*SUMMARY OF PRODUCT CHARACTERISTICS*
*(Guideline III/9163/89)*

## 1 NAME OF THE MEDICINAL PRODUCT

IMMUNORHO 200 mcg Powder and solvent for solution for injection
IMMUNORHO 300 mcg Powder and solvent for solution for injection
Human Anti Rho (D) immunoglobulin
Virus inactivated by solvent/detergent method

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

### 2.1 Active ingredient

Human anti Rho (D) immunoglobulin.

### 2.2 Quantitative composition

1 ml of solution obtained from the reconstitution of the lyophilised product with the vial of solvent included in the package, contains:
Human Protein not more than 180 mg
among which human immunoglobulins not less than 90%
with antibodies against erythrocytes Rho (D) corresponding to mcg 100 – 150 (corresponding to 500 – 750 I.U.) according to the presentation.

## 3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection.
Lyophilised product containing immunoglobulins mainly immunoglobulins G (IgG).

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Prophylaxis of anti-D (Rho) immunisation in Rh-negative (Rho, d) and in $D^u$-positive women.
The sensitization occurs particularly after childbirth, but may also occur during the course of the pregnancy. Besides, amniocentesis, external cephalic version, abdominal trauma, antepartum haemorrhage, ectopic pregnancy or chorionic villi sampling as well as miscarriage and abortion constitute potentially sensitizing episodes.
Prophylaxis of anti-D (Rho) immunization in negative Rho (D) persons after incompatible transfusion of Rh-positive blood (D) or with erythrocytes concentrates.

### 4.2 Posology and method of administration

#### 4.2.1 Posology

In connection with pregnancy, childbirth and gynaecological interventions:
Post-partum prophylaxis:

1000 - 1500 I.U. (200 - 300 mcg) are recommended as the optimum standard dose without previous testing for infiltration of HbF cells (Kleihauer-Betke test).
The injection should be given to the mother as soon as possible after delivery, and in any case not later than 72 hours post-partum.
Ante-partum and post-partum prophylaxis:
1000 - 1500 I.U. (200 - 300 mcg) during the 28$^{th}$ week of pregnancy; in some cases, it is justified to initiate prophylaxis earlier. A further dose of 1000 - 1500 I.U. (200 - 300 mcg) should be given within 72 hours of delivery if the newborn is Rh D positive.
After interruption of pregnancy, extrauterine pregnancy, or hydatid mole:

- before the 12$^{th}$ week of pregnancy: 600 - 750 I.U. (120 to 150 mcg) if possible within 72 hours of the event;
- after the 12$^{th}$ week of pregnancy: 1250 - 1500 I.U. (250 to 300 mcg) if possible within 72 hours of the event;
- after amniocentesis or chorion biopsy: 1250 - 1500 I.U. (250 to 300 mcg) if possible within 72 hours of the intervention.

Following a transfusion of Rh-incompatible blood:
administer 500 I.U. to 1250 I.U. (100 to 250 mcg) per 10 ml of transfused blood over a period of several days.

### 4.2.2 Method of administration

Only for intramuscular use.
In case of clotting disorders where intramuscular injections are contraindicated, human anti D immunoglobulin may be administered subcutaneously. After injection, careful manual pressure with a compress should be applied on the site.
If large total doses ( > 5 ml) are required, it is advisable to administer them in small doses to be injected in various sites.

## 4.3 Contraindications

Intolerance to blood or blood derivatives due to hypersensitivity to homologous immunoglobulins.
Allergic response related to any of the components.

## 4.4 Special warnings and precautions for use

Not to be administered intravenously (risk of shock). Injections must be intramuscular and care should be taken to draw back the plunger of the syringe before injection in order to be certain that the needle is not in a blood vessel.
True allergic responses to human anti D immunoglobulin given in the prescribed intramuscular manner are rare.
In the case of shock, treatment should follow the guidelines for shock therapy. Intolerance to immunoglobulins is likely to develop in the very rare cases of IgA deficiency when the patient has antibodies against IgA.
Patients should be observed for at least 20 minutes after administration.
Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of the injection.

