CINVANTI®
(aprepitant) injectable emulsion

Choose the IV NK_1 RA with the potential to improve practice efficiency[1]

CINVANTI—the only IV NK_1 RA approved as a 2-minute IV Push[1-3]

IV=intravenous; NK_1 RA=neurokinin-1 (NK_1) receptor antagonist.

INDICATION

CINVANTI is a substance P/neurokinin-1 (NK_1) receptor antagonist, indicated in adults, in combination with other antiemetic agents, 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 as a single-dose regimen; delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy (MEC) as a single-dose regimen; and nausea and vomiting associated with initial and repeat courses of MEC as a 3-day regimen.

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

IMPORTANT SAFETY INFORMATION

Contraindications

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

Concurrent use of pimozide with CINVANTI is contraindicated.

Please see additional Important Safety Information on page 9 and accompanying full Prescribing Information.

Organizations should be efficient and consider more than just drug acquisition cost

Selecting an NK_1 RA should be driven by clinical considerations, but must also take into account:

- Patient time in office
- Effective staff utilization (nurses, pharmacists, and pharmacy technicians)
- Capacity of high-demand compounding areas
- Optimal workflow and use of infusion suite capacity
- Impact on refrigerated storage capacity

Shortages of IV fluid and bags have disrupted the ability to use IV infusions

- Hurricane Maria caused a temporary loss of manufacturing, resulting in shortages of IV fluid and bags[1]
- From 2007 to 2017, there were 5 saline shortages in the United States—**1 of which remains unresolved as of May 2020**[4,5]

The American Society of Health-System Pharmacists recommends switching from IV infusion to IV push (injection of 5 minutes or less) whenever possible.[1,6]

IMPORTANT SAFETY INFORMATION (cont)

Warnings and Precautions

Clinically Significant CYP3A4 Drug Interactions

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

- Use of CINVANTI with other drugs that are CYP3A4 substrates may result in increased plasma concentration of the concomitant drug.
  - Use of pimozide with CINVANTI is contraindicated due to the risk of significantly increased plasma concentrations of pimozide, potentially resulting in prolongation of the QT interval, a known adverse reaction of pimozide.

CINVANTI is the only IV NK_1 RA that provides operational efficiency advantages due to 2-minute IV Push[1,2,7-9]

The importance of assessing the impact of operational advantages

- Lower acquisition costs of generic antiemetics can provide short-term savings, but there is more to consider than just the cost of the product when determining the right NK_1 RA for your practice
- Product selection for CINV prophylaxis should also be driven by the desire to deliver efficient patient care

Limitations of other NK_1 RAs[1-3]

- Other IV NK_1 RAs have to be administered as IV infusions over a longer duration of 20-30 minutes
- Other IV NK_1 RAs have to be prepared and mixed in infusion bags
- IV infusions require additional steps, time, and supplies vs CINVANTI 2-minute IV Push

CINV=chemotherapy-induced nausea and vomiting.

IMPORTANT SAFETY INFORMATION (cont)

Warnings and Precautions (cont)

- 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 CINVANTI.

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 reinitiate CINVANTI in patients who experience these symptoms with previous use.

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Workflow benefits of CINVANTI 2-minute IV Push were supported by a retrospective study[1]

Study background

- A large multisite community oncology practice with more than 80 providers[1]
- More than 700 employees who staff 13 infusion centers[1]
- An OCM-based practice with the goal of improving patient care, increasing overall value, and reducing the impact on patient cost[1,10]

Time, motion, and cost evaluation

A physician-owned community oncology practice conducted a time, motion, and cost evaluation to determine the overall impact and operational advantages of adopting CINVANTI 2-min IV Push.*[1]

The study focused on the precise timing of each step in the process of preparing and administering 30-minute IV infusions† vs 2-minute IV Push, and how stakeholders were impacted in the separate workflow steps.[1]

Key data points assessed were[1]:

- Staff time saved/expended
- Supplies saved/consumed
- What could be accomplished with reallocated time for impacted disciplines

OCM=Oncology Care Model.

*This study was funded by Heron Therapeutics, Inc.

†Thirty-minute IV infusions of NK_1 RAs included fosaprepitant or CINVANTI (aprepitant), as the practice was transitioning between the 2 products during the study period.

IMPORTANT SAFETY INFORMATION (cont)

Warnings and Precautions (cont)

