Rhophylac is now provided in a
TWIST OFF syringe closure system
Rhophylac Syringes:
Two Different Closure Systems

Up to September 2013, Rhophylac syringes were supplied with a white closure system known as V-OVS tamper-evident closure. Since September 2013, a different closure system has been implemented for Rhophylac syringes. An element of the BD Hypak™ PRTC system, this closure features a plastic rigid tip cap with a Luer-Lok™ adaptor.

Handling and Opening of The V-OVS (White) Closure System

1. Hold the syringe upright on the ribbed part of the white closure system.
2. With the other hand, take hold of the white cap of the closure system and gently tilt back and forth until the cap disconnects and can be pulled off (seal will be broken).
3. Remove the cap in straight upward direction.

Please see Important Safety Information on the back cover, and enclosed full prescribing information and boxed warning for ITP indication in pocket.
Twist Off PRTC Closure System

Handling and Opening of The PRTC (Transparent/Gray) Closure System

1. Hold the syringe upright on the glass barrel or on the transparent part of the closure system.
2. With the other hand, take hold of the grey cap of the PRTC closure system and unscrew until the cap can be pulled off.

Improper handling of the PRTC closure system can damage the syringe irreversibly (typically the luer conus will break).

IMPORTANT SAFETY INFORMATION

Rhophylac®, Rh(D), Immune Globulin Intravenous (Human), is indicated for suppression of rhesus (Rh) isoimmunization in:

- Pregnancy and obstetric conditions in non-sensitized, Rh(D)-negative women with an Rh-incompatible pregnancy, including routine antepartum and postpartum Rh prophylaxis and Rh prophylaxis in cases of obstetric complications, invasive procedures during pregnancy, or obstetric manipulative procedures.
- Incompatible transfusions in Rh(D)-negative individuals transfused with blood components containing Rh(D)-positive red blood cells.

For suppression of Rh isoimmunization, Rhophylac can be administered IM or IV. Consider IV administration if reaching the muscle is of concern.

Rhophylac is indicated to raise platelet counts in Rh(D)-positive, non-splenectomized adult patients with chronic immune thrombocytopenic purpura (ITP). For the treatment of ITP, Rhophylac must be administered IV.

Please see Important Safety Information on the back cover, and enclosed full prescribing information and boxed warning for ITP indication in pocket.

To order Rhophylac, call 1-800-683-1288.
For more information, visit Rhophylac.com

If you have any questions regarding this information, please call 1-855-877-0020.
Important Safety Information

Rhophylac®, Rh(D), Immune Globulin Intravenous (Human), is indicated for suppression of rhesus (Rh) isoimmunization in:

- Pregnancy and obstetric conditions in non-sensitized, Rh (D)-negative women with an Rh-incompatible pregnancy, including routine antepartum and postpartum Rh prophylaxis and Rh prophylaxis in cases of obstetric complications, invasive procedures during pregnancy, or obstetric manipulative procedures.

- Incompatible transfusions in Rh (D)-negative individuals transfused with blood components containing Rh(D)-positive red blood cells.

For suppression of Rh isoimmunization, Rhophylac can be administered IM or IV. Consider IV administration if reaching the muscle is of concern.

Rhophylac is indicated to raise platelet counts in Rh(D)-positive, non-splenectomized adult patients with chronic immune thrombocytopenic purpura (ITP). For the treatment of ITP, Rhophylac must be administered IV.

WARNING: INTRAVASCULAR HEMOLYSIS IN ITP
This warning does not apply to Rh(D)-negative patients treated for the suppression of Rh isoimmunization.

Intravascular hemolysis leading to death has been reported in Rh(D)-positive patients treated for immune thrombocytopenic purpura (ITP) with Rh(D) Immune Globulin Intravenous (Human) products. Intravascular hemolysis can lead to clinically compromising anemia and multi-system organ failure, including acute respiratory distress syndrome (ARDS); acute renal insufficiency, renal failure, and disseminated intravascular coagulation (DIC) have also been reported. Monitor patients for signs and symptoms of intravascular hemolysis in a healthcare setting for at least 8 hours after administration. See full prescribing information for complete boxed warning.

