

For the use of Registered Medical Practitioner or a Hospital only

*HemoRel-A*TM Dried Factor VIII fraction I.P.

DESCRIPTION

HemoRel-A is a sterile, nonpyrogenic, lyophilized powder preparation of dried human Factor VIII, which is reconstituted with 15 ml WFI (water for injection). Factor VIII is a protein produced by the liver which is one of the essential contributors to blood coagulation. Deficiency of Factor VIII causes haemophilia A (classical haemophilia). Haemophilia A is a genetic bleeding disorder characterised by haemorrhages, which may occur spontaneously or after minor trauma.

COMPOSITION

HemoRel-A contains 250 IU coagulation factor VIII after dissolution with WFI. One IU of Factor VIII activity is approximately equal to the level of Factor VIII found in 1.0 ml of fresh, pooled human plasma.

CLINICAL PHARMACOLOGY

Factor VIII is an essential cofactor in activation of Factor X leading ultimately to formation of thrombin and fibrin. After intravenous injection of *HemoRel-A* there is a rapid increase of plasma Factor VIII activity followed by decrease in plasma factor VIII activity by a two phase exponential decay, initially there is a rapid decrease in activity followed by a subsequent slower phase.

The circulating half-life of factor VIII is 10-12 hours, but in the first 36-48 hours post-operative or post-life-threatening trauma, the rate of factor consumption is relatively high. In such cases an every 8-hour dose should be maintained. Also this should be supported by laboratory assay as the response may vary between patients.

INDICATIONS

HemoRel-A is indicated for

- Haemophilia A/Classical haemophilia (congenital factor VIII deficiency)
- Acquired factor VIII deficiency

PRODUCT SAFETY

The manufacturing process for *HemoRel-A* uses plasma collected from approved blood banks where the donors are screened for their history as per guidelines laid down by Indian and International regulatory authorities. Their blood is screened for the mandatory infectious diseases. These are repeat donors whose samples are quarantined and retested. Only on being declared negative the plasma is used for processing.

After manufacturing, the product is tested by suitable methods to show freedom from viruses like HIV, HBV, HCV, Parvovirus and HAV. The testing is carried out at the raw material, intermediate and finished product stages to assure quality of the product. The manufacturing procedure incorporates the well-known time tested and proven method of Solvent Detergent Technology, which inactivates lipid-coated viruses. Multiple steps have been employed to assure product safety hence there is a very remote probability that unknown infectious agents may be present in these products like lesser known viruses and prions.

Validation studies were carried out to validate the efficiency of the manufacturing process to remove and/or inactivate viruses. The manufacturing processes with the incorporated viral inactivation procedures have been validated as per recommendations and guidelines provided by the committee for proprietary medicinal products (CPMP guidelines).

These studies were conducted using starting intermediate samples spiked with model viruses to represent the worst-case conditions. Appropriate samples were drawn for viral titre determinations from manufacturing intermediates keeping in mind the process parameters; characterizations and final product quality meet the pharmaco-regulatory requirement.

DOSAGE

Haemophilia A:

Dosage is based on the desired factor VIII increase (%): A 100% Factor VIII level is 1 international unit (IU) of Factor VIII per ml of plasma (1.0 IU/ml). Most bleeding is successfully treated if levels are >30% of normal. In life-threatening or surgical situations, initiate therapy to achieve 100% level and adjust so that the expected level 8 hours after infusion does not fall below 50% during the treatment schedule.

One can assume that 1 IU of Factor VIII/kg body weight will increase the patient's level by 2% (0.02 IU/ml). Therefore, if the patient's level is 1% or less (0.01 IU/ml), which is true in severe hemophilia, a dose of 40 IU/kg body weight will raise the level to 80%, in the absence of any inhibitors.

Hence the following formula provides a guide of dosage calculations for both adult and pediatric patients:

Number of AHF Required = Body weight (in kg) x desired Factor VIII increase (% normal) x 0.5 I.U.

Dosage and desired level of AHF vary depending upon the nature of the bleeding (hemarthrosis, intramuscular, neurological, surgical, etc) and therefore hematologic or transfusion medicine consultation is strongly recommended.

OVERDOSAGE

No symptoms of overdosage with human coagulation factor VIII have been reported till date.

CONTRAINDICATIONS

There are no absolute contraindications to the use of *HemoRel-A*. However, special caution is required if you have had a known allergic reaction to any constituent of *HemoRel-A*. If any allergic reaction occurs, administration of *HemoRel-A* should be discontinued immediately.

