

# **PARTOBULIN SDF**

**EU Summary of Product Characteristics  
SPC 0408**

**EU Labelling  
LAB 0408**

**EU Patient-friendly Package Leaflet  
PPI 0408**

**Based on Partobulin SDF CCDS1202 and the ‘Guideline on the cSPC for Human Anti-D Immunoglobulin for Intramuscular Use – Revision 1 (CPMP/BPWG/574/99 Rev.1)’ of 20 September 2007.**

**Note: Information in squared brackets relates to 1650 fill size.**

## **SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

Partobulin SDF 1250 IU/ml solution for injection  
[PARTOBULIN SDF 1650 IU/1.32 ml solution for injection]

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each syringe contains 1250 IU\* human Anti-D immunoglobulin.  
[Each syringe contains 1650 IU\* human Anti-D immunoglobulin.]

One ml contains 1250 IU human Anti-D immunoglobulin.

\*100 micrograms of human anti-D immunoglobulin corresponds to 500 international units (IU)

Human protein content: 100 – 170 mg/ml of which at least 90% is IgG.

Excipients: Glycine, sodium chloride

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection.

The solution is clear or slightly opalescent, colourless to pale yellow. During storage the product may show formation of slight turbidity or a small amount of particulate matter.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

#### Prevention of Rh(D) immunisation in Rh(D) negative women

- Antenatal prophylaxis
  - ▷ Planned antenatal prophylaxis
  - ▷ Antenatal prophylaxis following complications of pregnancy including: Abortion/threatened abortion, ectopic pregnancy or hydatidiform mole, intrauterine fetal death (IUFD), transplacental haemorrhage (TPH) resulting from ante-partum haemorrhage (APH), amniocentesis, chorionic biopsy, obstetric manipulative procedures e.g. external version, invasive interventions, cordocentesis, blunt abdominal trauma or fetal therapeutic intervention
- Postnatal prophylaxis
  - ▷ Delivery of a Rh(D) positive (D, D<sup>weak</sup>, D<sup>partial</sup>) baby

#### Treatment of Rh(D) negative persons after incompatible transfusions of Rh(D) positive blood or other products containing red blood cells e.g. platelet concentrate.

Consideration should also be given to other official guidance on the appropriate use of human anti-D immunoglobulin for intramuscular use.

## 4.2 Posology and method of administration

### Method of administration

For intramuscular use.

If a large volume (>2 ml for children or >5 ml for adults) is required, it is recommended to administer this in divided doses at different sites.

If intramuscular administration is contra-indicated (bleeding disorders), the injection can be administered subcutaneously if no intravenous anti-D product is available.

### Posology

The dose of anti-D immunoglobulin should be determined according to the level of exposure to Rh(D) positive red blood cells and based on the knowledge that 0.5 ml of packed Rh(D) positive red blood cells or 1 ml of Rh(D) positive blood is neutralised by approximately 10 micrograms (50 IU) of anti-D immunoglobulin.

The following doses are recommended based on the clinical studies performed with PARTOBULIN SDF.

Consideration should also be given to dose and dose schedules for human anti-D immunoglobulin for intramuscular use recommended in other official guidance.

#### Prevention of Rh(D) immunisation in Rh(D) negative women

- *Antenatal prophylaxis:* According to general recommendations, currently administered doses range from 50 – 330 micrograms or 250 – 1650 IU. For specific study details see section 5.1.
  - ▷ *Planned antenatal prophylaxis:*  
A single dose at 28 – 30 weeks of gestation or two doses at 28 and 34 weeks.
  - ▷ *Antenatal prophylaxis following complications of pregnancy:*  
A single dose should be administered as soon as possible and within 72 hours and if necessary repeated at 6 – 12 week intervals throughout the pregnancy.
- *Postnatal prophylaxis.* According to general recommendations, currently administered doses range from 100 – 300 micrograms or 500 – 1500 IU. For specific study details see section 5.1. If the lower dose (100 micrograms or 500 IU) is administered then testing of the amount of fetal maternal haemorrhage should be performed.

