at this time.

Conclusions

This study indicates that beyond the formal protection an OD status provides in terms of market exclusivity, this status also provides another layer of defence, through diminishing the attractiveness of Gx/Bx entry compared to non-OMPs. Various factors may contribute to this diminished attractiveness, such as the relatively small population sizes, and physician and patient loyalty to the originator brand. The extent of OMP brand loyalty may be linked with the therapy area, for example differences may be observed for acute vs chronic conditions. This aligns with the current observation where non-oncology OMPs face less competitive Gx entry than oncology OMPs. This is a topic worth exploration in future analysis.

[1] European public assessment reports (EPAR) database. EMA. (July 2021) Available at: https://www.ema.europa.eu/sites/default/files/Medicines_output_european_public_assessment_reports.xlsx

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Part 3

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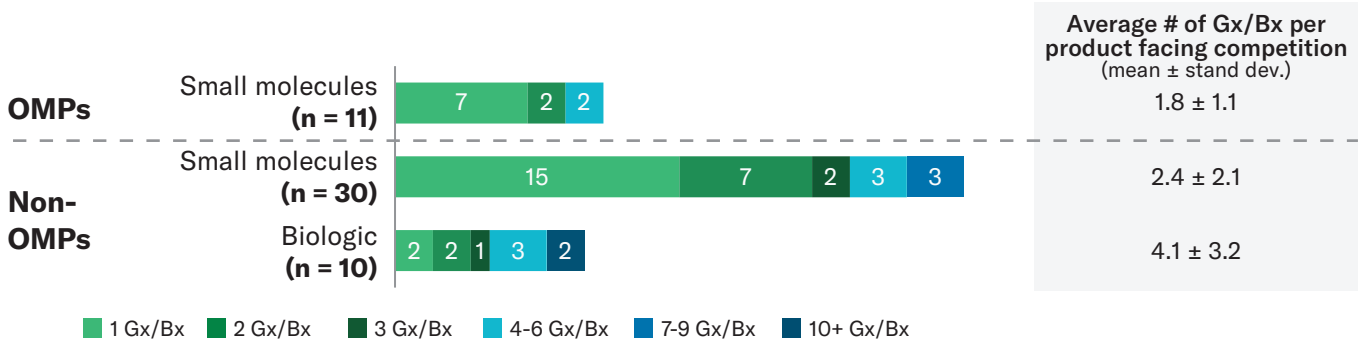
Results and discussion

Number of Gx/Bx entering per product for products that lost exclusivity and faced Gx entry from 2015-2020



To probe the attractiveness of Gx/Bx entry for OMPs, we compared the number of Gx/Bx that were approved centrally by the EMA for OMPs that lost market protection from 2015-2020, with the number of Gx/Bx that launched for non-OMPs that lost patent protection during the same timeframe. Analysis showed that a greater overall number of Gx/Bx have entered for non-OMPs than OMPs, indicating that OD indications represent a less attractive option for Gx/Bx manufacturers. For OMPs experiencing Gx competition, more than one Gx entered in ~35% of cases. Conversely, for non-OMPs more than one Gx/Bx entered for 50% of small molecules and for 80% of biologics. The difference in the average number of Gx/Bx per product facing competition is not significantly different for OMPs vs. non-OMPs, although there may be additional Gx/Bx launched outside of the EMA's central procedure (e.g., at the national level) which are not considered in this analysis. Interestingly, the OMPs with the highest number of Gx competitors (4 each) are both oncology products, supporting earlier observations that oncology OD indications may represent a more attractive Gx/Bx opportunity than non-oncology OD indications.

Conclusions

Overall, this study demonstrates that the OD status still provides significant opportunities for OMPs, even 20 years after its introduction, in terms of reducing the likelihood for Gx/Bx entry, as well as the number of competitors that launch. Moving forward, as the Bx landscape evolves, future analyses may assess whether biologic OMPs experience different competitive dynamics to small molecule OMPs post-loss of OD exclusivity. Differences could perhaps arise due to Bx development costs limiting entry into rare populations or alternatively increased appetite for Bx entry due to lower price erosion for Bx OMPs vs. Bx non-OMPs.

[1] European public assessment reports (EPAR) database. EMA. (July 2021) Available at: https://www.ema.europa.eu/sites/default/files/Medicines_output_european_public_assessment_reports.xlsx