PRIME
The European approach to expedited pathways

"Only when consensus among HTA bodies in Europe around how to consistently assess the relative effectiveness of a pharmaceutical product is reached, will the PRIME concept be able to fully deliver significant product level value to companies and patients alike."

A timely market introduction is a critical component of any drug development strategy – not only from a commercial stand point, where an early introduction can mean beating competition to market or simply significantly increased revenue, but also to patients awaiting better or alternative treatment options.

The debate around how regulators can facilitate this process on both sides of the Atlantic has resulted in new pathways for new medicines of major public interest. The FDA have the Breakthrough/RMAT pathways, and in the EU, EMA has put the PRIME process in place.

The regulator's toolbox

The European regulator has a few tools available in the expediting toolbox:

- Conditional Marketing Authorisation (CMA) has been around since the mid 2000's, providing a basic framework for accelerating the review process of particularly promising products. CMA's basic scope is products dealing with seriously debilitating or life-threatening disease, emergency situations or orphan products. In all cases the intention is to allow products with significant promise to reach the market with a smaller data package, with the caveat that additional, more comprehensive data is generated post approval.
- Accelerated assessment is EMA's equivalent to FDA's "priority review". It is granted prior to the assessment and follows the standard timetable for the initial review (120 days). After successful initial review the goal is to finalise the assessment within 150 days, as opposed to 210 days. The pathway has however only been successfully used in a few cases.
- The PRIME pathway is the latest addition to the toolbox, enabling early continual and strengthened regulatory dialogue between the applicant and the EU regulatory network. This helps improve the quality of the data package and to raise awareness of existing tools (e.g. parallel consultations, CMA) relevant to the development programme. One of the key benefits is the early appointment of an EMA rapporteur to provide continued support and help to build knowledge ahead of a marketing authorisation application (MAA). PRIME also focuses on the integration of HTA interaction in this early dialogue to help you avoid having to go back and redo or complement your studies to fulfil the payer requirements.

Is it really a pathway?

Interestingly the PRIME scheme is not so much a regulatory pathway on its own as it is a mechanism to facilitate early dialogue supported by already present components (CMA, scientific advice and accelerated approval). By getting the key stake holders in one room with the purpose of accelerating access for patients, it should hypothetically be possible to convince these stake holders of the value of approving and reimbursing a product based on a smaller initial data package – as long as everyone agrees on an alternative data generation strategy.

In the best of worlds this would work well from the outset and would have the same impact of the PRIME pathway on speed to market as the breakthrough designation/RMAT had in the US. Unfortunately, the intricacies of EU policy making and the independent will of 28 sovereign states with over 100 different HTA bodies make integration somewhat more difficult in the real world.

Experiences so far

Experiences from the PRIME scheme so far show that somewhat less than a fourth of the applications submitted were considered eligible (53 products out of 179)[1]. Approximately half of the products were oncology products followed by neurology and hematological products[2]. About half of the discussions have been with SME companies.

The primary reasons for rejection were either that the product was too advanced in the development, or issues with the robustness of presented data that did not sufficiently support the assumption of a major therapeutic advantage, or inconclusive/insufficient effect.

An increasing proportion of critical access related decisions are made elsewhere than within the regulatory agencies. For the regulators and the HTA bodies the concept of the PRIME pathway is a way to bridge that gap. For the HTA bodies to increase their impact over drug development decisions and priorities they have to move earlier in the development cycle. For both of these parties the PRIME pathway is of benefit just as much as it is for the companies involved.

At NDA we've supported several companies achieve PRIME designation, as well as the full range of regulatory interactions that this opens up. Through the NDA Joint Regulatory / HTA Advice option, companies have discovered a complement or an alternative to the formal process that has provided an efficient route to high quality advice and preparation for formal regulatory interactions.

Conclusion

Only when consensus among HTA bodies in Europe around how to consistently assess the relative effectiveness of a pharmaceutical product is reached, will the PRIME concept be able to fully deliver significant product level value to companies and patients alike. Until then we trust the brave and the curious to go through the process to experience, learn and help improve the way the process works, in order for this alignment to take place.

At NDA we are eagerly supporting this development through the support and services we deliver to clients on a regular basis, ensuring that our experiences become the benefits of small biotech and large pharma alike.

References

1. https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines (accessed 29 April 2019)
2. PRIME: a two-year overview, https://www.ema.europa.eu/en/documents/report/prime-two-year-overview_en.pdf (accessed 29 April 2019)