

DATA SHEET

RHESONATIV

NAME OF THE MEDICINE

Rhesonativ 625 IU/mL, solution for injection

DESCRIPTION

Rhesonativ contains 625 IU of human anti-D immunoglobulin. Rhesonativ is presented as a solution for injection. The Immunoglobulin A (IgA) content is $\leq 0.05\%$ of the total protein content.

Quantitative composition

1 mL of solution contains:

Human anti-D immunoglobulin	625 IU (125 μ g)
Human protein content	165 mg
Immunoglobulin G, at least	95%
IgA	$\leq 0.05\%$
Glycine	20 mg
Sodium chloride and Sodium acetate	
Corresponding to Sodium	1.6 mg
Tributyl phosphate	$\leq 3 \mu$ g
Polysorbate 80	$\leq 60 \mu$ g
Water for Injections	ad 1 mL

PHARMACOLOGY

Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins: Anti-D (Rh) immunoglobulin.

ATC code: J06B B01.

Anti-D immunoglobulin contains specific antibodies (IgG) against the D (Rh) antigen of human erythrocytes.

Pharmacokinetic properties

Measurable levels of antibodies are obtained approximately 20 minutes after intramuscular injection. Peak serum levels are usually achieved 2 to 3 days later.

The half-life in the circulation of individuals with normal IgG levels is 3 to 4 weeks.

IgG and IgG complexes are broken down in cells of the reticuloendothelial system.

INDICATIONS

- Prevention of Rh(D) immunisation in Rh(D) negative women.
 - Pregnancy/delivery of a Rh-positive baby.
 - Abortion/threatened abortion, ectopic pregnancy or hydatidiform mole.

- Transplacental haemorrhage (TPH) resulting from ante-partum haemorrhage (APH), amniocentesis, chorionic biopsy or obstetric manipulative procedures, e.g. external version, or abdominal trauma.
- Treatment of Rh(D) negative persons after incompatible transfusions of Rh(D) positive blood or other products containing red blood cells.

CONTRAINDICATIONS

Rhesonativ is contraindicated in any patient who has a hypersensitivity to any of the components.

PRECAUTIONS

When medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens and theoretically to Creutzfeldt-Jacob Disease (CJD) agents. The risk of transmission of infective agents is however reduced by:

- i. selection of donors by a medical interview and screening of individual donations and plasma pool for specific markers of infection
- ii. inactivation/ removal procedures included in the production process that have been validated using model viruses.

The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV, and for the non-enveloped virus HAV. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 may cause serious reactions in pregnant women who are sero-negative (foetal infection) and for individuals with immunodeficiency or increased red cell production (e.g. in haemolytic anaemia); however, there is reassuring clinical experience regarding the lack of hepatitis A or parvovirus B19 transmission with immunoglobulins and it is also assumed that the antibody content makes an important contribution to the viral safety.

The manufacturing process of Rhesonativ has been investigated for its capacity to remove prion proteins using an experimental agent of transmissible spongiform encephalopathy (TSE), considered to be a model for the CJD and vCJD agents. The manufacturing process has been shown to significantly reduce the amount of this experimental model agent. The TSE reduction steps are precipitation of fraction I, precipitation of fraction III, two different chromatography purification steps and filtration.

Do not inject this product intravenously (risk of shock). Injections must be given intramuscularly, and care should be taken to draw back on the plunger of the syringe before injection in order to be certain that the needle is not in a blood vessel.

In case of postpartum use, Rhesonativ is intended for maternal administration. It should not be given to the new-born infant.

The product is not intended for use in Rh(D) positive individuals.

Patients should be observed for at least 20 minutes after administration and for at least 1 hour after an accidental intravenous injection.

If symptoms of allergic or anaphylactic type reactions occur, immediate discontinuation of the administration is required.

True hypersensitivity reactions are rare but allergic reactions to anti-D immunoglobulin may occur. Patients should be informed of the early signs of hypersensitivity reactions including

hives, generalised urticaria, tightness of the chest, wheezing, hypotension and anaphylaxis. The treatment required depends on the nature and severity of the side effect. In case of shock, current medical standards for shock treatment should be observed.

Rhesonativ contains a small quantity of IgA. Although anti-D immunoglobulin has been used successfully to treat selected IgA deficient individuals, the attending physician must weigh the benefit against the potential risks of hypersensitivity reactions. Individuals deficient in IgA have a potential for development of IgA antibodies and anaphylactic reactions after administration of blood components containing IgA.

