Drugmakers accused of exploiting orphan drug incentives, fueling price problem

In January *Kaiser Health News* published a data-rich report focusing on the increase in approvals of orphan disease drugs, detailing how even high-volume products have reaped the tax breaks and market exclusivity that come with orphan drug status. The analysis by KHN, an editorially independent newsroom supported by the nonprofit Kaiser Family Foundation, based in Menlo Park, California, showed that more than 70 drugs that now have orphan designations, were approved first for mass market use and only later received orphan status. The investigation spurred Senator Chuck Grassley (R-Iowa), chairman of the senate committee on the judiciary, to open an inquiry into the Orphan Drug Act's potential misuses. Orphan drug rules "appear to be stretched beyond their original intent," which may be helping to stoke drug prices for commonly used drugs, Grassley said in a February 10 statement.

Ridge Carpenter

The government's accountability arm is looking into price tags for orphan drugs.

Both the report and inquiry arrive amid continuing turmoil over price points for newly approved drugs, particularly in orphan indications. On March 21, the Government Accountability Office, acting on a request from three US senators, launched an investigation into potential abuses of the Orphan Drug Act. The Orphan Drug Act was set in place in 1983 to encourage development of medicines to treat diseases affecting fewer than 200,000 people. The KHN analysis found that about a third of orphan approvals since the program began have been drugs with expanded indications, including best-selling biologic drugs Humira (adalimumab) and Enbrel (etanercept), or drugs with multiple orphan designations. For each approval, drugmakers receive government incentives plus seven years exclusivity for that rare disease. Orphan status became a commercial opportunity.

In early February, Marathon Pharmaceuticals drew criticism for the price of its newly approved corticosteroid drug Emflaza (deflazacort) for treating Duchenne muscular dystrophy (DMD). Deflazacort is not a new drug; it has been used for decades as an anti-inflammatory and immunosuppressant. Though it's not approved for DMD anywhere in the world, some 7–9% of US patient, had been importing it to treat the illness Marathon said. Northbrook, Illinois–based Marathon riled patients when it set the annual list price for its new drug Emflaza at $89,000, when the generic version generally cost less than $2,000 annually.

To gain Emflaza's approval, Marathon conducted 17 preclinical and clinical studies, and is entitled to profit from its efforts, but the price was a staggering increase over the generic deflazacort, and it fired up the DMD community. Facing heated criticism, less than a week after announcing the approval, Marathon released an "Open Letter to the Duchenne Community," saying it would "pause" the marketing process to meet with all interested parties and "move forward with commercialization based on a resulting plan of action." In mid-March, the company said it was selling the rights to Emflaza to PTC Therapeutics for $140 million in cash and stock. The new owner has not yet set a price for the drug.

Another recently approved DMD drug is also facing resistance over pricing. Advocacy groups had pressured the US Food and Drug Administration to clear Exondys 51 (eteplirsen), which the FDA did in September 2016 (*Nat. Biotechnol.* **34**, 675–676, 2016). The antisense drug had showed in clinical studies that dystrophin, the protein affected by the disease, increased in patients' skeletal muscles, yet had demonstrated no clinical benefit. The drugmaker Sarepta of Cambridge, Massachusetts, priced the RNA therapeutic at about $300,000 annually—lower than expected—but still it has met strong pushback from insurers.

Biogen's newly approved drug Spinraza (nusinersen) (*Nat. Biotechnol.* **35**, 99–100, 2017) has experienced similar reimbursement issues. The drug—in-licensed from Ionis in Carlsbad, California—did show clinical efficacy in a pivotal trial in early-onset spinal muscular atrophy. Treated patients achieved a sustained motor function improvement over those in the untreated group, and a greater percentage of patients survived compared with those in the control group. But the Boston biotech priced Spinraza at $125,000 a dose, which puts the first-year cost at ~$750,000, and about $375,000 per year after that, and thus payers have placed caveats around their coverage. Insurers Anthem of Indianapolis, and Humana, of Louisville, Kentucky, for example, said they will reimburse only patients with the most severe forms of the disease, and require proof that the drug is working before covering it beyond 6 months. UnitedHealth Group of Hopkins, Minnesota, will cover all disease forms, but is also requiring drugmakers to demonstrate sustained improvement for continued therapy.

These payers might soon have more clarity on what to weigh up when evaluating orphan drugs. The Institute for Clinical and Economic Review (ICER), a non-profit that examines the value proposition for various classes of drugs and has been warily eyed by both the biotech and pharmaceutical lobby groups, will in May hold a policy summit to discuss orphan drugs and pricing. ICER, which has already examined the non-small-cell lung cancer, hepatitis C and multiple myeloma spaces, among others, plans to release a report on value-based prices for rare conditions, examining Spinraza as a jumping-off point for the discussion.

Grassley has become the watchdog on industry drug prices and previously led the investigation into pricing for Foster City, California–based Gilead's hepatitis C drug, Sovaldi (sofosbuvir; *Nat. Biotechnol.* **32**, 501–502, 2014), and requested an explanation from Canonsburg, Pennsylvania–based Mylan Pharmaceuticals on the rapid increase in price for its EpiPen. In December he wrote a letter to president-elect Donald Trump, saying Trump's "strong leadership will be critical in helping to address the high cost of prescription drugs," after the inauguration. Indeed, high drug prices were an issue in the presidential election for both major political parties; it appears to be the rare bipartisan issue in the US.

And it isn't going away—Trump himself said in January this year that pharma companies are "getting away with murder" concerning drug prices. Marathon, Sarepta and Biogen are just the latest to test the limits of reimbursement in a long-running fight between drugmakers and payers over the perceived value of drugs, with patients sitting in the middle (*Nat. Biotechnol.* **34**, 1231–1241, 2016).

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