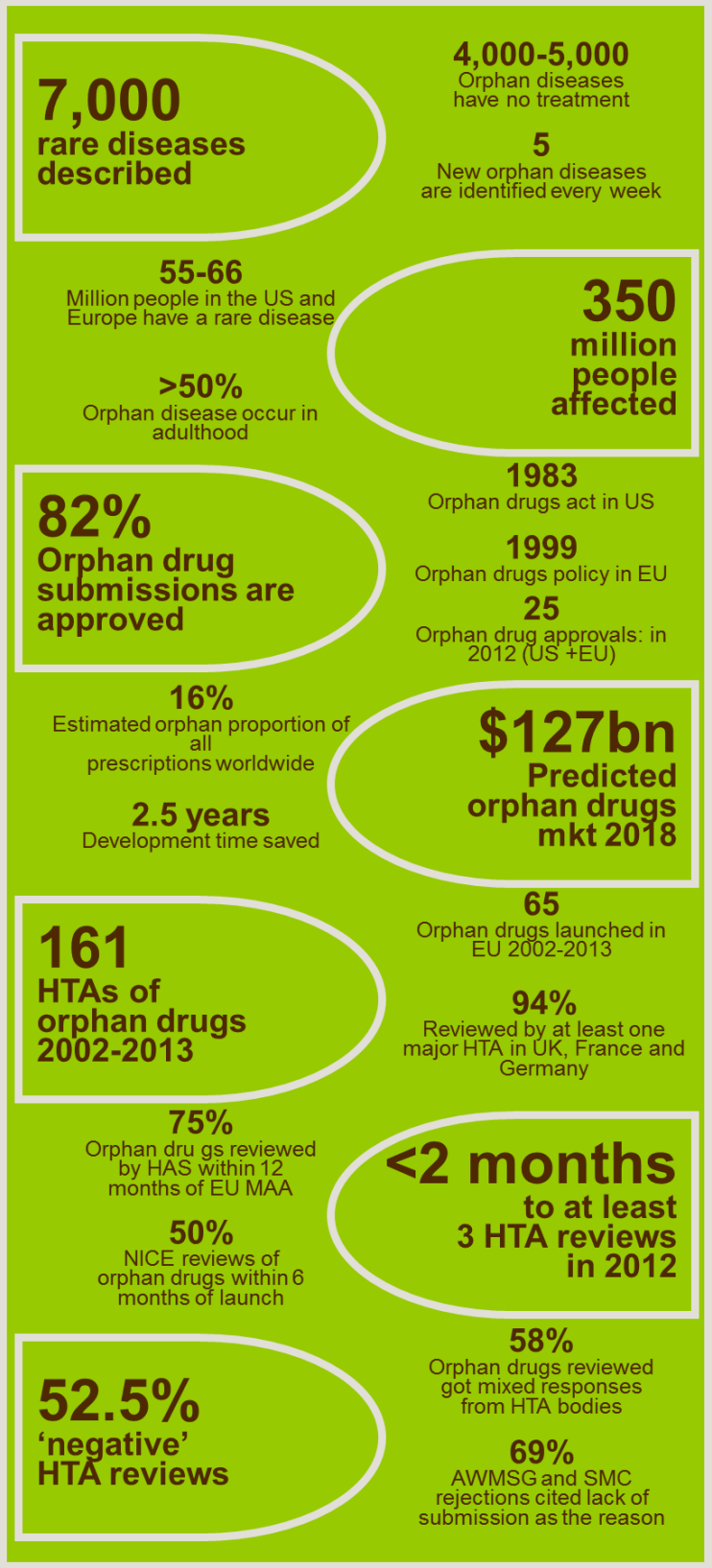
Orphan Drugs and Rare Diseases

Orphan indication? No easy access

Health technology assessment for orphan drugs continues to present challenges for pharmaceutical companies