For postnatal use, the product should be administered to the mother as soon as possible within 72 hours of delivery of an Rh positive (D, D<sup>weak</sup>, D<sup>partial</sup>) infant. If more than 72 hours have elapsed, the product should not be withheld but administered as soon as possible.

The postnatal dose must still be given even when antenatal prophylaxis has been administered and even if residual activity from antenatal prophylaxis can be demonstrated in maternal serum.

If a large fetomaternal haemorrhage (> 4 ml (0.7% - 0.8% of women)) is suspected, e.g. in the event of fetal/neonatal anaemia or intrauterine fetal death, its extent should be determined by a suitable method e.g. Kleihauer-Betke acid elution test to detect fetal HbF or flow cytometry which specifically identifies Rh(D) positive cells. Additional doses of anti-D immunoglobulin should be administered accordingly (10 micrograms or 50 IU) per 0.5 ml fetal red blood cells).

### Incompatible transfusions of red blood cells (RBCs)

The recommended dose is 20 micrograms (100 IU) anti-D immunoglobulin per 2 ml of transfused Rh(D) positive blood or per 1 ml of RBC concentrate. The appropriate dose should be determined in consultation with a specialist in blood transfusion. Follow-up tests for Rh D positive RBCs should be done every 48 hours and further anti-D administered until all Rh D positive RBCs have cleared from the circulation. A maximum dose of 3000 micrograms (15000 IU) is sufficient in the case of larger incompatible transfusions independent of whether the transfusion volume is greater than 300 ml of Rh(D) positive red blood cells.

The use of an alternative intravenous product is recommended, as it will achieve adequate plasma levels immediately. If no intravenous product is available, the large volume should be administered intramuscularly over a period of several days.

### **4.3 Contraindications**

Hypersensitivity to any of the components.  
Hypersensitivity to human immunoglobulins.

### **4.4 Special warnings and precautions for use**

Ensure that PARTOBULIN SDF is not administered into a blood vessel, because of the risk of shock.

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

The product is neither intended for use in Rh(D) positive women nor for women already immunised to Rh(D) antigen.

True hypersensitivity reactions are rare but allergic type responses to anti-D immunoglobulin may occur.

PARTOBULIN SDF contains a small quantity of IgA. Although anti-D immunoglobulin has been used successfully to treat selected IgA deficient individuals, individuals who are deficient in IgA have the potential for developing IgA antibodies and may have anaphylactic reactions after administration of plasma derived medicinal products containing IgA. The physician must therefore weigh the benefit of treatment with PARTOBULIN SDF against the potential risks of hypersensitivity reactions.

Rarely, human anti-D immunoglobulin can induce a fall in blood pressure with anaphylactic reaction, even in patients who have tolerated previous treatment with human immunoglobulin.

Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. In case of shock, standard medical treatment for shock should be implemented.

Patients in receipt of incompatible transfusion, who receive very large doses of anti-D immunoglobulin, should be monitored clinically and by biological parameters, because of the risk of haemolytic reaction.

PARTOBULIN SDF is made from human plasma. Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infectious agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV, and for the non-enveloped viruses HAV and parvovirus B19.

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.

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

#### **4.5 Interaction with other medicinal products and other forms of interaction**

##### Live attenuated virus vaccines

Active immunisation with live virus vaccines (e.g. measles, mumps or rubella) should be postponed for 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.

##### Interference with serological testing

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.

Passive transmission of antibodies to erythrocyte antigens, e.g. A, B, D may interfere with some serological tests for red cell antibodies, for example the antiglobulin test (Coombs' test) particularly in Rh(D) positive neonates whose mothers have received antenatal prophylaxis.

#### **4.6 Pregnancy and lactation**

This medicinal product is intended for use in pregnancy.

#### **4.7 Effects on ability to drive and use machines**

PARTOBULIN SDF has no influence on the ability to drive and use machines.