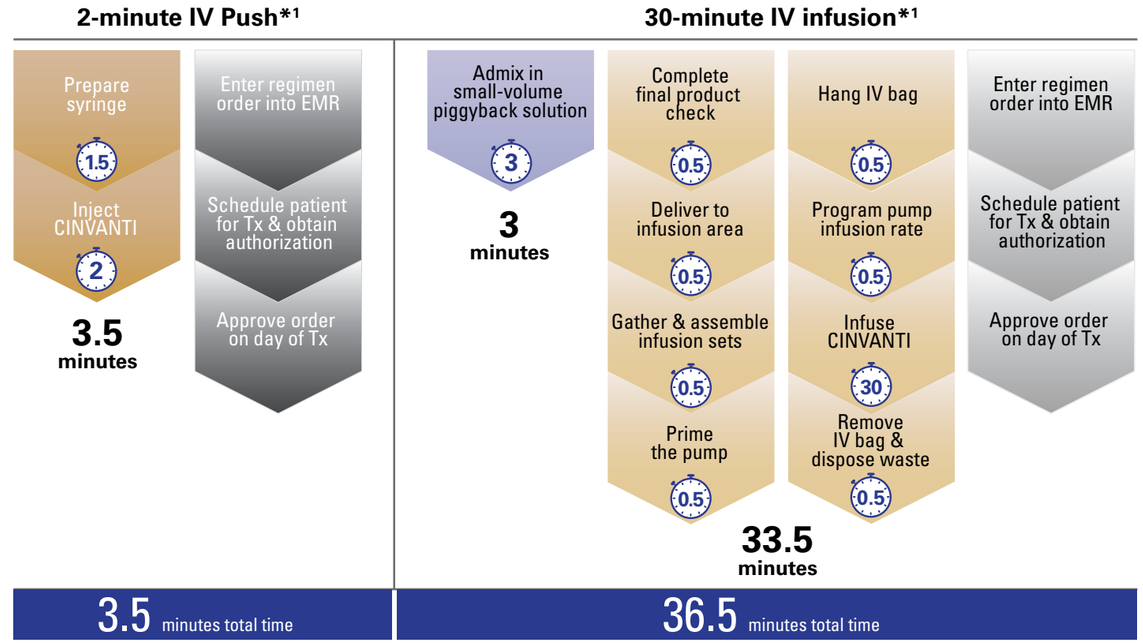
Decrease in INR with Concomitant Warfarin

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.

CINVANTI 2-minute IV Push streamlined nurse and pharmacy workflow vs 30-minute infusion, saving 33 minutes per dose[1]



Total time saved from CINVANTI 2-minute IV Push vs 30-minute IV infusion[1]

EMR=electronic medical record; Tx=treatment.

*Some common workflow steps for both methods of administration have not been included in this chart.

IMPORTANT SAFETY INFORMATION (cont)

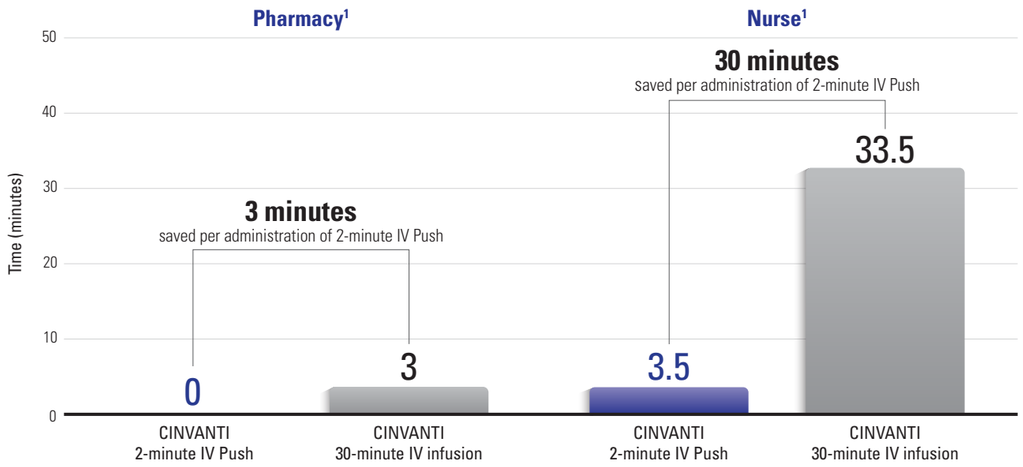
Use in Specific Populations

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.

Please see additional Important Safety Information on page 9 and accompanying full Prescribing Information.

CINVANTI 2-minute IV Push gave nurses the chance to reallocate 30 minutes per administration[1]

CINVANTI 2-minute IV Push eliminates key steps from the preparation and administration required for IV infusions[1]



Steps removed by using CINVANTI 2-minute IV Push vs 30-minute IV infusion*[1]:

Pharmacy	Nurse
Mixing small-volume parenteral solution	Verifying admixture is correct prior to administration
	Delivering to the infusion area
	Gathering and assembling infusion sets
	Priming the pump/tubing
	Hanging the IV bag
	Programming the pump infusion rate
	Infusing the product
	Removing the IV bag when completed and disposing of waste appropriately

*Observational study with inputs from nursing heads, pharmacy heads, and pharmacy technicians.

IMPORTANT SAFETY INFORMATION (cont)

Adverse Reactions

The most common adverse reactions are:

- Single-dose fosaprepitant with MEC (≥2%): fatigue, diarrhea, neutropenia, asthenia, anemia, peripheral neuropathy, leukopenia, dyspepsia, urinary tract infection, pain in extremity.

