GRIFOLS

Fanhdi®
250, 500 and 1000 I.U.

FACTOR VIII
Powder and solvent for solution for injection

Composition

Vial:

- Active ingredient:			
Factor VIII	250 I.U.	500 I.U.	1000 I.U.
(Total proteins	≤ 90 mg	≤ 90 mg	≤ 90 mg)
- Excipients:			
Arginine, Human albumin, Histidine			
Pre-filled syringe with solvent:			
Water for injections	10 ml	10 ml	10 ml

Pharmaceutical form and content

Powder and solvent for solution for injection, containing 250, 500 or 1000 I.U. of factor VIII.

Activity

Fanhdi® is a high purity and stable FVIII lyophilised concentrate obtained from human plasma by means of a continuous purification process consisting of a polyethylene glycol (PEG) precipitation followed by an affinity chromatography and sodium chloride and glycine precipitations.

The product in final vial has a specific activity of at least 2.5 to 10 I.U./mg of protein depending on potency (250, 500 or 1000 I.U.).

The specific activity excluding the natural stabiliser VWF and albumin is greater than 1000 I.U./mg of protein.

This product is obtained from plasma tested and found nonreactive for hepatitis B surface antigen (HBsAg) and negative for antibodies to HCV and antibodies to HIV-1 and HIV-2. ALT levels are also determined, rejecting those plasma units with an ALT level of greater than twice the upper limit of normal.

The process to manufacture Fanhdi® has been validated for viral inactivation/removal, using HIV and model viruses for enveloped and non-enveloped viruses. Two specific steps designed to inactivate any contaminating viruses, consisting of a treatment with tri(n-butyl) phosphate (TNBP) and Polysorbate 80 and a heat treatment for 72-74 h at 81 ± 1 °C, as well as two steps of the process related to inactivation/removal (polyethylene glycol precipitation and affinity chromatography) were studied, resulting altogether in a good viral inactivation/removal level.

Therapeutic indications

Fanhdi® is indicated for the prevention and control of bleeding in patients with moderate or severe factor VIII deficiency due to classical haemophilia A.

Contraindications

Caution is advised in patients with known allergic reactions to constituents of the preparation.

Precautions

If allergic or anaphylactic reactions occur, administration should be stopped immediately (the current specific guidelines of shock therapy should be followed).

After repeated treatment with human plasma coagulation factor VIII concentrate, the level of inhibitors in plasma should be determined.

When medicinal products prepared from human blood or plasma are administered, transmission of infective agents cannot be totally excluded. This also applies to pathogens of hitherto unknown nature.

To reduce the risk of transmission of infective agents, selection of donors and donations using suitable methods is performed. Besides, removal and inactivation procedures are included in the production process.

Vaccination guidelines for patients treated with blood or human plasma derivatives must be taken into consideration in all the patients receiving Fanhdi®.

Interactions and incompatibilities

Interactions

None known.

Incompatibilities

Fanhdi® should not be mixed with any other drugs.

Warnings

Pregnancy and lactation

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials.

Studies carried out in animal models are not sufficient to assess the safety with respect to reproduction, development of the embryo or foetus, the course of gestation and peri- and postnatal development.

Therefore, human plasma factor VIII concentrate may be used if clearly needed during pregnancy and lactation.

Effects on ability to drive

There are no indications that human plasma coagulation factor VIII concentrate may impair the ability to drive or to operate machines.

Posology

The dose and duration of Fanhdi® treatment must be adjusted according to each patient's needs.

The required dosage may be estimated using the following formula:

Number of factor VIII units required = Body weight x Desired factor VIII rise x 0.5
(I.U.) (kg) (%)

This calculation is based on the empirical finding that 1 I.U. of factor VIII per kg body weight raises the plasma factor VIII activity approximately 2% (i.e. 0.5 I.U./kg are required for 1% increase in plasma factor VIII level).

The patient's plasma factor VIII levels should be determined and monitored during treatment with Fanhdi®. This is particularly important in the case of surgical procedures.

Haemorrhagic event	Therapeutically necessary plasma level of FVIII activity	Period during which it is necessary to maintain the therapeutic plasma level of factor VIII activity
- Minor haemorrhages: - Haemorrhages into joints	30%	At least 1 day, depending on the severity of the haemorrhage
- Major haemorrhages: - Haemorrhages into muscles - Teeth extraction - Mild trauma capitis - Minor operations - Haemorrhages into the oral cavity	40 - 50%	3 - 4 days or until adequate wound healing
- Life-threatening haemorrhages: - Major operations - Gastro-intestinal bleeding - Intracranial, intra-abdominal or intrathoracic haemorrhages - Fractures	60 - 100%	During 7 days, then therapy for at least another 7 days

Patients with inhibitors

If plasma factor VIII does not reach the expected levels or if the bleeding cannot be controlled after the administration of the adequate dose, the presence of inhibitors should be suspected.

Haemophiliacs with antibodies against factor VIII (inhibitors) need a specific therapy. Immunotolerance can be achieved by treatment with human plasma coagulation factor VIII concentrate.

Prophylaxis

For long-term prophylaxis against bleeding in patients with severe haemophilia A, Fanhdi® should be administered at doses of 10 to 50 I.U./kg, given at intervals of 2 to 3 days. In some cases, especially in younger patients, shorter dosage intervals or higher doses may be necessary.

Instructions for use/handling

Do not use after expiry date given on the label.

Chemical and physical in-use stability has been demonstrated for 12 hours at 25 °C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and coditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Left-over product must never be kept for later use, nor stored in a refrigerator.

To prepare the solution:

1. Warm the vial and syringe but not above 30 ºC.
2. Attach plunger to syringe containing diluent.
3. Remove filter from packaging. Remove cap from syringe tip and attach syringe to filter.
4. Remove vial adaptor from packaging and attach to syringe and filter.
5. Remove cap from vial and wipe stopper with antiseptic wipe provided.
6. Pierce vial stopper with adaptor needle.
7. Transfer all diluent from syringe to vial.
8. Gently shake vial until all product is dissolved. As with other parenteral solutions, do not use if product is not properly dissolved or particles are visible.
9. Briefly separate the syringe/filter from vial/adaptor, to release the vacuum.
10. Invert vial and aspirate solution into syringe.
11. Prepare injection site, separate syringe and inject product using the set with butterfly needle provided or a sterile needle. Injection rate should be 3 ml/min into a vein and never more than 10 ml/min to avoid vasomotor reactions.

Do not re-use administration sets.

Overdose

The consequences of overdosage are not known since overdosage cases have not been reported.

Undesirable effects

- Allergic or anaphylactic reactions are observed in rare cases.
- Increase in body temperature is observed in rare cases.
- Development of antibodies to FVIII.
- Although the isoagglutinin content is very low, there is a risk of intravascular haemolysis.
- The transmission of infectious agents cannot be totally excluded (see item Precautions).

If any adverse reaction, not enclosed in this item, appears, inform your physician.

Storage

Do not store above 30 °C. Do not freeze.

Shelf-life

The expiry date of the product is given on the label.

Do not use after expiry date.

Sizes

Fanhdi® 250 I.U.
Fanhdi® 500 I.U.
Fanhdi® 1000 I.U.

Keep out of the reach and sight of children

Manufacturer

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