#### **4.8 Undesirable effects**

The following table lists the adverse reactions that have been reported for anti-D immunoglobulins in general and during post-marketing experience with PARTOBULIN SDF. The frequency of these adverse reactions is not known (cannot be estimated from the available data).

No adverse reactions related to the medicinal product were reported in clinical studies with PARTOBULIN SDF.

<b>MedDRA Standard System Organ Class</b>	<b>Adverse reaction</b>	<b>Frequency</b>
Immune system disorders	Anaphylactic shock, hypersensitivity	Not known
Nervous system disorders	Headache	Not known
Cardiac disorders	Tachycardia	Not known
Gastrointestinal disorders	Nausea, vomiting	Not known
Skin and subcutaneous tissue disorders	Skin reaction, erythema, itching, pruritus, rash	Not known

MedDRA Standard System Organ Class	Adverse reaction	Frequency
Vascular disorders	Hypotension	Not known
Musculoskeletal and connective tissue disorders	Arthralgia	Not known
General disorders and administration site conditions	Fever, malaise, chill At injection site: swelling, pain, erythema, induration, warmth, pruritus, rash, itching	Not known
Investigations	Rh(C) antibodies positive	Not known

#### 4.9 Overdose

Consequences of an overdose are not known.

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immune sera and immunoglobulins: anti-D (Rh) immunoglobulin, ATC code: J06BB01.

Anti-D immunoglobulin contains specific antibodies (IgG) against the D (Rh) antigen of human erythrocytes. It can also contain antibodies to other Rh antigens e.g. anti-Rh C antibodies.

During pregnancy, and especially at the time of childbirth, fetal red blood cells may enter the maternal circulation. When the woman is Rh(D)-negative and the fetus Rh(D)-positive, the woman may become immunised to the Rh(D) antigen and produce anti-Rh(D) antibodies which cross the placenta and may cause haemolytic disease of the newborn. Passive immunisation with anti-D immunoglobulin prevents Rh(D) immunisation in more than 99% of cases provided that a sufficient dose of anti-D immunoglobulin is administered soon enough after exposure to Rh(D)-positive fetal red blood cells.

The mechanism by which anti-D immunoglobulin suppresses immunisation to Rh(D)-positive red cells is not known. Suppression may be related to the clearance of the red cells from the circulation before they reach immunocompetent sites or, it may be due to more complex mechanisms involving recognition of foreign antigen and antigen presentation by the appropriate cells at the appropriate sites in the presence or absence of antibody.

Efficacy and safety of PARTOBULIN SDF was investigated in a clinical study in 108 Rh(D) negative women administered PARTOBULIN SDF 1250 IU post-partum. Most subjects received a single dose of 1250 IU within 72 hours after delivery; only 16 subjects who were evaluable for efficacy received two doses within 72 hours in one treatment course. The primary endpoint of the study was the elimination of fetal erythrocytes from the maternal circulation induced by routine administration of PARTOBULIN SDF post partum.

Within 3 days after treatment with PARTOBULIN SDF, 75.8% of the efficacy population (92 subjects) proved to be therapy responders, i.e. they showed a reduction of the initial fetal erythrocyte count of equal to or by more than 50%. 16.5% of subjects had a complete remission in spite of the fact that the observational period was only a maximum of three days, which is a rather short period to show relevant treatment effects of anti-D immunoglobulins. These data demonstrate the efficacy of PARTOBULIN SDF in eliminating fetal erythrocytes from the maternal circulation of Rh(D)-negative women. The study results therefore demonstrate that PARTOBULIN SDF can prevent the sensitisation of Rh(D) negative mothers, as the reduction of fetal erythrocytes and anti-D immunisation have been demonstrated to correlate.

#### 5.2 Pharmacokinetic properties

Human anti-D immunoglobulin for intramuscular administration is slowly absorbed into the recipient's circulation and reaches a maximum after a delay of 2-3 days.