CINVANTI 2-minute IV Push allows providers to reallocate time otherwise spent preparing and administering IV infusions[1]

CINVANTI 2-minute IV Push shortens infusion chair times

- Allows for savings on chair time that could be reused for other billable procedures[1]
- Optimizes infusion schedules, allowing a greater number of patients to be treated in a more timely fashion[1]
- Can help prevent unscheduled delays due to antiemetic preparation and complicated bottlenecking, helping to avoid frustration for employees and patients[1]
- Helps OCM practices reach their goals of providing high-quality patient care[1,10]

CINVANTI 2-minute IV Push may reduce administrative work

Nurses

- Are able to redirect time for enhanced patient care, thoroughly reviewing chemotherapy or other orders, and assisting other nurses[1]

Pharmacy

- Is able to complete other tasks such as organizing and cleaning the pharmacy, performing inventory management, drug ordering, and correcting charge documentation[1]

CINVANTI 2-minute IV Push can be delivered with fewer steps and in less time compared to a 30-minute IV infusion.[1]

IMPORTANT SAFETY INFORMATION (cont)

Adverse Reactions (cont)

- 3-day oral aprepitant with MEC (≥1% and greater than standard therapy): fatigue and eructation.
- Single-dose fosaprepitant with HEC: generally similar to 3-day oral aprepitant. In addition, infusion site reactions (3%) occurred.
- Single-dose CINVANTI (≥2%): 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.

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CINVANTI 2-minute IV Push reduces use of infusion supplies

CINVANTI 2-minute IV Push eliminates the need for materials such as tubing and bags of parenteral solution[1]

Supply item	Cost	CINVANTI 2-minute IV Push	CINVANTI 30-minute IV infusion
Single pair of gloves	$0.16	✓	✓
20 mL Luer Lock plastic syringe (sterile)	$0.27	✓	✓
18 ga needle (sterile)	$0.04	✓	✓
Alcohol swab (sterile)	$0.02	✓	✓
100 mL NS infusion bag (sterile)	$1.22	N/A	✓
Secondary tubing set (sterile)	$0.77	N/A	✓
Patient label	$0.03	✓	✓
Total		**$0.52**	**$2.51**

N/A=not applicable; NS=normal saline.

$1.99
saved per 2-minute IV Push administration

References: 1. Burns D, Kula J, Marshall S, Ashworth E, Ornelas M. Best practice approach to successful conversion of fosaprepitant to aprepitant IV in a large multisite community oncology infusion center: a retrospective analysis [published online May 23, 2020]. *Adv Ther.* doi:10.1007/s12325-020-01377-z. **2.** CINVANTI [prescribing information]. Heron Therapeutics, Inc., San Diego, CA; October 2019. **3.** Emend for injection [prescribing information]. Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ; April 2020. **4.** Mazer-Amirshahi M, Fox ER. Saline shortages—many causes, no simple solution. *N Engl J Med.* 2018;378(16):1472-1474. **5.** ASHP drug shortages list. American Society for Health-System Pharmacists website. https://www.ashp.org/Drug-Shortages/Current-Shortages/Drug-Shortages-List?page=CurrentShortages. Accessed May 11, 2020. **6.** American Society for Health-System Pharmacists and the University of Utah Drug Information Service. Small-volume parenteral solutions shortages suggestions for management and conservation. US Food and Drug Administration website. https://www.fda.gov/files/drugs/published/Small-Volume-Parenteral-SolutionsShortages-Suggestions-for-Managementand-Conservation.pdf. Published October 18, 2017. Accessed May 11, 2020. **7.** Fosaprepitant dimeglumine for injection [prescribing information]. Fresenius Kabi, Lake Zurich, IL; May 2016. **8.** Tsao NW, Lo C, Babich M, Shah K, Bansback NJ. Decentralized automated dispensing devices: systematic review of clinical and economic impacts in hospitals. *Can J Hosp Pharm.* 2014;67(2):138-148. **9.** Raajasekar AKA, Barola S, Tehrani L, Chandra AB. To push or not to push: the benefit of administering anti-emetics by intravenous push. *Blood.* 2015;126(23):3314. **10.** Oncology Care Model. Centers for Medicare & Medicaid Services website. https://innovation.cms.gov/innovation-models/oncology-care. Updated May 7, 2020. Accessed May 11, 2020. **11.** NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.2.2020. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed May 6, 2020. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Indication and Important Safety Information

INDICATION

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

Please see accompanying full Prescribing Information or visit www.CINVANTI.com.

CINVANTI® (aprepitant) injectable emulsion

Because drug acquisition cost isn't the only consideration for your practice or your patients

CINVANTI: the only IV NK_1 RA that demonstrates operational advantages due to 2-minute IV Push[1,2,7-9]

The unique formulation of CINVANTI is not interchangeable with fosaprepitant[2,3,11]	CINVANTI IV (aprepitant) injectable solution[1,2]	Generic fosaprepitant for injection[1,3,7]
	2-minute IV Push	30-minute IV infusion
Eliminates time-consuming preparation and administration steps required for IV infusions	✓	NO
Shortens infusion chair times for patients and staff	✓	NO
Helps conserve IV fluid during bag shortages	✓	NO
Vials can be stored at room temperature for up to 60 days, enabling storage in automated dispensing devices	✓	NO
Unique emulsion formulation requires no reconstitution	✓	NO

HERON CONNECT®

Heron provides comprehensive patient and practice support. Visit CINVANTI.com to learn more.

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