# $Rh_o$(D) Immune Globulin (Human)

## *RhoGAM®*

### Ultra-Filtered (300 µg)

## *MICRhoGAM®*

### Ultra-Filtered (50 µg)

**Rx Only**

For Intramuscular Injection Only
Preservative-free, latex-free delivery system

**DESCRIPTION**

RhoGAM® and MICRhoGAM® $Rh_o$(D) Immune Globulin (Human) are sterile solutions containing IgG anti-D (anti-Rh) for use in preventing Rh immunization. They are manufactured from human plasma containing anti-D. A single dose of RhoGAM contains sufficient anti-D (approximately 300 µg)* to suppress the immune response to 15 mL (or less) of Rh-positive red blood cells. A single dose of MICRhoGAM contains sufficient anti-D (approximately 50 µg)* to suppress the immune response to 2.5 mL (or less) of Rh-positive red blood cells. The anti-D dose is measured by comparison to the RhoGAM in-house reference standard, the potency of which is established relative to the International Reference Preparation 68/419.

The final product contains approximately 5 ± 1% gamma globulin, 2.9 mg/mL sodium chloride, 0.01% polysorbate 80 and 15 mg/mL glycine. Small amounts of IgA, typically less than 15 µg per dose, are present. The pH range is 6.20-6.55. The product contains no preservative and utilizes a latex-free delivery system.

*The anti-D content of RhoGAM/MICRhoGAM is expressed as µg per dose. It can be expressed as International Units (IU) per dose. The conversion factor is 1 µg = 5 IU.

**CLINICAL PHARMACOLOGY**

**Obstetrical Use**

The Rh-negative obstetrical patient may be exposed to red blood cells from her Rh-positive fetus during the normal course of pregnancy or after obstetrical procedures or abdominal trauma. Clinical studies have proven that the incidence of Rh immunization as a result of pregnancy was reduced to 1-2% from 12-13% when RhoGAM was given within 72 hours following delivery. Antepartum administration of Rh immune globulin at 28 weeks, as well as within 72 hours of delivery, has been shown to reduce the Rh immunization rate to about 0.1-0.2%.

Clinical studies demonstrated that administration of MICRhoGAM within three hours following abortion was 100% effective in preventing Rh immunization.

**Use after Rh Incompatible Transfusion**

An Rh-negative individual transfused with one unit of Rh-positive red blood cells has about an 80% likelihood of producing anti-D. However, Rh immunization can occur after exposure to < 1 mL of Rh-positive red blood cells. Protection from Rh immunization is accomplished by administering the appropriate dose of RhoGAM or MICRhoGAM, which is ≥ 20 µg per mL of Rh-positive red blood cells, within 72 hours of transfusion of incompatible red cells. (See **DOSAGE AND ADMINISTRATION** section.)

**INDICATIONS AND USAGE**

**Pregnancy and Other Obstetrical Conditions in Rh-Negative Women, Unless the Father or Baby are Conclusively Rh Negative**

- Pregnancy/delivery of an Rh-positive baby irrespective of the ABO groups of the mother and baby
- Abortion/threatened abortion at any stage of gestation
- Ectopic pregnancy
- Antepartum fetal-maternal hemorrhage (suspected or proven) resulting from antepartum hemorrhage (e.g., placenta previa), amniocentesis, chorionic villus sampling, percutaneous umbilical blood sampling, other obstetrical manipulative procedure (e.g., version) or abdominal trauma
- Transfusion of Rh incompatible blood or blood products

**Transfusion**

- Prevention of Rh immunization in any Rh-negative person after incompatible transfusion of Rh-positive blood or blood products (e.g., red cells, platelet concentrates, granulocyte concentrates)

**CONTRAINDICATIONS**

Individuals known to have had an anaphylactic or severe systemic reaction to human globulin should not receive RhoGAM®, MICRhoGAM® or any other $Rh_o$(D) Immune Globulin (Human).

