PANHEMATIN®
(HEMIN FOR INJECTION)

Dosing, preparation, and infusion instructions

OVER
30 YEARS *of*
U.S. CLINICAL EXPERIENCE

Order through **Canadian Blood Services** and **Héma-Québec**

For more information about PANHEMATIN or to access a dosing calculator, visit **www.panhematin.ca** and enter the password **AIP**.

About PANHEMATIN

PANHEMATIN is formatted as a sterile, lyophilized powder for intravenous administration
after reconstitution. Each dispensing vial of PANHEMATIN contains the equivalent of 268 mg hemin, 240 mg sodium carbonate and 335 mg of sorbitol. The pH may have been adjusted with hydrochloric acid. When mixed as directed with Sterile Water for Injection, USP, each 48 mL provides the equivalent of approximately 261 mg hematin (5.4 mg/mL). The product contains no preservatives.

PANHEMATIN is supplied as a sterile, lyophilized black powder in single dose dispensing vials in a carton. Prior to reconstitution, PANHEMATIN should be stored at 20-25°C (68-77°F).

Because PANHEMATIN contains no preservative and undergoes rapid chemical decomposition in solution, it must be reconstituted immediately before use.

Indication:

PrPANHEMATIN® (hemin for injection) is indicated for the amelioration of recurrent attacks of acute intermittent porphyria temporally related to the menstrual cycle in susceptible women, after initial carbohydrate therapy is known or suspected to be inadequate.

Limitations of Use:

- Before administering PANHEMATIN, consider an appropriate period of carbohydrate loading (i.e., 400 g glucose/day for 1 to 2 days).
- Attacks of porphyria may progress to a point where irreversible neuronal damage has occurred. PANHEMATIN therapy is intended to prevent an attack from reaching the critical stage of neuronal degeneration. PANHEMATIN is not effective in repairing neuronal damage.

Dosing PANHEMATIN

Dosing considerations

- PANHEMATIN should only be used by or in consultation with physicians experienced in the management of porphyrias.
- Before PANHEMATIN therapy is begun, the presence of acute porphyria must be diagnosed using the following criteria:
  1. Presence of clinical symptoms suggestive of acute porphyric attack.
  2. Quantitative measurement of porphobilinogen (PBG) in urine. The single-void urine sample should be refrigerated or frozen without additives and shielded from light for subsequent quantitative δ-aminolevulinic acid (ALA), PBG, and total porphyrin determinations. (Note: the classical Watson-Schwartz or Hoesch tests are considered to be less reliable).
- Clinical benefit from PANHEMATIN depends on prompt administration. For mild porphyric attacks (mild pain, no vomiting, no paralysis, no hyponatremia, no seizures), a trial of glucose therapy is recommended while awaiting hemin treatment or if hemin is unavailable. For moderate to severe attacks, immediate hemin treatment is recommended. Symptoms of severe attacks are severe or prolonged pain, persistent vomiting, hyponatremia, convulsion, psychosis, and neuropathy. In addition to treatment with PANHEMATIN, consider other necessary measures such as the elimination of triggering factors.
- Monitor urinary concentrations of the following compounds during PANHEMATIN therapy. Effectiveness is demonstrated by a decrease in one or more of the following compounds:
  ALA - δ-aminolevulinic acid
  PBG - porphobilinogen
  Uroporphyrin
  Coproporphyrin

Recommended dose and dosage adjustment

- The dose of PANHEMATIN is 0.8 to 3.1 mg/kg/day of hematin for 3 to 14 days based on the clinical signs.
- The standard dose in clinical practice is 2.3 to 3.1 mg/kg/day.
- In more severe cases this dose may be repeated no earlier than every 12 hours.
- Do not exceed 4.6 mg/kg of hematin in any 24 hour period.

Preparing PANHEMATIN

Calculate dose of reconstituted PANHEMATIN for infusion

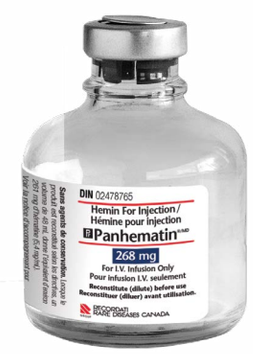
After reconstitution each mL of PANHEMATIN contains the equivalent of approximately 5.4 mg of hematin.