Developing drugs for rare diseases has its own set of challenges but, while the US continues to support orphan innovations through new policies like granting breakthrough status, European countries have increased barriers to entry and left biopharma companies in a quandary about how best to develop and commercialise. The development of treatments for rare diseases, so called orphan diseases, has been a significant challenge. The capital costs of the long and expensive pathway of drug development compared with the relatively small numbers of patients treated lead either to unattractive markets or to relatively high per patient prices. Nevertheless, the need to innovate in these diseases is clear. Since the 1990s and 2000s, the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) have recognised these issues and created a series of incentives (including protocol assistance, extended market exclusivity, changes to the fee structure for registration) for the development of pharmaceuticals with orphan designation. This has recently been extended in the US with the introduction in July 2012 of 'breakthrough status' which is intended to expedite the development and review of drugs for serious or life-threatening conditions. The case in Europe, though, looks very different. A once receptive market to these vital innovations is struggling with the question of when and what to pay: the answer so far has been a messy combination of drug rejections, government interventions and industry-funded patient access schemes. But what can the industry do to get more value from these groundbreaking therapies?

Who reviews orphan drugs and when?



The advent of health technology assessment (HTA) in Europe in the 1990s started a new trend for reviews. As time has moved on, more and more effort has been focused on the early assessment of all drugs coming to market. Over 80 per cent of orphan drugs launched between 2002 and 2013 have been through HTA by one of the major bodies in the UK (NICE, SMC, AWMSG), France (HAS) or Germany (IQWiG). HTA and pricing review times for orphan drugs have fallen from two to three years in the early 2000s to a few months by 2012. Good news if you are looking for a fast answer. But this news hides an underlying problem. While over 80 per cent of orphan drugs reviewed in the early 2000s led to a positive outcome (acceptance for use or, in the case of France, a high Improvement of Medical Benefit [ASMR] rating), that proportion has plummeted in the last decade with only around 20 per cent of orphan drug reviews in 2012 being positive - many of these involving patient access schemes to placate the payers involved. Orphan drugs can hope for a slightly easier ride in Germany, where the Social Code Book V deems the added medical benefit of orphan drugs to be proven by the fact that they have been approved. Consequently, of the eight drugs commented on

by IQWiG, seven have been assumed to have benefit. Only in the case of Intermune's idiopathic pulmonary fibrosis drug Esbriet (perfenidone) was the balance of benefit and risk to patients considered inadequate and 'no proven added benefit' found. Governments also intervene in some instances against HTA advice, for example in the case of Vertex Pharmaceuticals' Kalydeco (ivacaftor) for cystic fibrosis in Wales and Scotland, to make available treatments for very rare diseases - but this has been on a case by case basis and not a clear policy shift to help foster innovations. In other cases (Germany, England and Wales for Cancer), innovation funds have been set up to overcome the issues of underfunding and the poor fit of HTA methodologies with the data available for orphan drugs. Nevertheless, companies need to be ready to face severe challenges to access.

How to prepare?

Each orphan drug is unique but a review of all submissions, both successful and unsuccessful, leads to a set of fairly simple rules for successful market access.

1. Start early

Clear winners have carefully thought through the challenges of access during design of their clinical trials and have tried to address the three biggest challenges for orphan drugs: getting the right comparator, building a robust data set and proving applicability of the data. Of all the orphan drugs reviewed, most were criticised for the applicability of the clinical data, with 54 per cent of all drugs given low ASMR ratings (indicating marginal or no benefit over existing treatments) often due to the lack of comparative data.

2. Understand the local environment and play by the rules when you can

Knowing who will make decisions about your drug, when and with what information, is key. A good mapping of decision makers and the steps and data involved will give a sense of the data gaps and help in the process of submission and negotiation. Sixty nine per cent of all rejections by the SMC and AWMSG come about because the manufacturer fails to submit all or part of the information requested for review.

3. Break the rules - when you have to

Appealing above and beyond the HTA bodies can be successful (as in the case of Kalydeco) but having the right local support, in terms of all stakeholders from patients to key opinion leaders, and strong convincing arguments that go beyond emotional appeal are critical. With a shifting focus of HTA - including value-based pricing and more complex and numerous reviews - driving access will continue to be a challenge. Optimising your market access strategy should be a central part of development and launch planning for orphan drugs.

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