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

**Live attenuated virus vaccines**

Immunoglobulin administration may impair for a period of at least 6 weeks and up to 3 months the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella.

**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.

Results of blood typing and antibody testing, including the Coombs or anti-globulin test, are significantly affected by the administration of anti-D (Rho) immunoglobulin.

## 4.6 Pregnancy and lactation

This medicinal product is used during pregnancy. No harmful effects are known with respect to the course of pregnancy, the foetus and the neonate (category A).

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

There are no indications that anti D immunoglobulin may impair the ability to drive or use machines.

## 4.8 Undesirable effects

Local pain and tenderness may occur at the injection site; this can be prevented by dividing larger doses over several injection sites. Fever, cutaneous reactions and chills occur occasionally. Nausea, vomiting, hypotension, tachycardia, allergic or anaphylactic reactions, including shock, are rare.

When medicinal products prepared from human blood or plasma are administered, infectious diseases due to the 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, donors and donations are duly screened. Each unit of plasma used for the production of this hemoderivative has been controlled and resulted negative for HBsAg, $HIV_1$Ab, $HIV_2$Ab, HCVAb and has been screened for the ALT level; the plasma pool has also been controlled for the presence of HCV-RNA using a genic amplification technique and the result was non reactive. The production process includes procedures for the removal and inactivation of viruses. The product is virus inactivated by solvent/detergent method (TNBP/sodium cholate).

## 4.9 Overdose

Consequences of overdose are not known.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutical category: human anti D immunoglobulin.

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

## 5.2 Pharmacokinetic properties

Detectable levels of antibodies are obtained approximately 20 minutes after intramuscular injection. Peak serum levels are usually reached after 2 to 3 days.
The anti-Rho (D) immunoglobulin half-life in the circulation of individuals with normal IgG levels is of 3 to 4 weeks.
IgG and IgG-complexes are broken down in the cells of the reticuloendothelial system.

## 5.3 Preclinical safety data

Immunoglobulins are normal constituents of the human body.
In animals, single dose toxicity testing is of no relevance since higher doses result in overloading. Repeated dose toxicity testing and embryo-foetal toxicity studies are not practicable due to induction of, and interference with antibodies. Effects of the product on the immune system of the newborn have not been studied.
Since clinical experience provides no hint for tumorigenic and mutagenic effects of immunoglobulins, experimental studies, particularly in heterologous species, are not considered necessary.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Glycine
Sodium chloride
*Vial of solvent:*
Water for injections

## 6.2 Incompatibilities

Anti-Rho (D) immunoglobulin should not be mixed with other medicinal products.

## 6.3 Shelf life

In its intact packaging and if correctly stored as indicated in point 6.4, IMMUNORHO has a shelf life of 3 years from the date of preparation.

## 6.4 Special precautions for storage

Store at a temperature not higher than 25°C, protect from light.
Do not freeze.

## 6.5 Nature and contents of container

Card box containing one neutral glass vial of lyophilised product and one ampoule of 2 ml of solvent.
Vial of 2 ml 200 mcg.
Vial of 2 ml 300 mcg.

## 6.6 Instructions for use and handling

Draw the content of the vial of solvent into an injection syringe; remove the central protection from the rubber stopper of the vial containing the lyophilised product and inject the solvent into the vial; gently shake the vial of solution and draw the solution with the syringe; change the needle and inject.
The imperfect solubilization results in the loss of potency.
Do not use solutions which are cloudy or have deposits.
Once the lyophilised product has been reconstituted with the solvent the resulting solution must be used immediately.

## 7 MARKETING AUTHORISATION HOLDER

Kedrion S.p.A. - Loc. Ai Conti, 55020 Castelvecchio Pascoli, Barga (Lucca) Italy.

## 8 MARKETING AUTHORISATION NUMBERS

IMMUNORHO 200 mcg Powder and solvent for solution for injection
N° 022547020
IMMUNORHO 300 mcg Powder and solvent for solution for injection
N° 022547018

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

Renewal: June 2005

## 10 DATE OF REVISION OF THE TEXT

January 2008