Lybalvi™ (olanzapine/samidorphan) – New drug approval

- On June 1, 2021, Alkermes announced the FDA approval of Lybalvi (olanzapine/samidorphan), for the treatment of:

    - Schizophrenia in adults
    - Bipolar I disorder in adults: (1) as acute treatment of manic or mixed episodes as monotherapy and as adjunct to lithium or valproate or (2) maintenance monotherapy treatment.

- Lybalvi is a combination of olanzapine, an atypical antipsychotic, and samidorphan, a novel opioid antagonist.

- The efficacy of Lybalvi for the treatment of schizophrenia was established based, in part, upon previous adequate and well-controlled studies of orally administered olanzapine. Efficacy of Lybalvi was also evaluated in a 4-week, randomized, double-blind, placebo- and active-controlled study. In this study, adult patients were randomized to Lybalvi, olanzapine, or placebo. The primary efficacy endpoint was change from baseline in Positive and Negative Syndrome Scale (PANSS) total score at week 4. Total PANSS scores range from 30 to 210, with a higher score reflecting greater symptom severity.

    - The placebo-subtracted difference for Lybalvi in the total PANSS score was -6.4 (95% CI: -10.0, -2.8).

- In addition, an evaluation of weight changes in patients with schizophrenia was conducted in a 24-week study comparing Lybalvi and olanzapine. The co-primary endpoints were percent change from baseline in body weight and the proportion of patients who gained ≥ 10% body weight at week 24.

    - The olanzapine-subtracted difference for Lybalvi in percent change from baseline in body weight was -2.4 (95% CI: -3.9, -0.9).
    - The olanzapine-subtracted difference for Lybalvi in patients who gained ≥ 10% body weight was -13.7 (95% CI: -22.8, -4.6).

- The efficacy of Lybalvi in the treatment of adult patients with bipolar I disorder was based on previous adequate and well-controlled studies of orally administered olanzapine.

- Lybalvi carries a boxed warning for increased mortality in elderly patients with dementia-related psychosis.

- Lybalvi is contraindicated in patients:

    - Who are using opioids
    - Who are undergoing acute opioid withdrawal.

- Additional warnings and precautions for Lybalvi include cerebrovascular adverse reactions, including stroke in elderly patients with dementia-related psychosis; precipitation of severe opioid withdrawal in patients who are physiologically dependent on opioids; vulnerability to life-threatening opioid overdose; neuroleptic malignant syndrome; drug reaction with eosinophilia and systemic symptoms; metabolic changes; traditive dyskinesia; orthostatic hypotension and syncope; falls; leukopenia, neutropenia, and agranulocytosis; dysphagia; seizures; potential for cognitive and motor impairment;

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body temperature dysregulation; anticholinergic (antimuscarinic) effects; hyperprolactinemia; and risks associated with combination treatment with lithium or valproate.

- The most common adverse reactions (≥ 5% and at least twice placebo) with Lybalvi use for schizophrenia were increased weight, somnolence, dry mouth, and headache.

- Based on data from olanzapine, the most common adverse reactions with Lybalvi use (as monotherapy) for treatment of bipolar I disorder are asthenia, dry mouth, constipation, increased appetite, somnolence, dizziness, and tremor. Based on data from olanzapine, the most common adverse reactions with Lybalvi use (as adjunct to lithium or valproate) are dry mouth, dyspepsia, weight gain, increased appetite, dizziness, back pain, constipation, speech disorder, increased salivation, amnesia, paresthesia.

- The recommended initial dose of Lybalvi for treatment of schizophrenia is 5 mg/10 mg (contains 5 mg of olanzapine and 10 mg of samidorphan) or 10 mg/10 mg orally once daily. The recommended dosage is 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg once daily.

    — The dosage may be adjusted at weekly intervals of 5 mg (based on the olanzapine component) depending upon clinical response and tolerability, up to the maximum recommended dosage of 20 mg/10 mg once daily.

- The dosing recommendations for Lybalvi for bipolar I disorder include:

    — Monotherapy: Initiate at 10 mg/10 mg or 15 mg/10 mg once daily. The recommended dosage is 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg once daily. The maximum recommended dosage is 20 mg/10 mg once daily.
    — Maintenance monotherapy: Administer 5 mg/10 mg, 10 mg/10 mg, 15 mg/10 mg, or 20 mg/10 mg once daily.
    — Adjunctive to lithium or valproate: Initiate at 10 mg/10 mg once daily. The recommended dosage is 10 mg/10 mg, 15 mg/10 mg or 20 mg/10 mg, once daily.
    — Dosage may be adjusted at weekly intervals of 5 mg (based on the olanzapine component), depending upon clinical response and tolerability, up to the maximum recommended dosage of 20 mg/10 mg once daily.

- Alkermes plans to launch Lybalvi in 4th quarter 2021. Lybalvi will be available as 5 mg/10 mg, 10 mg/10 mg, 15 mg/10 mg, and 20 mg/10 mg tablets.