

Specialty Pipeline MONTHLY UPDATE

Critical updates in an ever-changing environment

February 2020

NEW DRUG INFORMATION

- **Tepezza™ (teprotumumab):** The U.S. Food and Drug Administration (FDA) granted approval to Horizon's Tepezza for treatment of thyroid eye disease (TED). It is the first FDA-approved medicine for the treatment of TED. Tepezza dosage is weight-based with eight infusions over six months. Horizon's approval of Tepezza is based on results from OPTIC, a Phase 3 confirmatory clinical trial where 83 patients either received eight intravenous infusions of Tepezza or placebo every three weeks for up to 21 weeks. OPTIC demonstrated patients treated with Tepezza had a meaningful improvement (>2 mm) in proptosis (bulging of the eye) as compared against placebo (82.9% vs 9.5% respectively).¹ These results were achieved within a six-month course of therapy. All secondary endpoints were met, including reduced diplopia, improved quality of life and reduction in degree of inflammation pain, swelling and redness. Horizon is currently conducting the OPTIC-X extension trial to gather further insight into long-term efficacy and safety of Tepezza. Horizon's Tepezza launched at a wholesale acquisition cost (WAC) of \$14,900 per vial; a patient weighing 80kg (176 pounds) will be approximately \$447,000 for eight infusions. Tepezza will be available through a limited network of specialty pharmacies.
- **Tazverik™ (tazemetostat):** The FDA granted accelerated approval of Epizyme's Tazverik for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection. Tazverik is the first FDA-approved EZH2 inhibitor and the only approved treatment specifically indicated for epithelioid sarcoma patients. The FDA based its approval on a Phase 2, single arm study that demonstrated an overall response rate of 15% (nine patients) among 62 patients who took 800mg of Tazverik twice daily. Serious adverse events occurred in 37% of patients and 34% needed to suspend dosing due to toxicity.² Tazverik's approval is contingent upon verification of safety and efficacy in a confirmatory trial. In addition, Epizyme is also conducting clinical pharmacology evaluations on liver function and is expanding enrollment in cohort studies. Tazverik is expected to launch with a specialty distribution network by the before the end of February with a WAC of \$186,000 a year.

- **Bynfezia pen™ (octreotide acetate):** Sun Pharmaceuticals' Bynfezia pen has been approved by the FDA for treatment of severe diarrhea/flushing episodes associated with metastatic carcinoid tumors in adult patients, treatment of profuse watery diarrhea associated with vasoactive intestinal peptide tumors (VIPomas) in adult patients, and for reduction of growth hormone (GH) and insulin-like growth factor 1 (IGF-1) [somatomedin C] in adult patients with acromegaly who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.³ Sun Pharmaceuticals approval is based via 505(b)(2) pathway which used Novartis' Sandostatin® (octreotide acetate) as the reference product. Octreotide is also available as a generic injection vial. Launch and pricing are pending.
- **Palforzia™ (peanut Allergen powder-dnfp):** The FDA has approved Aimmune Therapeutics' Palforzia for use in patients with a confirmed diagnosis of peanut allergy. Palforzia is first oral immunotherapy for mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut. Palforzia is administered orally by a registered prescribing physician in office with an initial dose escalation over one day (0.5mg to 6mg), followed by up-dosing to a maintenance dose of 300mg/day over several weeks. Patients must be monitored for 60 minutes after the first dose and each additional dose escalation. Palforzia's approval is based on two Phase 3 clinical trials. At trial entry, all patients could tolerate no more than 30mg (1/10 of a peanut kernel). By trial end, 67% could tolerate 600mg (two peanut kernels), 50% could tolerate 1000mg (four to five peanut kernels).⁴ Efficacy was not shown in participants 18 years of age or older. In July 2019, the Institute for Clinical and Economic Review (ICER) released their review for peanut allergy treatments, including Palforzia. They concluded "new peanut allergy therapies aren't as effective — or nearly as inexpensive — as abstinence. Overall, the body of evidence is not strong enough to suggest that Palforzia offers a superior net health benefit versus strict peanut avoidance." ICER voted 12 to 4 against net health benefit. In September 2019, the FDA AdCom evaluated Palforzia and voted efficacy 7 to 2, safety 8 to 1.⁵ The boxed warning for Palforzia includes an anaphylaxis warning. Palforzia is available only through a Risk Evaluation and Mitigation Strategy (REMS) program and will have a WAC of \$10,680 annually.

