Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Trinbelimab (Recombinant Anti Rho-D Immunoglobulin) 150 mcg/ml and 300 mcg/ml Liquid Injection.

2. Qualitative and quantitative composition

Each Vial / PFS contains:

Trinbelimab (Purified Liquid Bulk) In-House 150 / 300 mcg

It can also be expressed as International Units (IU) per dose. The conversion factor is 1 mcg = 5 IU.

For full list of excipients, see section 6.1

3. Pharmaceutical form

Trinbelimab (Recombinant Anti Rho-D Immunoglobulin) is a clear non pyrogenic, colorless and sterile solution.

4. Clinical particulars

4.1 Therapeutic indications

For use in preventing Rh immunization:

Pregnancy and other obstetrical conditions

For administration to Rh-negative women not previously sensitized to the Rho(D) factor, unless the father or baby are conclusively Rh-negative.

- Delivery of a Rh-positive baby irrespective of the ABO groups of the mother and baby
- Antepartum prophylaxis at 26 to 28 weeks gestation
- Antepartum fetal-maternal haemorrhage (suspected or proven) as a result of placenta previa, amniocentesis, chorionic villus sampling, percutaneous umbilical blood sampling, other obstetrical manipulative procedure (e.g., version) or abdominal trauma.
- Actual or threatened pregnancy loss at any stage of gestation
- Ectopic pregnancy
- Other sensitizing events.

Transfusion of Rh-incompatible blood or blood products

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

4.2 Posology and method of administration

Indication	Dose	Notes
Pregnancy and other obstetrical conditions		

Postpartum (if the newborn is Rh-positive) Administer within 72 hours of delivery. Antepartum: • Prophylaxis at 26 to 28 weeks gestation Administer within 72 hours of suspected or proven exposure to Rhpositive red blood cells resulting from: • Amniocentesis, chorionic villus sampling (CVS) and percutaneous umbilical blood sampling (PUBS) • Abdominal trauma or obstetrical manipulation • Ectopic pregnancy • Threatened pregnancy loss after 12 weeks gestation with continuation of pregnancy • Pregnancy termination (spontaneous or induced) beyond 12 weeks gestation	Trinbelimab (Recombinant Anti Rho-D Immunoglobulin). 300 mcg / 1500 IU	Additional doses of Trinbelimab are indicated when the patient has been exposed to > 15 mL of Rhpositive red blood cells. This may be determined by use of qualitative or quantitative tests for fetalmaternal hemorrhage. If antepartum prophylaxis is indicated, it is essential that the mother receive a postpartum dose if the infant is Rh-positive. If Trinbelimab is administered early in pregnancy (before 26 to 28 weeks), there is an obligation to maintain a level of passively acquired anti-D by administration of Trinbelimab at 12-week intervals.
Actual or threatened termination of pregnancy (spontaneous or induced) up to and including 12 weeks gestation.	Trinbelimab 150 mcg / 750 IU	Trinbelimab to be administered within 72 hours of exposure.

In cases of miscarriage in an advanced stage of pregnancy,	Trinbelimab 300 mcg / 1500 IU	Trinbelimab to be administered within 72 hours.
Other sensitizing events during pregnancy in Rh negative women at a risk of transplacental haemorrhage and not known to have been sensitized	Trinbelimab 150 mcg / 750 IU Or 300 mcg / 1500 IU	Trinbelimab to be administered
Transfusion of Rhincompatible blood or blood products		Administer Trinbelimab within 72 hours of suspected or proven exposure to Rh-positive red blood cells.
Indication	**Dose**	**Notes**
< 2.5 mL Rh-positive red blood cells	Trinbelimab 150 mcg / 750 IU	Administer Trinbelimab within 72 hours of suspected or proven exposure to Rh-positive red blood cells.
2.5 - 15.0 mL Rh-positive red blood cells	Trinbelimab 300 mcg / 1500 IU	Administer Trinbelimab within 72 hours of suspected or proven exposure to Rh-positive red blood cells.
> 15.0 mL Rh-positive red blood cells	Trinbelimab 300 mcg / 1500 IU (multiple injection)	Additional doses of Trinbelimab are indicated when the patient has been exposed to > 15 mL of Rhpositive red blood cells. Administer 20 mcg of Trinbelimab per mL of Rh-positive red blood cell exposure. 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.

Method of Administration

Route of administration - Intramuscular administration.

The administration of Trinbelimab ((Recombinant Anti Rho-D

Immunoglobulin) should be performed under the supervision of a physician.

4.3 Contraindications

Trinbelimab (Recombinant Anti Rho-D Immunoglobulin) is contraindicated in:

- Pregnant woman with positive ICT. (Indirect Coombs' test)
- Pregnant woman is Rh-D positive.
- Should not be given to an infant.

