



Heron Announces FDA Approval of Supplemental New Drug Application to Expand CINVANTI® Label for IV Push

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SAN DIEGO, Feb. 26, 2019 /PRNewswire/ -- Heron Therapeutics, Inc. (Nasdaq: HRTX), a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs, today announced that the U.S. Food and Drug Administration (FDA) has approved Heron's supplemental New Drug Application (sNDA) for CINVANTI (aprepitant) injectable emulsion, for intravenous (IV) use. The sNDA requested FDA approval to expand the administration of CINVANTI beyond the already approved administration method (a 30-minute IV infusion) to include a 2-minute IV injection.

CINVANTI is the first and only polysorbate 80-free, IV formulation of an NK₁ receptor antagonist (RA) indicated for the prevention of acute and delayed chemotherapy-induced nausea and vomiting (CINV). CINVANTI is the first IV formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK₁ RA to significantly reduce CINV in both the acute phase (0 – 24 hours after chemotherapy) and the delayed phase (24 – 120 hours after chemotherapy).

CINVANTI was initially approved based on data demonstrating the bioequivalence of CINVANTI to EMEND IV® (fosaprepitant), supporting its efficacy for the prevention of acute and delayed CINV following highly emetogenic cancer chemotherapy (HEC) and moderately emetogenic cancer chemotherapy (MEC). Results from two pivotal, randomized, cross-over, bioequivalence studies of CINVANTI and EMEND IV showed subjects receiving CINVANTI reported fewer adverse events than those receiving EMEND IV, including substantially fewer infusion-site reactions.

The new method of administration for CINVANTI was approved based on a third study demonstrating bioequivalence and a comparable safety profile for CINVANTI given as a 30-minute IV infusion and as a 2-minute IV injection, also referred to as an IV push.

"CINVANTI, delivering the efficacy of aprepitant, but without polysorbate 80, has been an important addition for the prevention of CINV. Notably, data now show that the 2-minute IV push has comparable safety to the 30-minute IV infusion. This approval will enable physicians to leverage the operational advantages of this method of administration and will contribute to a reduction in total patient time spent in the infusion suite," said Rudolph M. Navari, M.D., Ph.D., University of Alabama, Birmingham School of Medicine, Division of Hematology Oncology.

"We are pleased to have strengthened our CINV franchise with today's label expansion for CINVANTI, as we now have the only NK₁ RA that offers the benefits and flexibility of an IV push method of administration," said Barry Quart, Pharm.D., President and Chief Executive Officer of Heron.

"Administration of CINVANTI by 2-minute IV push is an important advantage for our customers compared to EMEND IV, which requires reconstitution and an IV bag for infusion."

About CINVANTI (aprepitant) injectable emulsion

CINVANTI, in combination with other antiemetic agents, is indicated in adults for the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy (HEC), including high-dose cisplatin, and nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC). CINVANTI is an IV formulation of aprepitant, a substance P/neurokinin-1 (NK₁) receptor antagonist (RA). CINVANTI is the first IV formulation to directly deliver aprepitant, the active ingredient in EMEND® capsules. Aprepitant (including its prodrug, fosaprepitant) is the only single-agent NK₁ RA to significantly reduce nausea and vomiting in both the acute phase (0 – 24 hours after chemotherapy) and the delayed phase (24 – 120 hours after chemotherapy). CINVANTI is the only IV formulation of an NK₁ RA indicated for the prevention of acute and delayed nausea and vomiting associated with HEC and nausea and vomiting associated with MEC that is free of polysorbate 80 or any other synthetic surfactant. The FDA-approved dosing administration included in the United States prescribing information for CINVANTI is a 30-minute infusion or a 2-minute injection.

Please see full prescribing information at www.CINVANTI.com.

Important Safety Information

Contraindications

CINVANTI is contraindicated in patients with hypersensitivity to any of the components of CINVANTI.

Concurrent use of pimozone with CINVANTI is contraindicated.

Warnings and Precautions

Clinically Significant CYP3A4 Drug Interactions

Aprepitant is a substrate, weak-to-moderate (dose-dependent) inhibitor, and an inducer of CYP3A4.

- Use with other drugs that are CYP3A4 substrates may result in increased plasma concentration of the concomitant drug.
 - Use of pimozone with CINVANTI is contraindicated due to the risk of significantly increased plasma concentrations of pimozone, potentially resulting in prolongation of the QT interval, a known adverse reaction of pimozone.
- Use of CINVANTI with strong or moderate CYP3A4 inhibitors (e.g., ketoconazole, diltiazem) may increase plasma concentrations of aprepitant and result in an increased risk of adverse reactions related to CINVANTI.
- Use of CINVANTI with strong CYP3A4 inducers (e.g., rifampin) may result in a reduction in aprepitant plasma concentrations and decreased efficacy of aprepitant.

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis during or soon after administration of CINVANTI have occurred. Symptoms including dyspnea, eye swelling, flushing, pruritus, and wheezing have been reported. If hypersensitivity reactions occur, discontinue CINVANTI. Do not reinstate CINVANTI in patients who experience these symptoms with previous use.

Decrease in INR with Concomitant Warfarin

Co-administration of CINVANTI 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 initiation of CINVANTI with each chemotherapy cycle.

Risk of Reduced Efficacy of Hormonal Contraceptives

The efficacy of hormonal contraceptives may be reduced during administration of and for 28 days following the last dose of CINVANTI. Advise patients to use effective alternative or back-up methods of non-hormonal contraception during treatment with CINVANTI and for 1 month following administration of CINVANTI or oral aprepitant, whichever is administered last.

Use in Specific Populations

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

Adverse Reactions

The most common adverse reactions with the 3-day oral aprepitant regimen in conjunction with MEC ($\geq 1\%$ and greater than standard therapy) were fatigue and eructation.

The most common adverse reactions with the single-dose intravenous fosaprepitant regimen in conjunction with HEC were generally similar to that seen in prior HEC studies with oral aprepitant. In addition, infusion site reactions (3%) occurred.

The most common adverse reactions with single-dose CINVANTI ($\geq 2\%$) were headache and fatigue. The safety profile of CINVANTI in healthy subjects who received a single 2-minute injection was similar to that seen with a 30-minute infusion.

About Heron Therapeutics, Inc.

Heron Therapeutics, Inc. is a commercial-stage biotechnology company focused on improving the lives of patients by developing best-in-class treatments to address some of the most important unmet patient needs. Heron is developing novel, patient-focused solutions that apply its innovative science and technologies to already-approved pharmacological agents for patients suffering from pain or cancer.

For more information, visit www.heronrx.com.

Forward-looking Statements

This news release contains "forward-looking statements" as defined by the Private Securities Litigation Reform Act of 1995. Heron cautions readers that forward-looking statements are based on management's expectations and assumptions as of the date of this news release and are subject to certain risks and uncertainties that could cause actual results to differ materially, including, but not limited to, those associated with: the commercial opportunity for CINVANTI IV push; and other risks and uncertainties identified in the Company's filings with the U.S. Securities and Exchange Commission. Forward-looking statements reflect our analysis only on their stated date, and Heron takes no obligation to update or revise these statements except as may be required by law.

Investor Relations and Media Contact:

David Szekeres
Senior VP, General Counsel, Business Development and Corporate Secretary
Heron Therapeutics, Inc.
dszekeres@heronrx.com
858-251-4447

 View original content: <http://www.prnewswire.com/news-releases/heron-announces-fda-approval-of-supplemental-new-drug-application-to-expand-cinvanti-label-for-iv-push-300802594.html>

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