Human anti-D immunoglobulin has a half-life of about 3-4 weeks. This half-life may vary from patient to patient.

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

### **5.3 Preclinical safety data**

Immunoglobulins are normal constituents of the human body.

The safety of PARTOBULIN SDF has been demonstrated in several non-clinical studies. Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology and toxicity.

Studies of repeated dose toxicity, genotoxicity, and toxicity to reproduction in animals are impracticable due to induction of and interference by developing antibodies to heterologous proteins. Since clinical experience provides no evidence for carcinogenic potential of immunoglobulins, no experimental studies in heterogeneous species were performed.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Glycine  
Sodium chloride  
Water for injections

### **6.2 Incompatibilities**

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

### **6.3 Shelf life**

2 years

### **6.4 Special precautions for storage**

Store in a refrigerator (2°C – 8°C).  
Do not freeze.  
Keep the syringe in the outer carton in order to protect from light.

### **6.5 Nature and contents of container**

1250 IU in 1 ml [or 1650 IU in 1.32 ml] solution in a glass syringe (Type I glass) with a plunger (bromobutyl) and needle (stainless steel).

Pack size: 1 syringe.

Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal and other handling**

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

The colour can vary from colourless to pale-yellow up to light brown. 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.

## **7. MARKETING AUTHORISATION HOLDER**

[To be completed nationally]

{Name and address }

<{tel}>

<{fax}>

<{e-mail}>

## **8. MARKETING AUTHORISATION NUMBER(S)**

[To be completed nationally]

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

{DD/MM/YYYY }

[To be completed nationally]

## **10. DATE OF REVISION OF THE TEXT**

{MM/YYYY }

[To be completed nationally]

PARTOBULIN is a trademark of Baxter AG, Vienna, Austria

Baxter is a trademark of Baxter International Inc.

## **LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**OUTER CARTON**

**1. NAME OF THE MEDICINAL PRODUCT**

PARTOBULIN SDF 1250 IU/1 ml solution for injection  
[PARTOBULIN SDF 1650 IU/1.32 ml solution for injection]

Human Anti-D immunoglobulin

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Human Anti-D immunoglobulin: 1250 IU (250 microgram)  
[Human Anti-D immunoglobulin: 1650 IU (330 microgram)]  
Human protein: 100 – 170 mg/ml of which at least 90% is IgG.

**3. LIST OF EXCIPIENTS**

Glycine  
Sodium chloride  
Water for injections

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection  
1250 IU/1 ml  
[1650 IU/1.32 ml]

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Intramuscular use.  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN**

Keep out of the reach and sight of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

EXP:

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.

Do not freeze.

Keep the container in the outer carton in order to protect from light.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE****11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

[To be completed nationally]

{Name and Address}

**12. MARKETING AUTHORISATION NUMBER(S)**

[To be completed nationally]

**13. BATCH NUMBER**

Lot:

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription.

**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

PARTOBULIN SDF 1250 IU

[PARTOBULIN SDF 1650 IU]

PARTOBULIN is a trademark of Baxter AG, Vienna, Austria

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS  
SYRINGE LABEL**

**1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

PARTOBULIN SDF

Human Anti-D immunoglobulin  
IM use.

**2. METHOD OF ADMINISTRATION**

**3. EXPIRY DATE**

EXP:

**4. BATCH NUMBER**

Lot:

**5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

1250 IU/1 ml  
[1650 IU/1.32 ml]

**6. OTHER**

**PACKAGE LEAFLET**

## PACKAGE LEAFLET: INFORMATION FOR THE USER

### **PARTOBULIN SDF 1250 IU/ml Solution for Injection** **[PARTOBULIN SDF 1650 IU/1.32 ml Solution for Injection]**

Human Anti-D immunoglobulin

**Read all of this leaflet carefully before you are given this medicine.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist, nurse or midwife.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, pharmacist, nurse or midwife.

