Rabies Immune Globulin (Human)

HyperRAB® S/D

Solvent/Detergent Treated

DESCRIPTION
Rabies Immune Globulin (Human) — HyperRAB® S/D treated with solvent/detergent is a colorless to pale yellow or pink sterile solution of antibodies against rabies virus for intramuscular administration; it is preservative-free and latex-free.

The manufacturing process involves separation from the plasma of donors hyperimmunized with rabies virus. The immune globulin is isolated from solubilized Cohn Fraction B. The Fraction B solution is adjusted to a final concentration of 50% (w/v) with 0.4M of tris(hydroxymethyl)aminomethane (TRIS) and 0.2% of sodium chloride. After the addition of solvent/detergent (TRIS and detergent sodium chloride), the solution is heated to 30°C and maintained at that temperature for not less than 90 hours. Due to the heating step, the solvent/detergent step, the racemization are removed by precipitation, filtration and final sterilization and dialfiltration. HyperRAB® S/D is formulated as a 15%–18% protein solution at a pH of 6.4–7.2 in 0.9% sodium chloride solution to be administered within 72 hours after manufacture. The solution is standardised against the U.S. Standard Rabies Immune Globulin to contain an average potency of 155 U/ml. The U.S. standard of potency is equivalent to the international (IU) unit for rabies antibody.

The removal and inactivation of soluble and non-soluble proteins during the manufacturing process of HyperRAB® S/D has been validated in laboratory studies. Human Immunodeficiency Virus, Type 1 H IV-1, was chosen as the relevant virus for blood products. Bovine Viral Diarrhea Virus (BVDV) was chosen to model Hepatitis C virus (HCV). A recombinant retrovirus (RoV) was chosen to model Human herpes viruses and a large eukaryotic retrovirus (RoV type 3) was chosen to model non-enveloped viruses and its resistant to physical and chemical inactivation. These viruses are not inactivated by the solvent/detergent treatment process leading to the collection of Cohn Fraction B: the precipitation and removal of Fraction C in the production of Cohn Fraction B and the precipitation and amphoteric inactivation in the processing of Cohn Fraction B. Significant inactivation of enveloped viruses is achieved at the time of freeze of solubilized Cohn Fraction B in TRIS and detergent sodium chloride.

Additionally, the manufacturing process was investigated for its capacity to decrease the infectivity of an experimental agent of transmissible spongiform encephalopathy (TSE), considered as a model for the vCJD and CJD agents.

Studies of the HyperRAB® S/D manufacturing process demonstrated that TSE clearance is achieved during the Pooled Solvent/Detergent Fractionation Process (P SPF) lag. These studies provide reasonable assurance that low levels of CJD/TSE agent, if present in the starting material, would be removed.

CLINICAL PHARMACOLOGY

The usefulness of prophylactic antibodies in preventing rabies in humans who, after being studied and exposed to animals, was dramatically demonstrated in a group of persons bitten by a rabid wolf in Iran. Similarly, beneficial results were later reported from the U.S.S.R. Studies coordinated by WHO (World Health Organization) helped determine the optimal conditions under which antirabies serum of equine origin and rabies vaccines can be used in man. These studies showed that serum can interfere to a variable extent with the active immunity induced by the vaccine, but could be minimized by booster doses of vaccine after the end of the usual dosage series.

Preparation of rabies immune globulin of human origin with adequate purity was reported by Calabrese et al. and later was completed in a number of laboratories. This globulin was prepared in these laboratories as a single fraction and distributed to U.S. military forces. These studies demonstrated that a human globulin dose of 30–40 IU of rabies immune antibodies per kg body weight is not associated with any observable adverse effects.

Two categories of exposure should be considered:

1. Species of biting animal

The animal should be euthanized and tested as soon as possible. Holding for observation is not recommended. Discontinue vaccine if immunofluorescence test results of the animal are negative.

2. Condition of animal

The following recommendations are only a guide. In applying them, take into account the animal species involved, the circumstances of the bite or other exposure, and the vaccination status of the animal, and presence of rabies in the region. Local or state public health officials should be consulted if questions arise about the need for rabies prophylaxis.

