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YOU KNOW THAT FACE. YOU KNOW WHAT IT'S TELLING YOU. AND NOW YOU HAVE A PROVEN OPTION.

Barhemsys® is the first and only antiemetic approved for rescue treatment of PONV despite prophylaxis.[1] **Learn more at Barhemsys.com**

Indications

Barhemsys is a selective dopamine-2 (D_2) and dopamine-3 (D_3) receptor antagonist indicated in adults for:
- prevention of postoperative nausea and vomiting (PONV), either alone or in combination with an antiemetic of a different class
- treatment of PONV in patients who have received antiemetic prophylaxis with an agent of a different class or have not received prophylaxis

Select Important Safety Information

Contraindication: Barhemsys is contraindicated in patients with known hypersensitivity to amisulpride.

QT Prolongation: Barhemsys causes dose- and concentration-dependent prolongation of the QT interval. The recommended dosage is 5 mg or 10 mg as a single intravenous (IV) dose infused over 1 to 2 minutes. Avoid Barhemsys in patients with congenital long QT syndrome and in patients taking droperidol. Electrocardiogram (ECG) monitoring is recommended in patients with pre-existing arrhythmias/cardiac conduction disorders, electrolyte abnormalities (e.g., hypokalemia or hypomagnesemia), congestive heart failure, and in patients taking other medicinal products (e.g., ondansetron) or with other medical conditions known to prolong the QT interval.

Adverse Reactions: Common adverse reactions reported in ≥ 2% of adult patients who received Barhemsys 5 mg (N=748) and at a higher rate than placebo (N=741) in clinical trials for the prevention of PONV were: chills (4% vs. 3%), hypokalemia (4% vs. 2%), procedural hypotension (3% vs. 2%), and abdominal distention (2% vs. 1%). Serum prolactin concentrations were measured in one prophylaxis study where 5% (9/176) of Barhemsys-treated patients had increased blood prolactin reported as an adverse reaction compared with 1% (1/166) of placebo-treated patients. The most common adverse reaction, reported in ≥ 2% of adult patients who received Barhemsys 10 mg (N=418) and at a higher rate than placebo (N=416), in clinical trials for the treatment of PONV was infusion site pain (6% vs. 4%).

Please see the Brief Summary of Prescribing Information for Barhemsys on next page.

1. Barhemsys [Prescribing Information], Indianapolis, IN. Acacia Pharma; 2020. Model used for illustrative purposes only.

Barhemsys® (amisulpride) injection 2.5 mg/mL

Delivers when it matters most™

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Barhemsys®
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Brief Summary of Prescribing Information for Barhemsys® (amisulpride) injection

See package insert for full Prescribing Information

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Dosage & Administration: The recommended adult dosage of Barhemsys:

- Prevention of PONV, either alone or in combination with another antiemetic: 5 mg as a single intravenous dose infused over 1 to 2 minutes at the time of induction of anesthesia.
- Treatment of PONV: 10 mg as a single intravenous dose infused over 1 to 2 minutes in the event of nausea and/or vomiting after a surgical procedure.

Protect from light. Barhemsys is subject to photodegradation. Administer Barhemsys within 12 hours of removal of the vial from the protective carton.
See full prescribing information for preparation and administration instructions.

Dosage Forms and Strength: Injection: 5 mg/2 mL (2.5 mg/mL) as a clear, colorless sterile solution in a single-dose vial.

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Drug Interactions:

- Barhemsys causes dose- and concentration-dependent QT prolongation. To avoid potential additive effects, avoid use of Barhemsys in patients taking droperidol.
- ECG monitoring is recommended in patients taking other drugs known to prolong the QT interval (e.g., ondansetron).
- Reciprocal antagonism of effects occurs between dopamine agonists (e.g., levodopa) and Barhemsys. Avoid using levodopa with Barhemsys.

Postmarketing Experience: The following adverse reactions have been identified during postapproval chronic oral use of amisulpride outside of the United States (Barhemsys is not approved for oral dosing or chronic use). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: *Blood and Lymphatic System Disorders:* agranulocytosis; *Cardiac Disorders:* bradycardia, torsades de pointes, ventricular tachycardia, prolonged QT by electrocardiogram; *General Disorders:* neuroleptic malignant syndrome; *Immune System Disorders:* angioedema, hypersensitivity, urticaria; *Hepatic Disorders:* increased hepatic enzymes; *Nervous System Disorders:* agitation, anxiety, dystonia, extrapyramidal disorder, seizure; *Psychiatric Disorders:* confusional state, insomnia, somnolence; *Vascular Disorders:* hypotension.