Throughout this leaflet PARTOBULIN SDF will be called PARTOBULIN.

#### **In this leaflet:**

1. What PARTOBULIN is and what it is used for
2. Before you have PARTOBULIN
3. How PARTOBULIN is given
4. Possible side effects
5. How to store PARTOBULIN
6. Further information

#### **1. WHAT PARTOBULIN IS AND WHAT IT IS USED FOR**

PARTOBULIN belongs to a group of medicines called ‘immunoglobulins’ or ‘antibodies.’ Antibodies are normally found in your blood. PARTOBULIN contains specific antibodies called ‘Anti-D immunoglobulins.’ It is used to prevent people with the blood type called ‘Rhesus negative’ reacting with blood containing the opposite blood type called ‘Rhesus positive’. This can happen during pregnancy or after a blood transfusion.

During pregnancy when a mother with Rhesus negative blood is carrying a baby with Rhesus positive blood, the mother’s blood can react with the child’s blood. This will not usually affect the child she is carrying but can affect further pregnancies, causing a condition known as ‘Haemolytic Disease of the Newborn’ which can be serious for the baby. Giving injections of PARTOBULIN to the mother can prevent this condition.

- Partobulin is used during pregnancy when a Rhesus negative women has experienced a situation such as:
  - during pregnancy before delivery of a Rhesus-positive child
  - if you have an abortion or risk of abortion
  - if you have a pregnancy where the baby forms outside of your womb (ectopic)
  - if you have certain defects during early pregnancy, such as ‘a hydatidiform mole’
  - if the baby dies inside the womb
  - if you are suffering from placental bleeding during pregnancy
  - if you have an ‘amniocentesis test’ (when the amniotic fluid is sampled) or sampling of placental tissue during an operation (chorionic biopsy)
  - if you have needed manipulations to rotate the baby before or during delivery
  - if you need surgery during pregnancy
  - if your baby’s blood is sampled during pregnancy (cordocentesis)

- if you have an injury to your stomach area.
- if your baby needs to get treatment during pregnancy
- PARTOBULIN is also given to Rhesus negative women after delivery of a Rhesus positive child.
- PARTOBULIN is also used in Rhesus negative men or women after transfusion of blood that is not compatible.

## **2. BEFORE YOU HAVE PARTOBULIN**

### **Do not have PARTOBULIN if**

- you are allergic to the active ingredients (immunoglobulins) or any other ingredients (listed in section 6). The signs of an allergic reaction may have been shortness of breath, wheezing, rash, itching or swelling of your face and lips.

Do not use PARTOBULIN if the above applies to you. If you are not sure talk to your doctor, nurse or midwife before having PARTOBULIN.

### **Take special care with PARTOBULIN**

Check with your doctor, nurse or midwife before having Partobulin if you have any of the problems listed below. They will take special care when giving you Partobulin or change the way you are given it.

- You have Rhesus positive blood or you have already reacted to Rhesus positive blood in the past. In this case you must not have Partobulin.
- You have reacted to human antibody preparations in the past. There is a small chance you may experience an allergic reaction or a sudden drop in your blood pressure ('anaphylactic reaction'). This may also happen very rarely if you have not reacted to medicines like PARTOBULIN in the past.
- Your doctor has ever told you that you have a reduced amount of a specific protein in your blood called IgA and antibodies against IgA. As PARTOBULIN contains small amounts of IgA, there is a risk you may experience an allergic reaction.
- You have a blood disorder that means you cannot have injections into your muscle.
- You are having a blood transfusion.
- You are going to have any blood tests to check your blood type or antibodies.

If you are not sure if any of the above applies to you, talk to your doctor, nurse or midwife before having PARTOBULIN.

### **Using other medicines**

Please tell your doctor, nurse or midwife if you are taking or have recently taken any other medicines, including medicines you have bought yourself without a prescription.

In particular, tell your doctor, nurse or midwife if you have had:

- a vaccination during the last 2 to 4 weeks or are planning to have a vaccination.