Dosage Calculation Table
1 mg hematin equivalent = 0.18 mL PANHEMATIN
2 mg hematin equivalent = 0.37 mL PANHEMATIN
3 mg hematin equivalent = 0.55 mL PANHEMATIN
4 mg hematin equivalent = 0.74 mL PANHEMATIN

Health Canada has not authorized an indication for pediatric use.

Supply List

Reconstitution	
1	Vial of PANHEMATIN (hemin for injection)
1	Bottle Sterile Water for Injection, USP
1	60 mL syringe with 18-20 gauge needle
2	Alcohol wipes
1	Protective gloves



Infusion	
1	Vial of reconstituted PANHEMATIN
1	Infusion pump
1	Primary infusion set (including IV administration tubing with "Y" site)
1	250 mL IV bag of 0.9% Sodium Chloride for Injection, USP
1	Sterile 0.45-micron or smaller filter
1	IV tubing with vented spike, or vented spike adapter
1	Huber needle and injection cap
1	Central line dressing kit
1	Saline flush syringe
2	Alcohol wipes
1	Protective gloves
1	IV bag label

Reconstituting PANHEMATIN

Reconstitute PANHEMATIN

Vial Size	Volume of Diluent to be Added to Vial	Approximate Available Volume	Nominal Concentration Hematin per mL
268 mg	48 mL	48 mL	5.4 mg/mL

When mixed as directed with Sterile Water for Injection, USP, each 48 mL provides the equivalent of approximately 261 mg hematin (5.4 mg/mL).

Because PANHEMATIN contains no preservative and undergoes rapid chemical decomposition in solution, it must be reconstituted immediately before use.

Using aseptic technique, remove caps from Sterile Water for Injection, USP bottle and PANHEMATIN vial. Clean rubber stoppers* with alcohol wipes.

Using the 60 mL syringe, withdraw 48 mL Sterile Water for Injection from bottle.

Inject the Sterile Water into the PANHEMATIN dispensing vial. Do not add other drug or chemical agent to a PANHEMATIN fluid admixture.

Immediately after adding diluent, shake the vial well for a period of 2 to 3 minutes to aid dissolution. Since reconstituted PANHEMATIN is not transparent, any undissolved particulate matter is difficult to see when inspected visually. Therefore, terminal filtration through a sterile 0.45 micron or smaller filter is recommended.

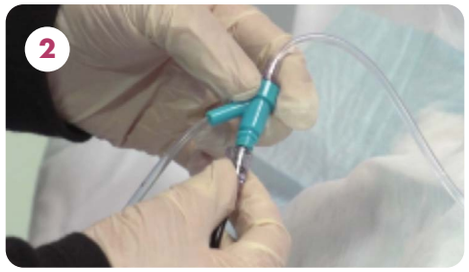
* The vial stopper of PANHEMATIN contains natural rubber latex, which may cause allergic reactions.

Administering PANHEMATIN

Refer to page 3 for a list of supplies needed to infuse PANHEMATIN.

Establish an IV Line

Protect patient's clothing with a towel or pad.



A large arm vein or a central venous catheter should be utilized for the administration of PANHEMATIN to minimize the risk of phlebitis.

Connect primary tubing to the 250 mL bag of 0.9% Sodium Chloride for Injection, USP, and prime.

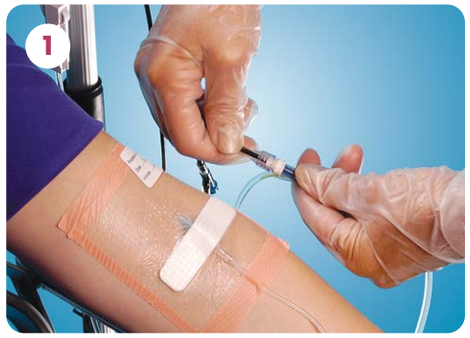
Verify blood return and flush IV to verify patency, then attach the line.