4.4 Special warnings and precautions for use

- Trinbelimab (Recombinant Anti Rho-D Immunoglobulin) is for intramuscular use only, do not inject intravenously.
- The product is intended for maternal administration.
- Do not inject the new-born infant.
- Administer with caution to patients who have had prior severe systemic allergic reactions to human immunoglobulin.

4.5 Interaction with other medicinal products and other forms of interaction

No drug-to-drug interactions studies were conducted with Trinbelimab.

4.6 Pregnancy and Lactation

Trinbelimab (Recombinant Anti Rho-D Immunoglobulin) does not harm the fetus or affect future pregnancies or the reproduction capacity of the maternal recipient. This medicinal product is intended for use in other sensitizing events during pregnancy. No studies have been done during lactation.

Geriatric Use:

It is not Indicated in Geriatric use.

Renal and Hepatic Impairment:

No study done on renal and hepatic Impairment Condition.

4.7 Effects on ability to drive and use machines

No Data available.

4.8 Undesirable effects

- Injection site reactions include swelling, induration, redness and mild pain or warmth.
- Fever, flushing, headache, and chills may rarely occur.
- Adverse events noted in the clinical study were pyrexia, abdominal pain, pruritus, hypertension, hypotension, abnormal White Blood Cell counts.
- Clinical experience adverse events seen during Phase III clinical study.
- In Anti D phase 3 study following adverse events were observed:

Adverse reaction System Organ Class Preferred Term	Trinbelimab (n=144)	Rhogam (n=71)

Any	4	4
General disorders and administration site conditions Pyrexia		
Gastrointestinal disorders, Abdominal pain	2	0
Skin and subcutaneous tissue disorders Pruritus	0	1
Vascular disorders, Hypertension	0	1
Hypotension	0	2
Investigations White blood cell counts abnormal	1	0

Reporting of suspected adverse reactions: Healthcare professionals are requested to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose

Overdosage can lead to any adverse events as listed above. No antidote for this drug. The stoppage of drug administration shall ameliorate the symptoms gradually.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Trinbelimab (Recombinant Anti Rho-D Immunoglobulin) is protein with a molecular weight of 145.5 kD and is stabilized with excipients to ensure the stability till the end of shelf life of 24 months from the date of manufacturing. Trinbelimab act by suppressing the immune response of Rh-negative individual to Rh positive red blood cells and hence prevents alloimmunization. Passive administration of r – anti D causes rapid non - inflammatory clearance of passive anti D coated red blood cells, which stops the inflammatory destruction of fetal red blood cells, evoking a natural immune response.
Additionally, suppression of the immune response lead to the down regulation of maternal immature dendritic cells or anti D specific B cells before the anti D response develops.

Trinbelimab (Recombinant Anti Rho-D Immunoglobulin) coated red cells are rapidly cleared from the maternal blood.
Trinbelimab is known to mediate Antibody- Dependent Cell Mediated Cytotoxicity (ADCC). Mononuclear phagocytic system is also thought to be responsible for clearance of anti-D-sensitized erythrocytes. There is more evidence building up in recent years that ADCC may not be the primary mode of red cell clearance in vivo. Antibody mediated B-cell inhibition is emerging as the possible mechanism for red cell clearance.
Inhibition of B cells by crosslinking heterologous receptors (co-inhibition):

• FcγRIIb inhibitory activity requires bridging to specific co-targets.
• Inhibition many activate pathways in both healthy and diseased B cells.
• Could result in potent suppression of B-cell responses without destroying B cells.

5.2 Pharmacokinetic properties

The PK parameters of Trinbelimab (Recombinant Anti Rho-D Immunoglobulin) are expected to be like a biologically similar preparation of monoclonal anti-D:
Pharmacokinetic parameters of monoclonal anti-D are as follows: Median T_{max} (h) - 168, Mean C_{max} (ng/mL) 42.83, Mean AUC_{0-t} (ng.h/mL) 30241.71, $AUC_{0-\infty}$ (ng.h/mL)

5.3 Preclinical safety data

A prospective, randomized clinical trial to confirm safety and efficacy of Trinbelimab (Recombinant Anti Rho-D Immunoglobulin) in prevention of isoimmunization in comparison with polyclonal anti-D immunoglobulin r-anti D was conducted in total of 215 subjects; 144 subjects were randomized to receive the recombinant anti-D (Test group) and 71 subjects were randomized to receive polyclonal anti D (Rhogam) (Reference group).
Each eligible subject received a single intramuscular injection either the Test or Reference anti-D IgG within 72 hours of delivery. Insignificant p value for Indirect Coomb's Test (ICT) for Day 90 (p=0.30) and Day 180 (p=0.49) was observed between Test and Reference in prevention of Rh isoimmunization in Rh (D) negative pregnant women delivering Rh (D) positive infant. Four subjects from each group experienced 1 adverse event. All the adverse events were mild in severity. No subject receiving Test developed antibodies to r-anti D post administration of drug. This study observed equal efficacy between Test and Reference as sensitization (as evaluated by positive ICT at Day 90 or 180) was not noted in any subject in both the groups. The safety profile was same in both groups with mild severity.