Ideally you should wait for 3 months after your treatment with PARTOBULIN has finished before having any vaccinations called 'live virus' vaccinations, such as measles, mumps or rubella to make sure the vaccination works properly.

### **Pregnancy and breast-feeding**

Medicines containing anti-D immunoglobulin like PARTOBULIN are intended for use in pregnant women.

### **Driving and using machines**

PARTOBULIN has no effect on your ability to drive or use machines.

### **Important information about some of the ingredients of Partobulin**

PARTOBULIN is made from human plasma (the liquid part of blood). This means blood from blood donors is used to make PARTOBULIN. When medicines are made from human blood or plasma, a number of measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/infections. Manufacturers of these products also include 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 administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken for the manufacture of PARTOBULIN are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A virus and parvovirus B19. PARTOBULIN also contains certain antibodies that can prevent an infection with hepatitis A virus and parvovirus B19.

## **3. HOW PARTOBULIN IS GIVEN**

### **The usual dose**

- Your doctor will decide how much you will need; this will depend on why you need to have PARTOBULIN.

### **How Partobulin is given**

- The solution will first be warmed to body temperature and then given as a slow injection deep into one of your muscles, or sometimes as an injection just under your skin.
- If you need to have several injections of PARTOBULIN at the same time (more than 2 ml for children or 5 ml for adults), your doctor or nurse will inject the medicine at several different sites of your body.

**If you have any questions about your treatment, ask your doctor, nurse or midwife.**

## **4. POSSIBLE SIDE EFFECTS**

Like all medicines, PARTOBULIN can cause side effects, although not everybody gets them. The following side effects may happen with this medicine:

### **Allergic reactions**

If you have an allergic reaction tell your doctor, nurse or midwife straight away. The signs may include:

- shortness of breath
- wheezing
- rash, itching
- swelling of your face and lips

In more serious cases you may get:

- wheezing (anaphylactic shock).

**Other possible side effects are:**

- headache
- fast heart beat
- feeling dizzy or light headed, because of a drop in your blood pressure
- feeling sick or being sick (nausea or vomiting)
- skin redness, itching, rash
- joint pain
- high temperature (fever)
- generally feeling unwell
- feeling cold (chill)
- change in blood tests (anti-Rh(C) antibodies positive).

At the site where PARTOBULIN was injected swelling, pain, redness, hardening, warmth, itching or rash may occur.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or midwife straight away.

**5. HOW TO STORE X**

- Keep out of the reach and sight of children.
- Store in a refrigerator (2°C to 8°C)
- Do not freeze.
- Keep the syringe in the outer carton to protect from light.
- Do not use PARTOBULIN after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.
- Do not use if the solution is more than slightly cloudy or contains bits (deposits).

**6. FURTHER INFORMATION**

**What PARTOBULIN contains**

- The active substance is Anti-D immunoglobulin (an antibody), 1250 International Units (250 micrograms) [1650 International Units (330 microgram)].
- The other ingredients are glycine, sodium chloride (saline) and water for injections.

**What PARTOBULIN looks like and contents of the pack**

- PARTOBULIN is a clear or slightly opalescent, colourless to pale yellow solution. It is supplied as a 1 ml [1.32 ml] pre-filled syringe with a needle.

**Marketing Authorisation Holder and Manufacturer**

The Marketing Authorisation holder is:  
[To be completed nationally]

{Name and address}

<{tel}>

<{fax}>

<{e-mail}>

PARTOBULIN is made at:

Baxter AG  
Industriestrasse 67  
A-1221 Vienna  
Austria

**This leaflet was last approved in {MM/YYYY}.**

[To be completed nationally]

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**The following information is intended for medical or healthcare professionals only:**

### **Method of administration**

If intramuscular administration is contraindicated (bleeding disorders), the injection can be administered subcutaneously, if no intravenous product is available.

