

Proven Protection for Rh-negative Pregnant Women

A patient's guide to the prevention of Rh sensitization and hemolytic disease of the newborn (HDN)



GRIFOLS

HyperRHO® S/D

Rh₀(D) Immune Globulin (Human)



Each year nearly 1 million pregnancies are impacted by the potential of Rh sensitization.^{1,2}

HyperRHO[®] S/D Full Dose (Rh₀[D] immune globulin [human]) is indicated for prevention of Rh hemolytic disease of the newborn (HDN) and the prevention of isoimmunization in Rh₀(D) negative individuals who have been transfused with Rh₀(D) positive red blood cells.

HyperRHO S/D Full Dose is made from human plasma. Because this product is made from human plasma, it may carry a risk of transmitting infectious agents, such as viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

Never administer HyperRHO S/D Full Dose intravenously. Inject only intramuscularly. Never administer to the neonate.

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Please see Important Safety Information on page 7 and accompanying HyperRHO[®] S/D Full Dose (Rh₀[D] immune globulin [human]) full Prescribing Information for complete prescribing details.

Understanding Rh Sensitization and Hemolytic Disease of the Newborn (HDN)

You received this brochure because test results show that your blood group is Rh negative. Having a different Rh blood group than your baby may be harmful if you are Rh negative and your baby is Rh positive.³ During pregnancy, there's a possibility that a small amount of your baby's blood could mix with your blood. If this happens, your immune system may perceive this difference in blood type as a threat and produce antibodies that fight against your baby's blood. This is known as Rh sensitization and may result in a blood disorder called hemolytic disease of the newborn (HDN).⁴

It's important to know that even if your body produces these antibodies, it may not cause HDN.⁵ However, if these antibodies enter the baby's bloodstream, they can attack the baby's red blood cells and lead to HDN—or rhesus (Rh) disease.⁶ HDN does not develop in the first baby, but future Rh-positive babies may be at risk if the mother is sensitized.⁷

If HDN develops, it could become serious.⁸ A baby born with HDN may develop jaundice or anemia, or may have permanent damage to the brain and central nervous system.⁵ HDN can also lead to mental handicaps, hearing loss, or cerebral palsy. The baby may also need an exchange transfusion to replace his/her blood.

How Does HDN Develop?



A mother with Rh-negative blood becomes pregnant with a baby with Rh-positive blood.⁹



Baby's Rh-positive blood enters the mother's bloodstream during delivery or other trauma.⁹ The mother's immune system responds, and she develops Rh-positive antibodies as an immune response to the baby's blood.



Mother's Rh-positive antibodies enter the baby's Rh-positive bloodstream during pregnancy or birth, causing HDN.^{3,5}

The administration of HyperRHO[®] S/D Full Dose (Rh₀[D] immune globulin [human]) substantially reduces the risk of HDN developing.⁵

For more information about preventing HDN, visit www.hyperRHO.com.

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When Can HDN Develop?

HDN can develop when your blood and your baby's blood mix.⁵ Most of the time this happens during labor and delivery, but it can also happen

- During amniocentesis⁵
- During chorionic villus sampling (CVS)⁸
- If you have vaginal bleeding when you're pregnant⁸
- If you sustain an injury to your belly while you're pregnant⁵
- If you have a miscarriage⁵
- If you have an ectopic pregnancy⁸
- If you have an abortion³

The administration of HyperRHO[®] S/D Full Dose (Rh_o[D] immune globulin [human]) within 72 hours of a full-term delivery of an Rh-positive infant by an Rh-negative mother reduces the rate of Rh sensitization from 12%-13% to 1%-2%.⁵

Rh_o(D) immune globulin (human) should be given with caution to patients with a history of prior systemic allergic reactions following the administration of human immunoglobulin preparations. Such persons have increased potential for developing antibodies to IgA and could have anaphylactic reactions to subsequent administration of blood products that contain IgA.

As with all preparations administered by the intramuscular route, bleeding complications may be encountered in patients with thrombocytopenia or other bleeding disorders.

A large fetomaternal hemorrhage late in pregnancy or following delivery may cause a weak mixed field positive DU test result. If there is any doubt about the mother's Rh type, she should be given Rh_o(D) immune globulin (human). A screening test to detect fetal red blood cells may be helpful in such cases.

If more than 15 mL of D-positive red blood cells are present in the mother's circulation, more than a single dose of HyperRHO S/D Full Dose is required. Failure to recognize this may result in the administration of an inadequate dose.

Please see Important Safety Information on page 7 and accompanying HyperRHO[®] S/D Full Dose (Rh_o[D] immune globulin [human]) full Prescribing Information for complete prescribing details.

What Is HyperRHO S/D Full Dose?

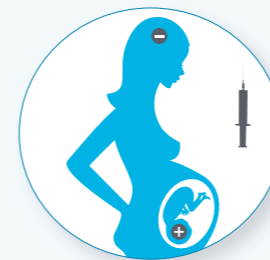
HyperRHO S/D Full Dose provides critical protection necessary to prevent Rh sensitization and HDN when you do not already have Rh-positive antibodies in your system.⁵ HyperRHO S/D Full Dose has been available for 45 years and is known as an immune globulin or hyperimmune.⁹

HyperRHO S/D Full Dose is preservative and latex free, and comes as a prefilled injection of approximately 1 mL.⁵ When injected intramuscularly, HyperRHO S/D Full Dose destroys any Rh-positive red blood cells that may have entered your body. HyperRHO S/D Full Dose also prevents your immune system from further production of Rh-positive antibodies, protecting you from becoming Rh sensitized and your baby from developing HDN.