Rhophylac is contraindicated in individuals with known anaphylactic or severe systemic reaction to human immune globulin products. Rhophylac is contraindicated in IgA-deficient patients with antibodies to IgA and a history of hypersensitivity to Rhophylac or any of its components.

Do not administer Rhophylac to the newborn infant of a mother who received Rhophylac postpartum.

Allergic or hypersensitivity reactions may occur with Rhophylac; early signs of hypersensitivity include generalized urticaria, chest tightness, wheezing, hypotension, and anaphylaxis.

Rhophylac is derived from human plasma. The risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

Suppression of Rh Isoimmunization: The most common adverse reactions in the suppression of Rh isoimmunization with Rhophylac (≥0.5% of patients) are nausea, dizziness, headache, injection-site pain, and malaise.

Immune Thrombocytopenic Purpura: The most serious adverse reactions in patients receiving Rh(D) immune globulin have been observed in the treatment of ITP. ITP patients being treated with Rhophylac should be alerted to and monitored for signs and symptoms of intravascular hemolysis, including back pain, shaking chills, fever, and hematuria. Potentially serious complications of intravascular hemolysis include clinically compromising anemia, acute renal insufficiency, and, very rarely, disseminated intravascular coagulation, and death.

The most common adverse reactions observed in the treatment of ITP (>14% of patients) are chills, pyrexia/ increased body temperature, headache, and hemolysis. In patients with preexisting anemia, Rhophylac may increase the severity of anemia.

Immunoglobulin administration may transiently interfere with the immune response to live virus vaccines, such as measles, mumps and rubella.

Please see enclosed full prescribing information for Rhophylac.
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use RHOPHYLAC safely and effectively. See full prescribing information for RHOPHYLAC.

RHOPHYLAC
Rh(D) Immune Globulin Intravenous (Human) 1500 IU (300 mcg) Solution for Intravenous (IV) or Intramuscular (IM) Injection
Initial US Approval: 2004

WARNING: INTRAVASCULAR HEMOLYSIS IN ITP
See full prescribing information for complete boxed warning. This warning does not apply to Rh(D)-negative patients treated for the suppression of Rh isoimmunization.

• Intravascular hemolysis leading to death has been reported in Rh(D)-positive patients treated for immune thrombocytopenic purpura (ITP) with Rh(D) Immune Globulin Intravenous (Human) products.
• Intravascular hemolysis can lead to clinically compromising anemia and multi-system organ failure including acute respiratory distress syndrome (ARDS); acute renal insufficiency, renal failure, and disseminated intravascular coagulation (DIC) have been reported.
• Monitor patients for signs and symptoms of intravascular hemolysis in a healthcare setting for at least 8 hours after administration.

RECENT MAJOR CHANGES

INDICATIONS AND USAGE
Rhophylac is an Rh(D) Immune Globulin Intravenous (Human) indicated for:

• Suppression of Rh isoimmunization.

Both Indications (5.1)
• IgA deficient patients with known antibodies to IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions (5.1.1).
• Rhophylac is made from human blood; therefore it may contain infectious agents; e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent (5.1.3).

ADVERSE REACTIONS
The most common adverse reactions, reported in ≥0.5% of subjects, are nausea, dizziness, headache, injection-site pain, and malaise (6.1).

ITP
The most common adverse reactions, reported in >14% of subjects, are chills, pyrexia, increased body temperature, headache, and hemolysis (increased bilirubin, decreased hemoglobin, or decreased haptoglobin) (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact CSL Behring Pharmacovigilance at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
Immunoglobulin administration may transiently interfere with the immune response to live virus vaccines, such as measles, mumps and rubella (7.1).

