APONVIE™ (aprepitant) injectable emulsion

ADMINISTRATION FACT SHEET

APONVIE IS ADMINISTERED VIA A SINGLE 30-SECOND IV PUSH

- APONVIE is administered via **a 30-second IV push.** Therapeutic plasma concentrations associated with **≥97% receptor occupancy in the brain are achieved within 5 minutes** for APONVIE—unlike oral aprepitant, which was taken 1 to 3 hours prior to induction of general anesthesia in clinical trials and does not reach maximum concentration until 3 hours after administration[1-4,a]
- **Plasma concentrations of aprepitant were higher than those of the oral formulation for approximately 3 hours.** By the 4-hour timepoint, the plasma concentrations for the 2 formulations converged, and remained similar.[5]
- At 48 hours, therapeutic plasma concentrations associated with NK_1 receptor occupancy is estimated to be **maintained at >90%**[2,5,a]
- Because IV administration allows the drug to enter directly into systemic circulation without the delay associated with absorption processes, it results in 100% bioavailability, making it the best way to deliver a drug rapidly and accurately[6]

[a]The relationship between receptor occupancy and efficacy has not been established.

STORAGE AND HANDLING[1]

APONVIE injectable emulsion is supplied as an opaque, off-white to amber emulsion in a single-dose 5 mL glass vial containing 32 mg/4.4 mL aprepitant:

- 10 single-dose vials per carton
- Refrigerate APONVIE at 2°C to 8°C (36°F to 46°F)
- APONVIE injectable emulsion vials can remain at room temperature up to 60 days (20°C to 25°C [68°F to 77°F])
- Do not freeze

INDICATION

APONVIE is a substance P/neurokinin-1 (NK_1) receptor antagonist, indicated for the prevention of postoperative nausea and vomiting in adults.

Limitations of Use: APONVIE has not been studied for treatment of established nausea and vomiting.

PREPARATION OF APONVIE FOR ADMINISTRATION[1]

- Aseptically withdraw 4.4 mL from the vial. Do not dilute.
- The infusion line should be flushed with normal saline before and after administration of APONVIE

IMPORTANT SAFETY INFORMATION

Contraindications:

APONVIE is contraindicated in patients with a history of hypersensitivity to aprepitant or any component of the product, and in patients taking pimozide. Increased pimozide levels may cause serious or life-threatening reactions, such as QT prolongation.

Please see additional Important Safety Information on the following page and full Prescribing Information.

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IMPORTANT SAFETY INFORMATION (cont)

Warning and Precautions:

Hypersensitivity Reactions: Serious hypersensitivity reactions, including anaphylaxis, during or soon after administration of aprepitant have occurred. Symptoms including dyspnea, eye swelling, flushing, pruritus, and wheezing have been reported. Monitor patients during and after administration. If hypersensitivity reactions occur, administer appropriate medical therapy. Do not administer APONVIE in patients who experienced these symptoms with previous use of aprepitant.

Clinically Significant CYP3A4 Drug Interactions: Aprepitant is a substrate, weak-to-moderate (dose-dependent) inhibitor, and an inducer of CYP3A4. Use of pimozide, a CYP3A4 substrate, with APONVIE is contraindicated. Use of APONVIE with strong CYP3A4 inhibitors (eg, ketoconazole) may increase plasma concentrations of aprepitant and result in an increased risk of adverse reactions related to APONVIE. Use of APONVIE with strong CYP3A4 inducers (eg, rifampin) may result in a reduction in aprepitant plasma concentrations and decreased efficacy of APONVIE.

Decrease in INR with Concomitant Warfarin: Use of aprepitant with warfarin, a CYP2C9 substrate, may result in a clinically significant decrease in the International Normalized Ratio (INR) of prothrombin time. Monitor the INR in patients on chronic warfarin therapy in the 2-week period particularly at 7 to 10 days, following administration of APONVIE.

Risk of Reduced Efficacy of Hormonal Contraceptives: The efficacy of hormonal contraceptives may be reduced for 28 days following administration of APONVIE. Advise patients to use effective alternative or back-up methods of non-hormonal contraception for 1 month following administration of APONVIE.

Use in Specific Populations:

Avoid use of APONVIE in pregnant women as alcohol is an inactive ingredient in APONVIE. There is no safe level of alcohol exposure in pregnancy.

Adverse Reactions:

Most common adverse reactions (incidence ≥3%) for APONVIE are constipation, fatigue, and headache and for oral aprepitant are constipation and hypotension.

Report side effects to Heron at 1-844-437-6611 or to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information.

REFERENCES: 1. APONVIE [package insert]. San Diego, CA: Heron Therapeutics Inc; 2022. **2.** Data on file. Summary of clinical pharmacology studies. San Diego, CA: Heron Therapeutics Inc; 2021. **3.** Van Laere K, De Hoon J, Bormans G, et al. Equivalent dynamic human brain NK1-receptor occupancy following single-dose i.v. fosaprepitant vs. oral aprepitant as assessed by PET imaging. *Clin Pharmacol Ther.* 2012;92(2):243-250. doi:10.1038/clpt.2012.62. **4.** EMEND [package insert]. Whitehouse Station, NJ: Merck & Co Inc; 2019. **5.** Data on file. Study HTX-019-111. San Diego, CA: Heron Therapeutics Inc; 2021. **6.** Ruiz ME, Scioli Montoto S. Routes of drug administration. In: Talevi A, Quiroga P, eds. *ADME Processes in Pharmaceutical Sciences*. Springer, Cham. Published December 1, 2018. doi.org/10.1007/978-3-319-99593-9_6.

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