PRIME THERAPEUTICS®

Drug Pipeline MONTHLY UPDATE

Critical updates in an ever-changing environment

January 2020

NEW DRUG INFORMATION

- **Dayvigo™ (lemborexant):** The U.S. Food and Drug Administration (FDA) approved Eisai/Purdue Pharma's Dayvigo for the treatment of insomnia. Dayvigo inhibits orexin signaling which is thought to regulate sleep and wake by dampening wakefulness, a similar mechanism to Merck's Belsomra™ (suvorexant). The FDA's approval was based on two, Phase 3 studies, that evaluated Dayvigo versus placebo at one month and six months. The primary efficacy endpoint was the mean change from baseline to end of treatment for log-transformed, patient-reported (subjective) sleep onset latency.[1] Both studies demonstrated Dayvigo 5mg and 10mg had a statistically significant improvement in the primary endpoint compared to placebo. Dayvigo will be classified as a controlled substance and will launch after DEA scheduling, with pricing to follow.

- **Ubrelvy™ (ubrogepant):** Allergan's Ubrelvy has been approved by the FDA for treatment of acute migraine with or without aura. Ubrelvy is the first oral calcitonin gene-related peptide (CGRP) receptor antagonist and the first CGRP indicated for acute migraine. Ubrelvy's place in therapy appears to follow the use or failure of triptans for acute migraines. Ubrelvy's approval is based on four clinical trials that established safety and efficacy of 50mg and 100mg tablets. Results show reduction of pain from migraine and provide relief from the most bothersome migraine-associated symptoms at two hours, compared with placebo.[2] On January 10, 2020 the Institute for Clinical and Economic Review (ICER) released an evidence report assessing the comparative clinical effectiveness and economic value of three CGRP agents; Eli Lilly's Reyvow™ (lasmiditan), Biohaven's rimegepant, and Allergan's Ubrelvy™ (ubrogepant). The evidence report found Reyvow, rimegepant and Ubrelvy all perform better than placebo, but evidence is not adequate to distinguish among them. Generic triptans remain the most effective option for acute treatment of migraine for most patients requiring prescription medications.[3] According to David Rind, MD, ICER's Chief Medical Officer, "These new therapies appear to be less effective overall than triptans and are expected to be much more expensive."[3] Pricing is unknown but ICER estimates one year of Ubrelvy between $2,200 – $3,200. Allergan plans to launch Ubrelvy by end of January 2020, pricing to follow.

- **Caplyta™ (lumateperone):** The FDA has approved Intra-Cellular Therapies' Caplyta for treatment of schizophrenia. Caplyta is a once daily, 42mg oral capsule that does not require titration. Caplyta is a first-in-class antipsychotic that acts through serotonergic, dopaminergic and glutamatergic systems. The FDA approval of Caplyta was based on two placebo-controlled trials, with a primary endpoint of change in Positive and Negative Syndrome Scale (PANSS) total score at Day 28. The two studies tested Caplyta 28mg, 42mg and 84mg verses placebo. Caplyta 42mg demonstrated a statistically significant change in PANSS compared to placebo; however, Caplyta 84mg and Caplyta 28mg groups did not separate from placebo.[4] Intra-Cellular Therapies also conducted two studies of Caplyta compared to risperidone, in which Caplyta was shown to be statistically significantly superior to risperidone on safety and tolerability measures.[5] Caplyta has a Boxed Warning for increase in death for elderly patients with dementia-related psychosis. Intra-Cellular Therapies plans to launch Caplyta in March 2020, pricing to follow.
- **Conjupri™ (levamlodipine):** Conjupro Biotherapeutics' Conjupri has been approved by the FDA for the treatment of hypertension in adults and pediatric patients 6 years and older, to lower blood pressure. Conjupri is an active isomer of amlodipine, a long-acting calcium channel blocker, which is available generically. Conjupro Biotherapeutics' applied for FDA approval of Conjupri using the 505(b)(2) pathway. It will be available as a 1.25mg, 2.5mg and 5mg oral tablet. Conjupri's launch and pricing are pending.
- **Valtoco™ (diazepam):** Neurelis' Valtoco has been approved by the FDA for the treatment of cluster or acute repetitive seizures in patients 6 years of age and older. Valtoco is a nasal spray that uses a combination of vitamin E-based solution and Intravail® technology. The FDA stated Valtoco was "clinically superior" to Valeant's Diastat™ (diazepam rectal gel) and granted seven years of orphan drug exclusivity. The FDA stated, "In the context of when this drug is to be given, typically in the middle of a seizure event, it is inherently easier to administer the drug to a patient intranasally than rectally."[7] Similar products include UCB's Nayzilam™ (midazolam nasal spray). Valtoco's launch and pricing are pending.

