CSL Behring

Package leaflet: Information for the user

Rhophylac® 300 micrograms / 2 ml, solution for injection in pre-filled syringe
Human anti-D immunoglobulin

Please read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or healthcare professional.
- If you get any side effects, talk to your doctor or healthcare professional. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Rhophylac is and what it is used for

What Rhophylac is
This medicine is a ready-to-use solution for injection, which comes in a pre-filled syringe. The solution contains special proteins, isolated from human blood plasma. These proteins belong to the class of "immunoglobulins", also called antibodies. The active ingredient of Rhophylac is a specific antibody called "anti-D (Rh) immunoglobulin". This antibody works against Rhesus fa ctor type D.

What Rhesus factor type D is
Rhesus factors are special characteristics of human red blood cells. About 85% of the populatio n carry the so called Rhesus factor type D (abbreviated "Rh(D)"). These people are called *Rh (D) positive*. People who do not carry Rhesus factor type D are called *Rh(D) negative*.

What anti-D (Rh) immunoglobulin is
Anti-D (Rh) immunoglobulin is an antibody, which works against Rhesus factor type D and is produced by the human immune system. When a Rh(D) negative person receives Rh(D) positiv e blood, their immune system will recognise the Rh(D) positive red blood cells as "foreign" to t heir body, and will attempt to destroy them. For this purpose, the immune system will build spe cific antibodies against Rhesus factor type D. This process is called "immunisation" and it usua lly takes some time (2–3 weeks). Therefore, the Rh(D) positive red blood cells will not be destr oyed upon the first contact, and no signs or symptoms are usually seen then. But when the sam e Rh(D) negative person receives Rh(D) positive blood a second time, the antibodies will be "r eady at hand" and their immune system will destroy the foreign Rh(D) positive red blood cells i mmediately.

How Rhophylac works
If a Rh(D) negative person is given a sufficient amount of human anti-D (Rh) immunoglobulin, isoimmunisation against Rhesus factor type D can be prevented. To achieve this, treatment wit h Rhophylac should commence before or early enough after the first contact to Rh(D) positive red blood cells. The anti-D (Rh) immunoglobulins contained in this medicine will then destroy the foreign Rh(D) positive red blood cells immediately. Thus, the person's immune system will not be prompted to build-up its own antibodies.

What Rhophylac is used for
This medicine is used in two distinct situations:

A) <u>You are a Rh(D) negative pregnant woman, who carries a Rh(D) positive baby</u>
In this special situation you may be immunised by Rh(D) positive red blood cells from yo ur baby passing over into your own blood circulation. If this happens, the first baby is usu ally not affected and fully healthy. However, in your next Rh(D) positive baby, your antib odies would destroy the baby's Rh(D) positive red blood cells during pregnancy. This may lead to complications in the development of your next baby, including its possible death.

For that reason, you may receive Rhophylac 300:
- when you carry or have just delivered a Rh(D) positive baby;
- when you lose a Rh(D) positive baby (death of the unborn child in the womb, miscarria ge, threatened miscarriage or abortion);
- when your pregnancy is severely complicated (ectopic pregnancy or a pregnancy with a non-viable fertilised egg (hydatidiform mole));
- when it is likely that your baby's Rh(D) positive red blood cells have passed over into y our own blood circulation (transplacental haemorrhage resulting from antepartum haem orrhage). This may, for example, happen when you experience vaginal bleedings durin g pregnancy;
- when your doctor needs to perform testing methods for foetal deformities (amniocentes is, chorionic biopsy, cordocentesis);
- when your doctor or midwife needs to try moving the baby from outside (e.g., external version of the baby or other obstetric manipulative procedures);
- when you have an accident hurting your stomach or gut (abdominal trauma).

This medicine is used also if you are a Rh(D) negative pregnant woman and it is not known if y our baby is Rh(D) positive.

B) <u>You are a Rh(D) negative adult, child or adolescent (0-18 years) who has accidentally rece ived infusions (transfusions) of Rh(D) positive blood or other preparations containing Rh (D) positive red blood cells like “platelet concentrate” (mismatched transfusion).</u>

2. What you need to know before you are given Rhophylac

➔ Read this section carefully. The information given should be taken into consideration by you and your doctor before you are given this medicine.

Do not take Rhophylac:

- If you are allergic (hypersensitive) to human immunoglobulins or any of the other ingredie nts of this medicine (listed in section 6).
  ➔ Tell your doctor or healthcare professional prior to treatment about any medicine which you have not well tolerated earlier.