NEW INDICATIONS

- **Tecentriq® (atezolizumab):** The FDA broadened the use of Genentech's Tecentriq to be used in combination with Celgene's Abraxane® (nab-paclitaxel) and carboplatin chemotherapy for first-line treatment of metastatic non-small cell lung cancer (NSCLC) for patients who do not have EGFR or ALK genomic tumor aberrations.
- **Xtandi® (enzalutamide):** The FDA expanded the indication for Pfizer/Astellas Pharma's Xtandi to include the treatment of metastatic hormone-sensitive prostate cancer (mHSPC).
- **Botox® (onabotulinumtoxinA):** The FDA expanded its indication for Allergan's Botox to include lower limb spasticity in patients ages two to 17. Previously Botox was only approved for ages 12 and older.
- **Fiasp® (insulin aspart injection):** The FDA expanded the population for Novo Nordisk's Fiasp to include mealtime insulin for children and adolescents with type 1 diabetes.
- **Sabril® (vigabatrin):** The FDA expanded the indication of Lundbeck's Sabril to include children two years of age and older with refractory complex partial seizures. Previously Sabril was approved for patients 10 years of age and older.

FEBRUARY NEWS

- In a Phase II study of 106 patients with pulmonary arterial hypertension (PAH), Acceleron's experimental drug sotatercept hit its primary endpoint: a significant reduction in pulmonary vascular resistance. The drug also met three different secondary endpoints, including the six-minute walking test.⁶
- Late last year, two therapies received FDA approvals in quick succession. Novartis' crizanlizumab, branded Adakveo, was given the FDA nod for its ability to prevent vaso-occlusive crises (VOCs) — periodic episodes of debilitating pain that occur when sickle-shaped red blood cells get stuck inside blood vessels and deprive the body of oxygen-rich blood. Soon after, Global Blood Therapeutics' voxelotor, christened Oxbryta, was approved on the basis of data that showed it increased hemoglobin levels, although its use was not associated with fewer pain crises. The list prices for the three treatments were the main driver of the cost-effectiveness results, with average annual costs of \$88,000 for crizanlizumab, \$84,000 for voxelotor and \$24,000 for L-glutamine, ICER noted. Combined with relatively small improvements in quality-adjusted-life-years (QALYs) gained — 0.85 for crizanlizumab, 0.96 for voxelotor, and 0.10 for L-glutamine — all incremental cost-effectiveness ratios were estimated to be over \$1 million per QALY, ICER calculated, highlighting that none of the analyses undertaken lowered the estimated cost per QALY to less than the benchmark price of \$150,000 per QALY.⁷
- Takeda's Alunbrig, or brigatinib, which targets anaplastic lymphoma kinase genetic mutations, was granted priority review status by the FDA as a first-line treatment for ALK-positive metastatic non-small cell lung cancer.⁸
- The drug, roxadustat, which is designed to stimulate the production of red blood cells by mimicking the effect of high altitude in humans was approved in China last year — marking perhaps the first instance of a multinational pharmaceutical company AstraZeneca paving the way for the sale of a medicine in China, before the United States or Europe. FibroGen and AstraZeneca are locked in a race with Akebia, whose experimental drug vadadustat has a similar mechanism of action. But pivotal vadadustat data are not expected until later in 2020. The dominant drugs for anemia in the United States are red blood cell-boosting erythropoiesis-stimulating agents (ESA) from Amgen. The standard of care does, however, come with high cardio risks — but given the steep overall mortality rate for this patient population, it is a risk regulators consider acceptable.⁹

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