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BELVIQ and BELVIQ XR (lorcaserin HCl) CIV – Pennsylvania State Medicaid Testimony

May 23, 2017

Dear Committee Members,

I am Elena Nikonova, Medical Director for BELVIQ, US Medical Affairs. On behalf of Eisai, I appreciate your time reviewing our product that could potentially help patients in PA who have tried and failed (some multiple times) on diet and exercise alone to achieve their goals. I would like to highlight the following:

Introduction:

- BELVIQ (lorcaserin HCl) CIV was approved for use by the FDA in 2013 on the basis of three pivotal clinical trials which used lorcaserin 10 mg immediate release tablets administered twice daily.
- BELVIQ XR (lorcaserin HCl) CIV was approved in 2016 on the basis of bioequivalence data comparing the 20mg XR formulation once daily versus lorcaserin 10 mg twice daily.

Mechanism of Action:

- BELVIQ and BELVIQ XR® is believed to decrease food consumption and promote satiety by selectively activating serotonin 2C ($5\text{-}HT_{2c}$) receptors in the hypothalamus. The exact mechanism of action is not known.

Indication:

- BELVIQ and BELVIQ XR is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:
  - 30 kg/m^2 or greater, or
  - 27 kg/m^2 or greater with at least one weight-related comorbid condition

Limitations of use:

- The safety and efficacy of co-administration of BELVIQ and BELVIQ XR with other products intended for weight loss including prescription drugs (e.g., phentermine), over-the-counter drugs, and herbal preparations have not been established.
- The effect of BELVIQ and BELVIQ XR on cardiovascular morbidity and mortality has not been established.

Key points:

1. **Efficacy:** from pivotal studies using lorcaserin 10mg immediate release twice daily, it has been shown that patients reach weight loss (WL) of either ≥5 or ≥10% twice as effectively as diet and exercise alone (placebo). Long-term 2-year data show that more patients (67.9%, or 258/380) who continued taking BELVIQ for two years maintained a weight loss of ≥5% versus those started on BELVIQ and switched to placebo (50.3%, or 88/175)

    a. BELVIQ was evaluated in three randomized, double-blind, placebo-controlled trials with nearly 8,000 patients with overweight (OW) and comorbidities or obesity.
    b. In the pooled BLOOM and BLOSSOM trials, patients with overweight/obesity without diabetes taking BELVIQ immediate release twice daily:
        i. Lost more weight than patients taking placebo (5.8 kg vs 2.5 kg, respectively),

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ii. More BELVIQ vs. placebo patients lost ≥5% of their body weight (47.1% vs. 22.6%, p<0.0001; OR 3.1, p<0.0001) and ≥10% of their body weight (22.4% vs 8.7%, p<0.0001; OR 3.1, p<0.0001) at 1 year.

iii. Patients taking BELVIQ also demonstrated improvements in cardiometabolic risk factors, including decreases in blood pressure (systolic: -1.8 vs -1.0 mmHg, p=0.007; diastolic: -1.6 vs -1.0 mmHg, p=0.003) and total cholesterol (-0.9% vs 0.4%) versus placebo.

c. BLOOM-DM (N=604) evaluated the safety and efficacy of BELVIQ immediate release twice daily as adjunctive therapy for weight loss in OW (BMI ≥27) adult patients with T2D who were treated with metformin and/or a sulfonylurea (SFU). At 1 year:
   i. More BELVIQ vs placebo patients lost ≥5% (37.5% vs 16.1%; p<0.001; OR 3.1, p<0.0001) and ≥10% of their body weight (16.3% vs 4.4%; p<0.001; OR 4.1 p<0.0001) at 1 year.
   ii. BELVIQ patients also had significantly greater mean weight loss than placebo patients (4.7kg vs 1.6kg; p<0.001).
   iii. Glycemic improvements were significantly greater with BELVIQ vs placebo in HbA1C (0.9% vs 0.4%) and fasting glucose (27.4mg/dl vs 11.9mg/dl) (p<0.001).
   iv. There were changes from baseline in heart rate (-2.0 vs -0.4 bpm) treated with BELVIQ and placebo.