It is strongly recommended that every time Rhesonativ is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

Use in pregnancy and lactation

Rhesonativ is used in pregnancy.

Interactions with other medicines

Active immunisation with live virus vaccines (e.g. measles, mumps or rubella) should be postponed until 3 months after the last administration of anti-D immunoglobulin, as the efficacy of the live virus vaccine may be impaired.

If anti-D immunoglobulin needs to be administered within 2-4 weeks of a live virus vaccination, then the efficacy of such a vaccination may be impaired.

Effects on laboratory tests

After injection of immunoglobulin the transitory rise of the various passively transferred antibodies in the patient's blood may result in misleading positive results in serological testing.

The results of blood typing and antibody testing including the Coombs or antiglobulin test, are significantly affected by the administration of anti-D immunoglobulin.

Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

ADVERSE EFFECTS

The following adverse reactions have been observed with Rhesonativ:

Uncommon ($\geq 0.1\%$ and $< 1.0\%$)

Local pain and tenderness can be observed at the injection site; this can be prevented by dividing larger doses over several injection sites.

Very Rare ($< 0.01\%$)

Fever, malaise, headache, cutaneous reactions and chills may occur. Nausea, vomiting, hypotension, tachycardia and allergic or anaphylactic type reactions, including dyspnoea and shock, are reported, even when the patient has shown no hypersensitivity to previous administration.

For information on viral safety, see **PRECAUTIONS**.

DOSAGE AND ADMINISTRATION

In connection with pregnancy, child birth and gynaecological interventions, the following doses should be given to the pregnant woman:

Prophylaxis before child birth:

1250 IU (250 µg) during week 28-30 of pregnancy.

Prophylaxis after child birth:

For postnatal use, the product should be administered as soon as possible within 72 hours of delivery. If a large foeto-maternal haemorrhage is suspected, its extent should be determined by a suitable method and additional doses of anti-D should be administered as indicated.

Standard dose: 1250 IU (250 µg).

The dose should be administered as soon as possible and not later than 72 hours after delivery.

In the following special situations:

Spontaneous or induced abortion, ectopic pregnancy, hydatidiform mole or other risk of foeto-maternal haemorrhage, e.g. external version or abdominal trauma:

- before the 12th week of pregnancy: 625 IU (125 µg)
- after the 12th week of pregnancy: 1250 IU (250 µg)
- after amniocentesis or chorionic biopsy: 1250 IU (250 µg)

The dose should be administered as soon as possible and no later than 72 hours after the event.

Following a transfusion of Rh-incompatible blood the dose recommended is 1250 IU (250 µg) per 15 mL of transfused red blood cells. If required, a specialist in blood group serology and transfusion medicine should be consulted.

Administration

Rhesonativ should be injected intramuscularly.

In case of haemorrhagic disorders where intramuscular injections are contraindicated, Rhesonativ may be administered subcutaneously. Careful manual pressure with a compress should be applied to the site after injection.

If large total doses (>5 mL) are required, it is advisable to administer them in divided doses at different injection sites.

Instructions for Use, Handling and Disposal

Rhesonativ contains no antimicrobial agent. It must, therefore, be used immediately after opening and on one occasion only. Any remaining contents must be discarded.

The product should be brought to room or body temperature before use.

The solution should be clear or slightly opalescent. Do not use solutions that are cloudy or have deposits.

Any unused product or waste material should be disposed of in accordance with local requirements.

Incompatibilities

Rhesonativ must not be mixed with other medicinal products.

OVERDOSAGE

No data are available on overdosage.

Patients with incompatible transfusion who receive an overdose of anti-D immunoglobulin, should be monitored clinically and by biological parameters, because of the risk of haemolytic reaction.

In other Rh(D) negative individuals, overdosage should not lead to more frequent or more severe undesirable effects than the normal dose.

PRESENTATION

Rhesonativ is supplied as 1 mL and 2 mL solution in type I glass ampoules. Rhesonativ is available in 3 pack sizes:

- 1 x 1 mL;
- 1 x 2 mL; and
- 10 x 2 mL

STORAGE CONDITIONS

Shelf life is 30 months.

Store at 2°C to 8°C (Refrigerate. Do not freeze).

Protect from light.

Do not use after expiry date.

The content of an opened ampoule should be used immediately.

Medicine Classification

Prescription Medicine

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Date of Preparation

3 October 2007