Use in Specific Populations: Pregnancy—*Risk Summary:* Available data with amisulpride use in pregnant women are insufficient to establish a drug associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In animal reproduction studies, there were no adverse developmental effects observed with oral administration of amisulpride in rats and rabbits during the period of organogenesis at exposures about 43 and 645 times, respectively, the exposure delivered by the highest recommended human dose *(see Data)*. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. *Data—Animal Data:* Reproduction studies of amisulpride were conducted in pregnant rats administered oral doses up to 160 mg/kg/day (43 times the exposure based on area under the curve (AUC) at the highest recommended dose of 10 mg) throughout the period of organogenesis. No adverse embryo-fetal developmental effects were observed at any dose level. Maternal animals exhibited a dose-related decrease in overall mean body weight gain. In rabbits administered amisulpride throughout the period of organogenesis, oral doses up to 210 mg/kg/day (645 times the exposure based on AUC at the highest recommended dose of 10 mg) had no adverse developmental effects on the fetus. Maternal animals exhibited reduced mean body weight gain at doses of 100 and 210 mg/kg/day and reduced food intake was observed at 210 mg/kg/day. The pre- and post-natal developmental effects of amisulpride were assessed in rats administered oral doses of 60, 100 or 160 mg/kg/day during the periods of organogenesis and lactation. At 160 mg/kg/day (43 times the exposure based on AUC at the highest recommended dose of 10 mg), maternal animals exhibited a reduction in mean body weight gain and decrease in food intake during lactation. Amisulpride had no effect on maternal pregnancy parameters, litter survival or pup growth, development or maturation at any dose tested.
Lactation—*Risk Summary:* Based on case reports in published literature, amisulpride is present in human milk at concentrations that are 11- to 20-fold higher than human plasma in patients taking multiple oral doses of amisulpride (200 to 400 mg/day). The estimated infant daily dose ranged from 5% to 11% of the maternal dose. There are ways to minimize drug exposure to a breastfed infant *(see Clinical Considerations)*. There are no reports of adverse effects on the breastfed child and no information on the effects of amisulpride on milk production. The pharmacological action of amisulpride, a dopamine-2 (D_2) receptor antagonist, may result in an increase in serum prolactin levels, which may lead to a reversible increase in maternal milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Barhemsys and any potential adverse effects on the breastfed child from Barhemsys or from the underlying maternal condition. *Clinical Considerations:* A lactating woman may consider interrupting breastfeeding and pumping and discarding breast milk for 48 hours after Barhemsys administration to minimize drug exposure to a breastfed infant.
Females and Males of Reproductive Potential—*Infertility:* In animal fertility studies, administration of repeated doses of amisulpride over a 10-day period to female rats resulted in infertility that was reversible. **Pediatric Use**—Safety and effectiveness in pediatric patients have not been established. **Geriatric Use**—No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. **Renal Impairment**—Avoid Barhemsys in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2). The pharmacokinetics of amisulpride in patients with severe renal impairment have not been adequately studied in clinical trials. Amisulpride is known to be substantially excreted by the kidneys, and patients with severe renal impairment may have increased systemic exposure and an increased risk of adverse reactions. No dosage adjustment is necessary in patients with mild to moderate renal impairment (eGFR ≥ 30 mL/min/1.73 m^2).

Overdosage: Doses of oral amisulpride (Barhemsys is not approved for oral dosing) above 1200 mg/day have been associated with adverse reactions related to dopamine-2 (D_2) antagonism, in particular:

- cardiovascular adverse reactions (e.g., prolongation of the QT interval, torsades de pointes, bradycardia and hypotension).
- neuropsychiatric adverse reactions (e.g., sedation, coma, seizures, and dystonic and extrapyramidal reactions).

There is no specific antidote for amisulpride overdose. Management includes cardiac monitoring and treatment of severe extrapyramidal symptoms. Since amisulpride is weakly dialyzed, hemodialysis should not be used to eliminate the drug.

How Supplied/Storage and Handling: Barhemsys is supplied as follows: Package of 10 cartons (NDC 71390-125-20). Each carton (NDC 71390-125-21) contains one single-dose vial of clear, colorless, sterile solution of Barhemsys, 5 mg in 2 mL (2.5 mg/mL). Store vials at 20°C to 25°C (68°F to 77°F) [see USP Controlled Room Temperature].

Patient Counseling Information: QT Prolongation—Instruct patients to contact their healthcare provider immediately if they perceive a change in their heart rate, if they feel lightheaded, or if they have a syncopal episode. **Drug Interactions**—Advise patients to report to their healthcare provider if they are taking drugs which prolong the QT interval. **Lactation**—Women may consider reducing infant exposure through pumping and discarding breastmilk for 48 hours after Barhemsys administration.

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