### **Posology**

The dose of anti-D immunoglobulin should be determined according to the level of exposure to Rh(D) positive red blood cells and based on the knowledge that 0.5 ml of packed Rh(D) positive red blood cells or 1 ml of Rh(D) positive blood is neutralised by approximately 10 micrograms (50 IU) of anti-D immunoglobulin.

The following doses are recommended based on the clinical studies performed with PARTOBULIN SDF.

- **Prevention of Rh(D) immunisation in Rh(D) negative women**

*Antenatal prophylaxis:* According to general recommendations, currently administered doses range from 50 – 330 micrograms or 250 – 1650 IU. For specific study details see section 5.1.

- Planned antenatal prophylaxis:  
A single dose at 28 – 30 weeks of gestation or two doses at 28 and 34 weeks.
- Antenatal prophylaxis following complications of pregnancy:  
A single dose should be administered as soon as possible and within 72 hours and if necessary repeated at 6 – 12 week intervals throughout the pregnancy.

*Postnatal prophylaxis.* According to general recommendations, currently administered doses range from 100 – 300 micrograms or 500 – 1500 IU. For specific study details see section 5.1. If the lower dose (100 micrograms or 500 IU) is administered then testing of the amount of fetal maternal haemorrhage should be performed.

For postnatal use, the product should be administered to the mother as soon as possible within 72 hours of delivery of an Rh positive (D, D<sup>weak</sup>, D<sup>partial</sup>) infant. If more than 72 hours have elapsed, the product should not be withheld but administered as soon as possible.

The postnatal dose must still be given even when antenatal prophylaxis has been administered and even if residual activity from antenatal prophylaxis can be demonstrated in maternal serum.

If a large fetomaternal haemorrhage (> 4 ml (0.7% - 0.8% of women)) is suspected, e.g. in the event of fetal/neonatal anaemia or intrauterine fetal death, its extent should be determined by a suitable method e.g. Kleihauer-Betke acid elution test to detect fetal HbF or flow cytometry which specifically identifies Rh(D) positive cells. Additional doses of anti-D immunoglobulin should be administered accordingly (10 micrograms or 50 IU) per 0.5 ml fetal red blood cells).

- **Incompatible transfusions of red blood cells (RBCs)**

The recommended dose is 20 micrograms (100 IU) anti-D immunoglobulin per 2 ml of transfused Rh(D) positive blood or per 1 ml of RBC concentrate. The appropriate dose should be determined in consultation with a specialist in blood transfusion. Follow-up tests for Rh D positive RBCs should be done every 48 hours and further anti-D administered until all Rh D positive RBCs have cleared from the circulation. A maximum dose of 3000 micrograms (15000 IU) is sufficient in the case of larger incompatible transfusions independent of whether the transfusion volume is greater than 300 ml of Rh(D) positive red blood cells.

The use of an alternative intravenous product is recommended, as it will achieve adequate plasma levels immediately. If no intravenous product is available, the large volume should be administered intramuscularly over a period of several days.

### **Special precautions for use**

- Ensure that Partobulin is not administered into a blood vessel, because of the risk of shock.
- In the case of postnatal use, the product is intended for maternal administration. It should not be given to the newborn infant.
- Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection. In case of shock, standard medical treatment for shock should be implemented.
- Patients in receipt of incompatible transfusion, who receive very large doses of anti-D immunoglobulin, should be monitored clinically and by biological parameters, because of the risk of haemolytic reaction.
- It is strongly recommended that every time that Partobulin is administered to a patient, the name and batch number of the product be recorded in order to maintain a link between the patient and the batch of the product.
- In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

### **Interference with serological testing**

Passive transmission of antibodies to erythrocyte antigens, e.g. A, B, D may interfere with some serological tests for red cell antibodies, for example the antiglobulin test (Coombs' test) particularly in Rh(D) positive neonates whose mothers have received antenatal prophylaxis.

### **Overdose**

Consequences of an overdose are not known.

### **Special precautions for disposal**

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