**WARNINGS**

**RhoGAM® and MICRhoGAM® are made from human plasma. Because these products are made from human blood, they may carry a risk of transmitting infectious agents, e.g., viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections and by removing certain viruses during the manufacturing process. Following fractionation, an additional viral-clearance filtration step is incorporated into the manufacturing process. This filtration step removes viruses via a size-exclusion mechanism utilizing a patented Viresolve† 180 ultrafiltration membrane with a defined pore-size distribution of 12-18 nanometers. The filter is inert to the product. This virus removal process has been shown in laboratory spiking studies to reduce the levels of some viruses ranging from 18-200 nanometers in size, including enveloped viruses as well as non-enveloped viruses. All of the above steps are designed to increase product safety by reducing the risk of transmission of lipid-enveloped and non-lipid-enveloped viruses. Despite these measures, such products can still potentially transmit disease. There is also the possibility that unknown infectious agents may be present in such products. ALL infections thought by a physician possibly to have been transmitted by these products should be reported by the physician or other healthcare provider in the United States to Ortho-Clinical Diagnostics, Inc. at 1-800-421-3311. Outside the United States, the company distributing these products should be contacted. The physician should discuss the risks and benefits of these products with the patient. RhoGAM and MICRhoGAM are manufactured and distributed by Ortho-Clinical Diagnostics, Inc., Raritan, NJ 08869.**

**PRECAUTIONS**

**For intramuscular use only. Do not inject RhoGAM® or MICRhoGAM® intravenously. In the case of postpartum use, the product is intended for maternal administration. Do not inject the newborn infant.**

Patients should be observed for at least 20 minutes after administration.

Allergic responses to RhoGAM or MICRhoGAM may occur. Patients should be informed of the early signs of hypersensitivity reactions, including hives, generalized urticaria, tightness of the chest, wheezing, hypotension and anaphylaxis. The treatment depends upon the nature and severity of the reaction.

RhoGAM and MICRhoGAM contain a small quantity of IgA (less than 15 µg per dose). Although high doses of intravenous immunoglobulin containing IgA at levels of 270-720 µg/mL have been given without incident during treatment of patients with high-titered antibodies to IgA, the attending physician must weigh the benefit against the potential risks of hypersensitivity reactions.

The presence of passively acquired anti-D in the maternal serum may cause a positive antibody screening test. This does not preclude further antepartum or postpartum prophylaxis.

Some babies born of women given $Rh_o$(D) Immune Globulin (Human) antepartum have weakly positive direct antiglobulin (Coombs) tests at birth.

Fetal-maternal hemorrhage may cause false blood typing results in the mother. Late in pregnancy or following delivery, there may be sufficient fetal Rh-positive red blood cells in the circulation of the Rh-negative mother to cause a positive antiglobulin test for weak D ($D^u$). When there is any doubt as to the patient's Rh type, RhoGAM or MICRhoGAM should be administered.

**Pregnancy Category C**

Animal reproduction studies have not been conducted with RhoGAM or MICRhoGAM. The available evidence suggests that $Rh_o$(D) Immune Globulin (Human) does not harm the fetus or affect future pregnancies or the reproduction capacity of the maternal recipient.

**ADVERSE REACTIONS**

Adverse experience (AE) complaints related to RhoGAM® Ultra-Filtered and MICRhoGAM® Ultra-Filtered are received at a rate of approximately one complaint per 60,000 doses distributed for use. These AE complaints are split between reports of anti-D formation despite RhoGAM or MICRhoGAM administration and reports of local reactions at the site of administration.

Local AE reactions include swelling, induration, redness and mild pain at the site of injection, and a small number of patients have noted a slight elevation in temperature. Rarely, these reactions have been treated with antihistamines or corticosteroids. Systemic reactions to RhoGAM or MICRhoGAM are extremely rare. There have been no reported fatalities due to anaphylaxis or any other cause related to RhoGAM or MICRhoGAM administration.

As with any $Rh_o$(D) Immune Globulin (Human), administration to patients who have received Rh-positive red blood cells may result in signs and symptoms of a hemolytic reaction, including fever, back pain, nausea and vomiting, hypo- or hypertension, hemoglobinuria/emia, elevated bilirubin and creatinine and decreased haptoglobin.

**DOSAGE AND ADMINISTRATION**

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

† Viresolve is a trademark of Millipore Corporation.

A single dose (approximately 50 µg)* is contained in each prefilled syringe of MICRhoGAM. This dose will suppress the immune response to 2.5 mL of Rh-positive red blood cells. MICRhoGAM is therefore indicated within 72 hours after termination of pregnancy up to and including 12 weeks' gestation. At or beyond 13 weeks' gestation, RhoGAM should be administered instead of MICRhoGAM.