GENERIC DRUG INFORMATION

- **Travatan Z® (travoprost ophth soln, 0.004%):** Multiple manufacturers have launched their generic version of Alcon/Novartis' Travatan Z for glaucoma or ocular hypertension. Travatan Z generated $544 million in U.S. annual sales in 2018.
- **Aczone 7.5%® (dapsone gel, 7.5%):** Taro launched their authorized generic version of Allergan's Aczone 7.5% for treatment of acne. Taro is eligible for 180-day exclusivity. Multiple manufacturers are set to launch their generics in 2021. Aczone 7.5% generated $263 million in U.S. annual sales in 2018.
- **Exelderm soln® (sulconazole nitrate solution, 1% and sulconazole nitrate cream, 1%):** JG Pharma launched their authorized generic version of Ranbaxy Pharmaceuticals' Exelderm solution and cream for treatment of tinea corporis and tinea pedis. True generic launch dates are unknown. U.S. annual sales are unknown for Exelderm solution and cream.
- **Silenor® (doxepin hcl):** Multiple manufacturers have launched their generic version of Somaxon Pharmaceuticals' Silenor for treatment of insomnia. Silenor generated $47 million in U.S. annual sales in 2018.
- **Zohydro ER caps® (hydrocodone bitartrate 12-hour abuse-deterrent):** Macoven Pharmaceuticals launched their authorized generic version of Pernix Therapeutics Zohydro ER for treatment of pain. Multiple manufacturers are planned to launch their generics first quarter 2020. Zohydro ER generated $42 million in U.S. annual sales in 2018.
- **Jadenu®+ (deferasirox tab):** Multiple manufacturers have launched their generic version of Novartis' Jadenu for treatment of chronic iron overload. Jadenu generated $474 million in U.S. annual sales in 2018.
- **Depen Titratabs® (penicillamine tab):** Par/Endo have launched their generic version of Meda Pharmaceuticals Depen Titratabs for treatment of cystinuria hepatic encephalopathy and Wilson's disease. Depen Titratabs generated ‹$10 million in U.S. annual sales in 2018.

+ Specialty medication

REFERENCES

1. http://eisai.mediaroom.com/2019-12-23-U-S-FDA-Approves-Eisais-DAYVIGO-TM-lemborexant-for-the-Treatment-of-Insomnia-in-Adult-Patients.
2. https://www.allergan.com/News/Details/2019/12/Allergan%20Receives%20US%20FDA%20Approval%20for%20UBRELVY%20for%20the%20Acute%20Treatment%20of%20Migraine%20with%20or%20without%20Au.
3. https://icer-review.org/announcements/acute_migraine_evidence_report/.
4. https://ir.intracellulartherapies.com/news-releases/news-release-details/fda-approves-intra-cellular-therapies-novel-antipsychotic.
5. https://www.psychcongress.com/posters/lumateperone-iti-007-treatment-schizophrenia-overview-placebo-controlled-clinical-trials.
6. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212895s000lbl.pdf.
7. https://endpts.com/clinical-superiority-diszepam-nasal-spray-illustrates-fda-parameters-for-orphan-drug-exclusivity/.