Local Treatment of Wounds:
Immediate and thorough washing of all bite wounds and scratches with soap and water is perhaps the most effective measure for preventing rabies. Local or state public health officials should be consulted if questions arise about the need for rabies prophylaxis.

Only documented cases of rabies from human-to-human transmission have occurred in patients who received corneas transplanted from persons who died from rabies and history of rabies in the United States result from exposure to rabid animals.

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A properly immunized animal has only a minimal chance of developing rabies and transmitting the virus.

RECOMMENDATIONS

Rabies Immune Globulin (Human) — HyperRAB® S/D is prepared by cold ethanol fractionation from the plasma of donors hyperimmunized with rabies vaccine. The final product is then incubated in the final container for 21–28 days at 2°C–7°C. The product is standardised against the U.S. Standard Rabies Immune Globulin to contain an average potency of 155 U/ml. The U.S. standard of potency is equivalent to the international (IU) unit for rabies antibody.

Vaccination status of the animal, and presence of rabies in the region. Local or state public health officials should be consulted if questions arise about the need for rabies prophylaxis.

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**WARNINGS**

Rabies Immune Globulin (Human) — HyperRAB® S/D is made from human plasma. Products made from human plasma may contain certain infectious agents, such as viruses, and, theoretically, the Creutzfeldt-Jakob Disease (CJD) agent that can cause disease. The risk that such products will transmit an infectious agent is extremely low because of the methods used to process the plasma. But no testing exists for all potential infectious agents. It is not possible to completely remove these infectious agents. Some can be removed by inactivation processes, but other infectious diseases cannot be removed by these processes. Some infectious diseases can be transmitted from cell donations. The attending physician who wishes to administer HyperRAB® S/D to persons with isolated immunoglobulin A (IgA) deficiency must weigh the benefits of treatment against the potential risk of hypersensitivity reactions. Such persons have increased potential for developing antibodies to IgA and could have antibody 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 thrombocytopения or other bleeding disorders.

**PREDICTIONS**

General

HyperRAB® S/D should not be administered intravenously because of the potential for serious reactions. Although systemic reactions to immunoglobulin preparations are rare, epinephrine should be available for treatment of acute anaphylactic reactions.

Drug Interactions

Repeated doses of HyperRAB® S/D should not be administered once vaccine treatment has been initiated as this could prevent the full expression of active immunity expected from the rabies vaccine.

Other antibodies in the HyperRAB® S/D preparation may interfere with the response to vaccines such as measles, mumps, polio or rubella. Therefore, immunization with live vaccines should not be given within 3 months after HyperRAB® S/D administration.

**Pregnancy Category C**

Animal reproduction studies have not been conducted with HyperRAB® S/D. It is also not known whether HyperRAB® S/D can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

HyperRAB® S/D should be given to a pregnant woman only if clearly needed.

**Pediatric Use**

Safety and effectiveness in the pediatric population have not been established.

**ADVERSE REACTIONS**

The recommended dose for HyperRAB® S/D is 20 ml/kg (133 mL/kg) of body weight given pre- or post-exposure. If it may also be given through the seventh day after the first dose of vaccine is given. It is not known whether the full dose of HyperRAB® S/D should be thoroughly infused in the area around the wound and the rest should be administered intramuscularly in the deltoid muscle of the upper arm or other thigh muscle. The global region should be thoroughly flushed with 10 ml saline to reduce the risk of the rare side effects from the small-particle HyperRAB® S/D preparation. HyperRAB® S/D should never be administered in the deltoid area or in the same anatomical site as vaccine.

**STORAGE**

HyperRAB® S/D should be stored under refrigeration (2–8°C, 36–46°F). Solution that has been frozen should not be used.

**HOW SUPPLIED**

HyperRAB® S/D is packaged in 2 ml and 10 ml single dose vials with an average potency of 150 international units per mL (IU/ml). The 2 ml vial contains a dose of 6,000 IU (3 IU/kg) of antirabies immune globulin for a child weighing 15 kg. The 10 ml vial contains a total of 150 IU that is sufficient for an adult weighing 75 kg. HyperRAB® S/D is preservative-free and latex-free.

**REFERENCES**


27. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.


29. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.

30. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.


32. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.

33. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.

34. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.

35. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.

36. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.

37. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.

38. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.


40. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.

41. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP): General recommendations on immunization.