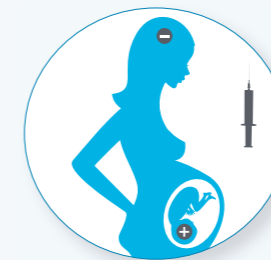
To prevent antibodies from forming against the baby's red blood cells, which could lead to HDN, HyperRHO S/D Full Dose is administered as an injection during week 28 of the pregnancy.⁵ Then, if the baby is Rh-positive, another dose is administered to you within 72 hours after the baby is born.

NEVER ADMINISTER HYPERRHO S/D FULL DOSE INTRAVENOUSLY. INJECT ONLY INTRAMUSCULARLY.
NEVER ADMINISTER TO THE NEONATE.

How Does HyperRHO S/D Full Dose Prevent HDN?⁵



Mother receives a HyperRHO S/D Full Dose injection during week 28 of the pregnancy, before Rh-positive antibodies have formed.



HyperRHO S/D Full Dose protects the mother and baby by preventing the development of Rh-positive antibodies.



Within 72 hours after the baby's delivery, the mother receives a second dose of HyperRHO S/D Full Dose.

Reactions to Rh_o(D) immune globulin (human) are infrequent in Rh_o(D)-negative individuals and consist primarily of slight soreness at the site of injection and slight temperature elevation. While sensitization to repeated injections of human immunoglobulin is extremely rare, it has occurred.

For more information about preventing HDN, visit www.hyperRHO.com.

Grifols: Committed to Safety From Plasma to Product

To produce our plasma-derived medicines, Grifols only uses plasma from qualified donors. A qualified donor is one who has passed a physical exam along with a comprehensive health screening at one of our plasma donation centers. The donors need to make two separate plasma donations (within a six-month period) that must undergo rigorous testing for transmissible diseases. Having two separate donations allows us to more easily confirm that donors are healthy enough to donate. Without a second plasma donation, the first donation cannot be used and will be discarded.

Each unit of plasma is tested after each donation using FDA-approved protocols to verify the donors' health status and determine the safety of the donated plasma.

The individually tested plasma units are then pooled together in preparation for the carefully controlled, multiphase manufacturing process. The pooled plasma is subjected to rigorous testing. Through a process known as fractionation, the various proteins in the plasma are separated. The individual proteins are then purified and subjected to manufacturing steps with the capacity to remove or inactivate viruses before the proteins are transformed into finished products.

For more information about Grifols' commitment to safety, visit www.grifolsusa.com.

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Please see Important Safety Information on page 7 and accompanying HyperRHO® S/D Full Dose (Rh₀[D] immune globulin [human]) full Prescribing Information for complete prescribing details.

Important Safety Information

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If more than 15 mL of D-positive red blood cells are present in the mother's circulation, more than a single dose of HyperRHO S/D Full Dose is required. Failure to recognize this may result in the administration of an inadequate dose.

Although systemic reactions to human immunoglobulin preparations are rare, epinephrine should be available for treatment of acute anaphylactic symptoms.

Administration of live virus vaccines (eg, MMR) should be deferred for approximately 3 months after Rh₀(D) immune globulin (human) administration.

HyperRHO S/D Full Dose should be given in pregnant women only if clearly needed because animal reproduction studies have not been conducted.

Reactions to Rh₀(D) immune globulin (human) are infrequent in Rh₀(D)-negative individuals and consist primarily of slight soreness at the site of injection and slight temperature elevation. While sensitization to repeated injections of human immunoglobulin is extremely rare, it has occurred.

Elevated bilirubin levels have been reported in some individuals receiving multiple doses of Rh₀(D) immune globulin (human) following mismatched transfusions. This is believed to be due to a relatively rapid rate of foreign red cell destruction.

Please see HyperRHO S/D Full Dose Prescribing Information for complete prescribing details inside pocket or visit www.hyperRHO.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

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Prevention Is Possible

Visit www.hyperRHO.com for more information about the prevention of HDN.

Talk to your healthcare provider about the risks of HDN.⁸

Ask how you can move forward with prevention.

References: **1.** The safety of RhIG in the prevention of haemolytic disease of the newborn" T.G. Hirose and D.A Mays. *Journal of Obstetrics and Gynaecology*, August 2007; (6):545-557. **2.** National Center for Health Statistics, December 2015. **3.** American College of Obstetricians and Gynecologists. <http://www.acog.org/-/media/For-Patients/faq027.pdf?dmc=1&ts=20170607T1126412307>. Accessed July 14, 2017. **4.** OB Focus. RH Disease and Red Blood Cell Alloimmunization (Isoimmunization). http://www.obfocus.com/high-risk/Rh_disease/RH%20Disease%20And%20Isoimmunization.htm. Accessed July 14, 2017. **5.** HyperRHO® S/D Full Dose (Rh₀[D] Immune globulin (human) [package insert]. Research Triangle Park, NC: Grifols Therapeutics, Inc; 2014. **6.** Boston Children's Hospital. Hemolytic Disease of the Newborn. <http://www.childrenshospital.org/conditions-and-treatments/conditions/hemolytic-disease>. Accessed July 14, 2017. **7.** Dean L. Blood groups and red cell antigens. Hemolytic disease of the newborn. National Center for Biotechnology Information website. https://www.ncbi.nlm.nih.gov/books/NBK2266/pdf/Bookshelf_NBK2266.pdf. Accessed July 14, 2017. **8.** March of Dimes. Rh Disease. <http://www.marchofdimes.org/complications/rh-disease.aspx>. Accessed July 14, 2017. **9.** Baxter D. Active and passive immunity, vaccine types, excipients and licensing. *Occup Med (Lond)*. 2007;57(8):552-556.

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