- You must not receive injections into a muscle, if you suffer from a severe reduction in the number of platelets (thrombocytopenia) or any other severe blood clotting disorder.
  ➔ Tell your doctor or healthcare professional prior to treatment if this applies to you. In t his case this medicine may be given to you only by injection into a vein.

Warnings and Precautions
➔ Talk to your doctor or healthcare professional before you are given Rhophylac.

- For protecting Rh(D) negative women after delivery of a Rh(D) positive baby, this medici ne is always given to the mother, not to the new-born baby.
- This medicine is not intended for use in Rh(D) positive persons, nor for individuals already immunised to Rh(D) antigen.

<u>When stopping the administration may be required</u>
- Rhophylac may trigger hypersensitivity reactions (allergic-type). In rare cases, allergic rea ctions such as a sudden fall in blood pressure or shock may occur (see also section 4 'Possi ble side effects') even if you have previously received human immunoglobulins and tolerat ed them well.
  ➔ Tell your doctor or healthcare professional immediately if such reactions occur. He or she will t hen stop the administration of the product and treat you depending on the nature and severi ty of the side effect.

<u>Your doctor or healthcare professional will take special care</u>
- if you have low levels of the IgA type immunoglobulins you are more likely to experience a hypersensitivity reaction.
- ➔ Tell your doctor or healthcare professional if you have low levels of IgA. He or she will then very thoroughly weigh the benefit of treatment with this medicine against the incr eased risk of hypersensitivity reactions.
- if you are treated with this medicine after a mismatched transfusion, you may receive quite a large amount of the product (up to 3000 micrograms, equivalent to 20 ml or 10 syringes). In this case a so called haemolytic reaction occurs. This results from the intended destructi on of the foreign Rh(D)-positive red blood cells. For this reason, your doctor or healthcare professional will monitor you closely and may need to do special blood tests.
- if your body mass index (BMI) is greater or equal to 30 (calculated by dividing your body mass by the square of your height), the injection of Rhophylac into a muscle may not be fully effective. In this case, your doctor or healthcare professional should rather inject this medicine into a vein.

<u>Information on safety with respect to infections</u>
This medicine is made from human blood plasma (this is the liquid part of the blood).
When medicines are made from human blood or plasma, certain measures are put in place to pr event infections being passed on to patients. These include:
- careful selection of blood and plasma donors to make sure those at risk of carrying infecti ons are excluded,

- the testing of each donation and pools of plasma for signs of virus/infections,
- the inclusion of steps in the processing of the blood or plasma that can inactivate or remove viruses.

Despite these measures, when medicines prepared from human blood or plasma are administer ed, the possibility of passing on infection cannot be totally excluded. This also applies to any u nknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodefi ciency virus (HIV, the AIDS virus), hepatitis B virus and hepatitis C virus.
The measures taken may be of limited value against non-enveloped viruses such as hepatitis A virus and parvovirus B19.

Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections, possi bly because the antibodies against these infections, which are contained in the product, are prot ective.
It is strongly recommended that every time you receive a dose of Rhophylac, the name and bat ch number of the product are recorded in order to maintain a record of the batches used.

Blood tests
➔ Tell your doctor or healthcare professional that you were treated with Rhophylac if you or your new-born baby have any blood tests (serological testing).

After you were given this medicine, the results of some blood tests may be altered for a certain period of time. If you are a mother having received this medicine before delivery, the results of some blood tests in your new-born baby may also be affected.

Other medicines and Rhophylac
➔ Tell your doctor or healthcare professional if you are taking, have recently taken or might ta ke any other medicines. This also applies to medicines obtained without a prescription.

Vaccinations
➔ Tell your doctor or healthcare professional prior to treatment if you have just had a vaccinat ion within the last 2 to 4 weeks. Also inform your vaccinating doctor after the treatment. He or she can then plan to check the efficacy of your vaccination.

This medicine may impair the efficacy of vaccinations with live virus vaccines, for example ag ainst measles, mumps, rubella (German measles) or varicella. Such vaccinations should therefo re not be given for 3 months after you were last given Rhophylac.

Pregnancy and breast-feeding
This medicinal product is used in pregnancy or early after delivery.
Immunoglobulins are excreted in human milk. In clinical studies, 432 mothers received this me dicine before delivery and 256 of them again after delivery, and no side effects were seen in the ir children.

