Voquezna® (vonoprazan) – New drug approval

- On November 1, 2023, Phathom Pharmaceuticals announced the FDA approval of Voquezna (vonoprazan):
    - For healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults
    - To maintain healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults
    - In combination with amoxicillin and clarithromycin for the treatment of *Helicobacter pylori* (*H. pylori*) infection in adults
    - In combination with amoxicillin for the treatment of *H. pylori* infection in adults.
- Voquezna is a single-ingredient formulation of vonoprazan, a potassium-competitive acid blocker.
- Vonoprazan was previously approved as part of a co-packaged product with amoxicillin and clarithromycin (Voquezna Triple Pak) and amoxicillin (Voquezna Dual Pak).
    - Voquezna Triple and Dual Pak are approved for the treatment of *H. pylori* infection in adults.
- The efficacy of Voquezna for healing of erosive esophagitis and relief of heartburn was established in a randomized, active-controlled, double-blind study (U.S. and Europe) in 1,024 adult patients with erosive esophagitis. Patients were randomized to Voquezna 20 mg once daily or lansoprazole 30 mg once daily for 2 to 8 weeks. The primary endpoint was endoscopically confirmed complete healing of all grades of erosive esophagitis at week 2 or week 8. The percentage of 24-hour heartburn-free days through week 8 was evaluated as a secondary endpoint.
    - Voquezna demonstrated non-inferiority vs. lansoprazole for the rate of healing of erosive esophagitis at week 2 or 8. The healing rates were 93% and 85% with Voquezna and lansoprazole, respectively (difference 8, 95% CI: 4.5, 12.2).
    - Voquezna demonstrated non-inferiority vs. lansoprazole for percentage of 24-hour heartburn-free days. The mean heartburn-free days were 67% and 64% for Voquezna and lansoprazole, respectively (difference 3, 95% CI: -1.6, 7.0).
- Two additional randomized, active-controlled, double-blind studies conducted outside of the U.S., of similar design to the U.S. trial, also demonstrated non-inferiority of vonoprazan 20 mg once daily compared to lansoprazole 30 mg once daily for the primary endpoint of healing of all grades of erosive esophagitis by week 8.
- Patients who completed the healing phase of the erosive esophagitis study and showed endoscopically confirmed healed erosive esophagitis at week 2 or week 8 were rerandomized in the maintenance phase to either Voquezna 10 mg once daily, a higher dosage of Voquezna, or lansoprazole 15 mg once daily. The primary endpoint was maintenance of healed erosive esophagitis (all grades) through week 24. The percentage of 24-hour heartburn-free days through week 24 was evaluated for non-inferiority as a secondary endpoint.
    - Voquezna 10 mg demonstrated non-inferiority and superiority vs. lansoprazole for the rate of maintenance healing at week 24. Maintenance healing rates were 79% and 72% for Voquezna and lansoprazole, respectively (difference 7, 95% CI: 0.2, 14.1).

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  - Voquezna 10 mg demonstrated non-inferiority vs. lansoprazole for percentage of 24-hour heartburn-free days through week 24. The mean heartburn-free days were 81% and 79% for Voquezna and lansoprazole, respectively (difference 2, 95% CI: -2.3, 6.8).
  - The higher Voquezna dose group did not demonstrate additional treatment benefit compared to Voquezna 10 mg once daily.

- Two additional randomized, active-controlled, double-blind studies conducted outside of the U.S., of similar design to the U.S. trial, also demonstrated non-inferiority of vonoprazan 10 mg once daily compared to lansoprazole 15 mg once daily for the primary endpoint of maintenance of healed erosive esophagitis (all grades) through week 24.

- Voquezna is contraindicated:

  - In patients with a known hypersensitivity to vonoprazan or any component of Voquezna
  - With rilpivirine-containing products.

- Warnings and precautions for Voquezna include presence of gastric malignancy; acute tubulointerstitial nephritis; *Clostridioides difficile*-associated diarrhea; bone fracture; severe cutaneous adverse reactions; vitamin B12 deficiency; hypomagnesemia and mineral metabolism; interactions with diagnostic investigations for neuroendocrine tumors; and fundic gland polyps.

- The most common adverse reactions (≥ 2%) with Voquezna use for healing of erosive esophagitis were gastritis, diarrhea, abdominal distension, abdominal pain, and nausea.

- The most common adverse reactions (≥ 3%) with Voquezna use for maintenance of healed erosive esophagitis were gastritis, abdominal pain, dyspepsia, hypertension, and urinary tract infection.

- For healing of erosive esophagitis and relief of heartburn, the recommended adult oral dosage of Voquezna is 20 mg once daily for 8 weeks.

- For maintenance of healed erosive esophagitis and relief of heartburn, the recommended adult oral dosage of Voquezna is 10 mg once daily for up to 6 months.

- Phathom Pharmaceuticals plans to launch Voquezna in December 2023. Voquezna will be available as a 10 mg and 20 mg tablet.

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