Start the sodium chloride infusion at a "keep vein open" (KVO) rate.

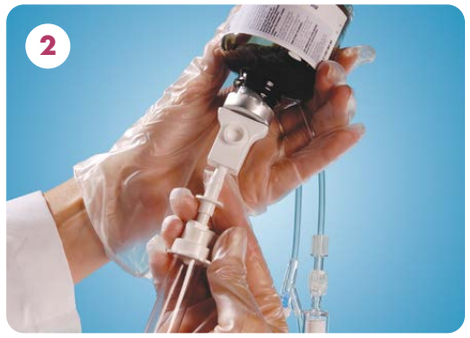
Infuse PANHEMATIN

Verify the dose of PANHEMATIN the patient will be receiving. Use an infusion pump to ensure accuracy of dosing and administration time.

Infuse the reconstituted PANHEMATIN immediately. PANHEMATIN contains no preservative and undergoes rapid chemical decomposition in solution.



Attach the 0.45-micron filter to the IV tubing, since undissolved particulate matter is difficult to see in PANHEMATIN. If the tubing is not vented, attach a vented spike adapter, and then insert the spike into the evacuated PANHEMATIN vial.



Prime the IV and filter system with PANHEMATIN. Attach IV line to the "Y" site on the primary infusion line, and stop the saline infusion.

Open the clamp on the IV tubing and begin infusion. The prescribed dose of PANHEMATIN should be infused over a period of at least 30 minutes.

After the full dose has been given, stop the infusion. Disconnect the PANHEMATIN at the "Y" site, and remove the vial and PANHEMATIN tubing. Rinse the vein with 100 mL 0.9% Sodium Chloride for Injection, USP. Discard any remaining PANHEMATIN solution.

Clinical use:

Pediatrics (< 16 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of PANHEMATIN in pediatric patients has not been established; therefore, Health Canada has not authorized an indication for pediatric use.

Geriatrics (≥ 65 years of age): Clinical data for subjects aged 65 and over was not sufficient to determine whether they respond differently from younger subjects. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Contraindications:

PANHEMATIN is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.

Relevant warnings and precautions:

- Do not use in patients with known hypersensitivity to PANHEMATIN.
- Risk of phlebitis.
- Risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jacob disease (vCJD) agent, and theoretically the Creutzfeldt-Jacob disease (CJD) agent.
- Transient, mild anticoagulant effects may occur. Avoid concurrent anticoagulant therapy.
- Elevated iron and serum ferritin may occur. Monitor iron and serum ferritin in patients receiving multiple administrations of PANHEMATIN.
- Reversible renal shutdown has been observed in a case where an excessive hematin dose (12.2 mg/kg) was administered in a single infusion. Recommended dosage guidelines should be strictly followed.
- Should be given to a pregnant woman only if clearly needed. Avoid administering hematin in severe pre-eclampsia.
- The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for PANHEMATIN and any potential adverse effects on the breastfed child from PANHEMATIN or from the underlying maternal condition.
- Avoid CYP inducing drugs (such as estrogens, barbituric acid derivatives and steroid metabolites) while on PANHEMATIN therapy.

For more information:

Please consult the Product Monograph at http://www.recordatirarediseases.com/sites/www.recordatirarediseases.com/files/inline-files/panhematin-product-monograph-ENG.pdf for important information related to adverse reactions, interactions and dosing information which has not been discussed in this document.

The Product Monograph is also available by calling McKesson Specialized Distribution at **1-877-827-1306** or email customersupport@gmdpharma.ca.

Order through **Canadian Blood Services** and **Héma-Québec**

For medical questions, please email **medinfocanada@recordatirarediseases.com**.

You are encouraged to report adverse events to Health Canada.
Visit **https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html**, or call toll-free: **1-866-234-2345**.

For more information about PANHEMATIN please email **infocanada@recordati.com** or visit **www.panhematin.ca** and enter the password **AIP**.

References
Recordati Rare Diseases Canada Inc. PANHEMATIN® Product Monograph. July 13, 2018.

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