Driving and using machines
No effects of Rhophylac on the ability to drive and use machines are expected.

Rhophylac contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per syringe, that is to say essentially "sodium-free".

3. How to use Rhophylac

This medicine will be injected by your doctor or healthcare professional into a muscle or directly into a vein. Your doctor will decide how much Rhophylac you should receive, and which is the appropriate route of administration. For example, if your body mass index (BMI) is greater or equal to 30, he or she should rather inject this medicine directly into a vein (see also section 2).

The syringe should be brought to room temperature (25°C) before use.
One syringe should be used for **one patient** only (even if product is left over then).

You should be observed for at least 20 minutes after having received Rhophylac.

If you receive more Rhophylac than you should
Consequences of an overdosage are not known.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Suc h side effects may occur even if you previously received human immunoglobulins and tolerate d them well.

Allergic reactions (hypersensitivity reactions) have been observed **rarely** (affects 1 to 10 users in 10,000). Early signs may appear as small itching bubbles on your skin (hives) or all over your body (generalised urticaria). They may progress to severe hypersensitivity / anaphylactic reactions such as a sudden fall in blood pressure or shock (e.g. you may feel light-headed, dizzy, faint on standing, cold in the hands and feet, sense an abnormal heart beat or chest pain, tightness of the chest, wheezing or have blurred vision) even when you have shown no hypersensitivity on previous administrations.

➔ Tell your doctor or healthcare professional immediately if you notice such signs during the administration of Rhophylac. He or she will decide to stop the administration completely and start the appropriate treatment.

If you are given this medicine into a muscle, you may feel local pain and tenderness at the injec tion site.

The following side effects were **uncommon** (affects 1 to 10 users in 1000):
- fever and chills (shivering),
- generally feeling unwell (malaise),
- headache,
- skin reactions, redness of the skin (erythema), itching (pruritis).

The following side effects were **rare** (affects 1 to 10 users in 10,000):
- allergic reactions, anaphylactic shock
- nausea and/or vomiting,
- low blood pressure (hypotension),

- rapid heartbeat or pulse rate (tachycardia),
- joint pain (arthralgia),
- difficulty in breathing (dyspnoea)
- reactions at the injection site.

Reporting of side effects
If you get any side effects, talk to your doctor or healthcare professional. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects, you can help provide more information on the safety of this medicine.

UK:
Yellow Card Scheme.
Website: www.mhra.gov.uk/yellowcard
or search for MHRA Yellow Card in the Google Play or Apple App store

Malta: ADR Reporting Website:
www.medicinesauthority.gov.mt/adrportal

Ireland:
HPRA Pharmacovigilance Section
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 676 4971
Fax: +353 1 676 2517
Website: www.hpra.ie
Email: medsafety@hpra.ie

5. How to store Rhophylac

- Keep out of the sight and reach of children.
- Store in a refrigerator (+2 to +8 °C).
- Do not freeze.
- Keep the syringe in the outer carton (in its sealed plastic pack) in order to protect from lig ht.
- Do not use this medicine if you notice that the solution is cloudy or has deposits.
- Do not use this medicine after the expiry date which is stated on the outer carton and the s yringe label after EXP. The expiry date refers to the last day of that month.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What this medicine contains

- The active substance is human anti-D (Rh) immunoglobulin (antibodies of the IgG type agai nst the Rhesus factor type D).
- The other ingredients are human albumin, glycine, sodium chloride and water for injections.
- This product contains a maximum of 30 mg/ml of human plasma proteins of which 10 mg/m l is human albumin as stabiliser. At least 95% of the other plasma proteins are human immu noglobulins (antibodies) of the IgG type. Rhophylac contains not more than 5 micrograms/ ml human immunoglobulins (antibodies) of the IgA type.
- Rhophylac contains no preservatives.

What Rhophylac looks like and contents of the pack

This medicine is a clear or slightly pearly and colourless or pale yellow solution for injection. Rhophylac 300 is provided in a pre-filled glass syringe with 2 ml of ready-to-use sterile solutio n containing 300 micrograms (1500 IU) of anti-D immunoglobulin.

Rhophylac is available in single packs containing 1 pre-filled syringe and 1 injection needle, both packed in one blister pack (a clear plastic container sealed with a paper foil) or in multipacks comprising 5 single packs. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last revised in: 06/2019