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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 or 1500 IU)* to suppress the immune response to 15 mL (or less) of Rh-positive red blood cells.[2,3] A single dose of MICRhoGAM contains sufficient anti-D (approximately 50 µg or 250 IU)* 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 US/WHO/EP Standard Anti-D Immunoglobulin Rh_o(D) Immune Globulin (Human) CBER Lot 4: NIBSC Lot 01/572 (285 IU/ampoule).

All donors are carefully screened by history and laboratory testing to reduce the risk of transmitting blood-borne pathogens from infected donors. Fractionation of the plasma is performed by a modification of the cold alcohol procedure that has been shown to significantly lower viral titers.[4] 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 defined pore-size distribution of 12-18 nanometers. The ultrafiltration step utilizes tangential flow filtration to permit filtration of IgG while effectively retarding enveloped and non-enveloped viruses above the pore-size distribution cutoff. The filter is inert to the product. Non-enveloped viruses are known to be resistant to chemical and physical inactivation.[5,6] Laboratory spiking studies have shown that the cumulative viral removal capability of the RhoGAM/MICRhoGAM manufacturing process exceeds 13 logs for human immunodeficiency virus (HIV). Clearance of model viruses for hepatitis C virus (HCV), hepatitis B virus (HBV) and parvovirus B19 (a non-enveloped

virus) exceeds 11 logs.[4] The donor selection process, the fractionation process and the Viresolve ultrafiltration step are designed to increase product safety by reducing the risk of transmission of enveloped and non-enveloped viruses. Rh_o(D) Immune Globulin (Human) intended for intramuscular use and prepared by cold alcohol fractionation has not been reported to transmit hepatitis or other infectious diseases.[7]

The safety of Rh_o(D) Immune Globulin (Human) has been further shown in an empirical study of viral marker rates in female blood donors in the United States.[8] This study revealed that Rh-negative donors, of whom an estimated 55-60% had received Rh_o(D) Immune Globulin (Human) for pregnancy-related indications, had prevalence and incidence viral marker rates similar to those of Rh-positive female donors who had not received Rh_o(D) Immune Globulin (Human). However, even after the fractionation and virus-filtration steps, there remains a risk of contracting blood-borne pathogens from a plasma-derived product.

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.[9] The pH range is 6.20-6.55. The product contains no preservative and utilizes a latex-free delivery system.

REFERENCES

*The anti-D content of RhoGAM/MICRhoGAM is expressed as µg per dose or as International Units (IU) per dose. The conversion factor is 1 µg = 5 IU.[1] †Viresolve is a trademark of Millipore Corporation.

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