2. **Safety:**
   a. Contraindication:
      i. BELVIQ and BELVIQ XR is contraindicated during pregnancy, because weight loss offers no potential benefit to a pregnant woman and may result in fetal harm.
      ii. BELVIQ and BELVIQ XR is contraindicated in patients with prior hypersensitivity reactions to lorcaserin or to any of the product components. Hypersensitivity reactions have been reported.
   b. Warnings and Precautions:
      i. Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS)-like Reactions,
      ii. Valvular Heart Disease,
      iii. Cognitive Impairment,
      iv. Psychiatric Disorders,
      v. Potential Risk of Hypoglycemia in T2D Patients,
      vi. Priapism, hematological changes, prolactin elevation, pulmonary hypertension,
      vii. Heartrate decreases
   c. Most Common Adverse Reactions:
      i. In the BLOOM and BLOSSOM studies, upper respiratory infections, headache, nasopharyngitis, dizziness, nausea, and fatigue were the most common adverse events that occurred more frequently in patients taking BELVIQ 10mg twice daily than placebo.
      ii. In the BLOOM-DM study, headache, back pain, nasopharyngitis, and nausea were the most common adverse events that occurred with greater incidence in patients taking BELVIQ 10mg twice daily than placebo. Hypoglycemia was also more frequent in patients taking BELVIQ 10mg twice daily than placebo, particularly if on a concomitant sulfonylurea.
      iii. Common side effects in patients on BELVIQ XR were similar to those seen in patients on BELVIQ.

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d. BELVIQ and BELVIQ XR is not a stimulant or narcotic. It is a federally controlled substance (CIV) because it may be abused or lead to dependence.

For more information about BELVIQ and BELVIQ XR, including Important Safety Information, please refer to the provided full Prescribing Information.

Belviq XR Bioequivalence:

- BELVIQ XR 20 mg administered once daily was compared with immediate-release lorcaserin hydrochloride 10 mg tablet administered twice daily under fasted conditions in 34 healthy subjects in an open label, randomized, crossover clinical trial.
    - At steady state, the time to reach peak plasma concentrations of lorcaserin (tmax) following BELVIQ XR 20 mg once daily was approximately 10 hours compared with 1.5 hours for immediate-release lorcaserin hydrochloride 10 mg tablet twice daily.
    - A single dose administration of BELVIQ XR 20 mg resulted in comparable total plasma exposure ($AUC_{0-\infty}$), but approximately 25% lower peak exposures (Cmax) relative to two doses of immediate-release tablets administered 12 hours apart.
    - At steady state, however, both Cmax,ss and area under the plasma concentration versus time curve ($AUC_{0-24,ss}$) of BELVIQ XR 20 mg administered once daily were bioequivalent to immediate-release lorcaserin hydrochloride 10 mg tablets administered twice daily under fasted conditions.

- Intake of high fat, high calorie breakfast before a single 20 mg oral dose of BELVIQ XR resulted in approximately 46% increase in Cmax and 17% increase in AUC0-∞ but no change in tmax. At steady state, however, there was no significant food effect on the rate or extent of absorption of BELVIQ XR.

Dosing:

- The recommended dose of BELVIQ is 10 mg twice daily.
- BELVIQ XR is 20 mg administered orally once daily. BELVIQ XR tablet must be swallowed whole and must not be chewed, crushed, or divided.
- BELVIQ and BELVIQ XR can be taken with or without food.

3. Focus on long-term rather than short-term benefits of weight management had been emphasized and appreciated by many professional organizations. As there is no 'one size fits all' treatment and diet and exercise continue to underperform for some patients with overweight (plus >=1 comborbidity) and obesity, health care professionals need additional tools to meet those patients' needs. Pharmacotherapy recommended in AACE guidelines as an adjunct therapy to diet and exercise can be such a powerful tool. As multidisciplinary clinicians use patient-centered approach, the question will be which drug provides the most appropriate benefit-risk profile for their patients.

CONCLUSION: BELVIQ and BELVIQ XR is believed to decrease food consumption and promote satiety by selectively activating serotonin 2C (5-HT2c) receptors in the hypothalamus. The exact mechanism of action is not known. In clinical trials, lorcaserin immediate release tablets was proven more than twice as effective at helping patients lose ≥5 and ≥10% of body weight over diet and exercise alone. In addition, in patients without type 2 diabetes, there was a decrease in blood pressure and cholesterol vs. placebo. In patients with diabetes, there were changes from baseline in heart rate treated with BELVIQ and placebo.

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Eisai recommends that PA state add BELVIQ and BELVIQ XR as covered medications for appropriate patients.

Thank you very much for your time and consideration. I would be happy to address your questions, if any.

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