ADVERSE REACTIONS

HemoRel-A is usually tolerated without reaction, but may have some cases of hypersensitivity or allergic reactions. These include: rash, hives, itching, tightness of the chest, breathing difficulty, throat tightness, and low blood pressure. If allergic/anaphylactic reactions occur, the infusion should be discontinued and appropriate treatment given as required. Increase in body temperature is observed in rare cases.

In some cases, inhibitors of Factor VIII may occur. An inhibitor is an antibody (part of our body's normal immune defenses) that forms in response to infusions of Factor VIII that inhibits the Factor VIII activity. These inhibitors can lead to a reduced response, or to no response to Factor VIII therapy. This is not an uncommon complication in the treatment of people with Hemophilia A.

WARNING AND PRECAUTIONS

Medical products prepared from human plasma carry a very remote risk of transmission of infective agents that are reduced by several methodologies.

Appropriate vaccination (Hepatitis A and B) for patients in receipt of plasma derived Factor VIII concentrates is recommended.

Solutions of *HemoRel-A* should not be used if it gels on reconstitution. Contents must not be used more than 2 hours after the container has been penetrated. Discard unused portion.

If hypersensitivity reactions occur during administration of *HemoRel-A* the infusion/injection should be stopped.

INTERACTIONS WITH OTHER MEDICINES

No interactions of *HemoRel-A* with other medications are known. However, do not mix *HemoRel-A* with any other solutions or medicines.

PREGNANCY AND LACTATION

Pregnancy Category C: Animal reproduction studies have not been conducted with *HemoRel-A*. It is also not known whether it can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. This preparation should be given to a pregnant and lactating woman only if clearly needed.

STORAGE AND SHELF LIFE

Store between 2 - 8°C. Do not freeze. Protect from light. Keep out of reach of children. Discard any unused material or half empty vial. The shelf life of *HemoRel-A* is 2 years. The reconstituted product should be used within 2 hours.

INSTRUCTION FOR USE

The *HemoRel-A* pack contains

- A vial of dried Factor VIII fraction
- One 23 G infusion set
- Package insert
- WFI (20 ml) in a plastic container
- One syringe filter
- One Alcohol swab
- One 20 ml syringe
- Two 20 G needles

RECONSTITUTION AND ADMINISTRATION

Use aseptic Technique

1) Dissolution

- Bring the vial containing *HemoRel-A* and WFI plastic container to room temperature (not above 37°C (98°F)).
- Remove flip off seal from *HemoRel-A* vial to expose the centers of the rubber stoppers.
- Disinfect the stoppers with an alcohol swab and allow it to dry.
- Aspirate 15ml of water from the WFI plastic container using the syringe and one needle.
- Gently push it into the *HemoRel-A* vial. The vacuum in the vial helps easy withdrawal of water.
- Swirl the *HemoRel-A* vial gently and continuously by rotating it at an angle of 45° until it is completely dissolved. Do not shake. Check to make sure the factor concentrate is completely dissolved. The solution is slightly opalescent with occasional un-dissolved proteins.
- Dissolution normally takes about 25 to 30 minutes at room temperature. The solution should be used within 2 hours of reconstitution.

2) Filtration and intravenous injection

- Re-disinfect the stopper of the *HemoRel-A* vial.
- Attach the filter between the needle and the syringe.
- Push the needle through the stopper of HemoRelA vial.
- Turn the vial upside down and draw all the solution into the 20 ml syringe slowly. Point the needle up and remove any air bubbles by gently tapping the syringe with your finger and slowly and carefully pushing air out of the syringe.
- Detach the filter needle from the syringe.
- Perform venipuncture using the 23 G infusion set, allow its plastic tube to fill with blood and connect the tube to the syringe.
- Inject the *HemoRel-A* solution slowly into the vein. The recommended maximum rate of infusion is 1 to 2 ml/min.

REFERENCES

National Hemophilia Society, Medical and Scientific Advisory Committee Recommendations Concerning the Treatment of Hemophilia and Other Bleeding Disorders (Revised March 2003)

Lusher JM. Congenital disorders of clotting proteins and their management, in Rossi's Principles of Transfusion Medicine, Third edition, 2002. Ed. Simon, Dzik, Snyder, et al; pp. 448-462, Lippincott, Williams and Williams, Philadelphia.

C.F. Abilgaard, J.V. Simone, J.J. Corrigan, et al., Treatment of Hemophilia with Glycine Precipitated Factor VIII, New Eng J Med, 275 (1966), p. 471.

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