A single dose (approximately 300 µg)* is contained in each prefilled syringe of RhoGAM. This is the usual dose for the indications associated with pregnancy unless there is clinical or laboratory evidence of a fetal-maternal hemorrhage (FMH) in excess of 15 mL of Rh-positive red blood cells. RhoGAM should be administered within 72 hours of known or suspected exposure to Rh-positive red blood cells. The indications and recommended dosage for RhoGAM and MICRhoGAM are summarized in the following table.

**Indications and Recommended Dosage**

| Indication | Indicated Dose[a] (approximately) |
|---|---|
| Postpartum (if the newborn is Rh-positive) | 300 µg[b] |
| Antepartum: Prophylaxis at 26 to 28 weeks' gestation[c] | 300 µg |
| Antepartum: Amniocentesis, chorionic villus sampling (CVS) and percutaneous umbilical blood sampling (PUBS) | 300 µg |
| Antepartum: Abdominal trauma or obstetrical manipulation | 300 µg |
| Antepartum: Ectopic pregnancy[d] | 300 µg |
| Antepartum: Abortion or threatened abortion at any stage of gestation with continuation of pregnancy[d] | 300 µg |
| Transfusion of Rh-incompatible blood or blood products[d] | 300 µg |

[a] Additional doses of RhoGAM are indicated when the patient has been exposed to > 15 mL of Rh-positive red blood cells. This may be determined by use of qualitative or quantitative tests for FMH (see below).

[b] See **DESCRIPTION** section.

[c] If antepartum prophylaxis is indicated, it is essential that the mother receive a postpartum dose if the infant is Rh-positive.

[d] If abortion or termination of pregnancy occurs up to and including 12 weeks' gestation, or less than 2.5 mL of Rh-incompatible red blood cells were administered, a single dose of MICRhoGAM $Rh_o$(D) Immune Globulin (Human) (approximately 50 µg)* may be used instead of RhoGAM.

If RhoGAM is administered for one of the above indications early in pregnancy (before 26 to 28 weeks), there is an obligation to maintain a level of passively acquired anti-D by administration of RhoGAM at 12-week intervals. RhoGAM should be administered within 72 hours of delivery or exposure to Rh-positive red blood cells. There is little information concerning the effectiveness of Rh Immune Globulin when given beyond this 72-hour period. In one study, Rh Immune Globulin provided protection against Rh immunization in about 50% of subjects when given 13 days after exposure to Rh-positive cells. If delivery occurs within three weeks after the last antepartum dose, the postpartum dose may be withheld, but a test for FMH should be performed to determine if exposure to > 15 mL of red cells has occurred.

Multiple doses of RhoGAM are required if an FMH exceeds 15 mL, an event that is possible but unlikely prior to the third trimester of pregnancy and is most likely at delivery. Patients known or suspected to be at increased risk of FMH should be tested for FMH by qualitative or quantitative methods. In efficacy studies, RhoGAM was shown to suppress Rh immunization in all subjects when given at a dose of ≥ 20 µg per mL of Rh-positive red blood cells. Thus, a single dose of RhoGAM will suppress the immune response after exposure to ≤ 15 mL of Rh-positive red blood cells. However, in clinical practice, laboratory methods used to determine the amount of exposure (volume of transfusion or FMH) to Rh-positive red blood cells are imprecise. Therefore, administration of more than 20 µg of RhoGAM per mL of Rh-positive red blood cells should be considered whenever a large FMH or red cell exposure is suspected or documented.

When multiple doses are required, consult your pharmacy for pooling directions. Multiple doses may be administered at the same time or at spaced intervals, as long as the total dose is administered within three days of exposure.

**Overdosage**

Patients who receive RhoGAM or MICRhoGAM for Rh-incompatible transfusion should be monitored by clinical and laboratory means due to the risk of a hemolytic reaction.

**STORAGE**

Store at 2 to 8°C. Do not store frozen.

*NOTE: For complete prescribing information, see package insert.*

Ortho-Clinical Diagnostics, Inc.
a Johnson & Johnson company
Raritan, New Jersey 08869


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