Animal Toxicology or Pharmacology Preclinical Safety Data:
Toxicity studies were performed on animals – rats, mice, rabbits, and dogs. Single dose toxicity, acute toxicity and repeat dose toxicity studies have been performed. All safety and toxicity studies show no adverse effect in animals.

Toxicity:
Acute toxicity studies of r – anti D were conducted on Swiss Albino mice using single dose of 2400 mcg/kg body weight, administered either intramuscularly or subcutaneously. Similar studies were performed using Wistar rats. These rodents were observed for clinical signs of toxicity, body weight and mortality, for a period of 14 days. Treated rodents did not reveal treatment attributed behaviour alterations, clinical

signs, gross pathological abnormalities, preterminal deaths and adverse effects on body weight gain. In conclusion, r – anti D is safe substance for given dose level of 2400 mcg/kg body weight in treated rodents when administered intramuscularly or subcutaneously.

Repeat dose toxicity study was performed in Wistar rats at selected doses of 15, 50, and 150 mcg/kg administered intramuscularly over a period of 14 days. Repeat dose administration did not show any clinical signs and mortality in any of the treated animals. The body weight gain, hematological parameters and clinical biochemistry parameters in all the treatment groups were comparable with control group animals. Gross pathology and histopathology did not reveal any significant changes related to treatment at 150 mcg/kg body weight/day when compared with control group animals. It was concluded, No Observed Adverse Effect Level (NOAEL) for Recombinant Anti Rho-D Immunoglobulin is 150 mcg/kg body weight in rats.

Similar results were observed in repeat dose toxicity study conducted on New Zealand White Rabbits at a dose of 15, 50, 150 mcg/kg administered intramuscularly over a period of 14 days.
Repeated dose toxicity study on Beagle Dogs at a dose of 1500 and 2000 mcg/dog/day for 14 consecutive days had no effect on general health of the animal. There were no toxicity signs, changes in body weight, feed consumption, haematology and clinical chemistry parameters. It was concluded that No Observed Adverse Effect Level (NOAEL) for Trinbelimab is 2000 mcg/dog/day.

The allergenicity study in Guinea pigs to estimate sensitizing potential of ranti D was conducted.
There was no skin reaction observed at topical challenge exposure site. The reaction score found was 0 - 8 % i.e. grading-1, hence r-anti D Immunoglobulin was classified as a weak sensitizer.

Carcinogenicity and genotoxicity IgG is a normal constituent in human plasma and has not been reported to be associated with any embryo-foetal toxicity or oncogenic/ carcinogenic potential. No study was done for evaluating carcinogenicity or genotoxicity.

6. Pharmaceutical Particulars

6.1 List of Excipients

Glycine
Sodium Chloride
Sodium Hydroxide
Hydrochloric acid
Water for Injection

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

24 months from the date of manufacturing.

6.4 Special Precautions for storage

Store at 2°C to 8°C. Do not freeze.

6.5 Nature and Content of container

• Each Vial Pack contains:

Sterile, ready-to-use, non-pyrogenic 2.0 ml USP Type-I glass vial having clear, colorless, solution of Recombinant Anti Rho-D Immunoglobulin Injection 300 mcg. One blister contains one labeled vial. One Carton contains one unit pack with one insert & sealed with hologram sticker on both sides.

• Each PFS Pack contains:

Sterile, ready-to-use, non-pyrogenic 1.0 ml USP Type-I siliconized glass prefilled syringe with tip cap having clear, colorless, solution of Recombinant Anti Rho-D Immunoglobulin Injection 300 mcg, with a sterile hypodermic single use needle.

6.6 Special precautions for disposal and other handling

7. Marketing Authorization Holder

Bharat Serums and Vaccines Limited,
Plot No: K-27, K-27 Part and K-27/1, Anand Nagar, Jambivili Village, Additional MIDC, Ambernath (E) - 421506, Thane, Maharashtra, India.

8. Marketing Authorization Number

H2025/CTD10930/23547

9. Date of first authorization/renewal of the authorization

27/10/2025

10. Date of revision of the text

27/10/2025