USE IN SPECIFIC POPULATIONS

PATIENT COUNSELING INFORMATION

Sections or subsections omitted from the full prescribing information are not listed.
Rhophylac®
Rh0(D) Immune Globulin Intravenous (Human)

**INDICATIONS AND USAGE**

Rhophylac is an Rh0(D) Immune Globulin Intravenous (Human) (anti-D) product that is indicated for the suppression of Rh isoimmunization in non-sensitized Rh0(D)-negative women with an Rh-incompatible pregnancy, including:

- Routine antepartum prophylaxis
- Postpartum prophylaxis (required only if the newborn is Rh0(D)-positive)

Additional doses of Rhophylac must be given if the patient is exposed to >15 mL of Rh0(D)-positive blood or blood components containing Rh0(D)-positive RBCs.

**Incompatible transfusions**

Rhophylac is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of Rhophylac or any of its components.

**Contraindications**

- Rhophylac is contraindicated in IgA-deficient patients with antibodies to IgA and a history of anaphylactic or severe systemic reaction.
- Rhophylac is contraindicated in patients who have had an anaphylactic or severe systemic reaction to Rhophylac or any of its components.

**DOSAGE AND ADMINISTRATION**

**Preparation and Handling**

- Rhophylac is a clear, colorless solution.
- Do not use if the solution is cloudy or contains particulates.
- Prior to intravenous use, ensure that the needle-free intravenous administration system is compatible with the tip of the Rhophylac glass syringe.
- Do not freeze.
- Rhophylac should be administered by intravenous or intramuscular injection.

**Monitoring**

- Monitor patients for signs and symptoms of hemolysis in a healthcare setting for at least 8 hours after administration.
- Perform a dipstick urinalysis at baseline, 2 hours and 4 hours after administration, and prior to the end of the monitoring period.
- Alert patients to monitor their back pain, shaking chills, fever, and discolored urine or hematuria.

**Administration**

- Rhophylac should be administered at a rate of 2 mL per 15 to 60 seconds.

**Injection Sites**

- Do not administer Rhophylac subcutaneously into the fatty tissue.
- It is advisable to administer Rhophylac in divided doses at different sites.

**Dosage**

The dose of Rhophylac must be increased if the patient is exposed to >15 mL of Rh0(D)-positive blood.

**Routine antepartum prophylaxis**

- At Week 28-30 of gestation: 1500 IU (300 mcg)
- Within 72 hours of birth: 1500 IU (300 mcg)

**Obstetric complications**

- Within 72 hours of complication: 1500 IU (300 mcg)

**Invasive procedures during pregnancy**

- Within 72 hours of procedure: 1500 IU (300 mcg)

**Excessive fetomaternal hemorrhage (>15 mL)**

- Within 72 hours of complication: 1500 IU (300 mcg)

**ADVERSE REACTIONS**

- Intravascular hemolysis: leading to death has been reported in Rh0(D)-positive patients.
- Acute renal failure, renal failure, and disseminated intravascular coagulation (DIC) have been reported.
- Absence of these signs and/or symptoms within 8 hours does not indicate IVH cannot occur subsequently.

**Special Populations**

- Rhophylac is not recommended for children weighing less than 5 kg.
- Rhophylac is not recommended for Rh0(D)-positive women with an Rh-incompatible pregnancy.

**Dosage Forms**

- Rhophylac is available in a 2 mL prefilled, ready-to-use, glass syringe for IV or IM use.

**Strengths**

- Dose (IU) x body weight (kg) = Total IU / 1500 IU per syringe = Number of syringes

**REFERENCES**

- A 1500 IU (300 mcg) dose of Rhophylac will suppress the immunizing potential of <15 mL of Rh0(D)-positive RBCs.
- The dose of Rhophylac must be increased if the patient is exposed to >15 mL of Rh0(D)-positive RBCs; in this case, follow the dosing guidelines for excessive fetomaternal hemorrhage.
5 WARNINGS AND PRECAUTIONS

5.1 Both Indications

5.1.1 Hypersensitivity

Severe hypersensitivity reactions may occur even in patients who have tolerated previous administrations. If symptoms of allergic or early signs of hypersensitivity reactions (including generalized urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis) occur, discontinue Rhophylac administration immediately and institute appropriate treatment. Medications such as epinephrine should be available for immediate treatment of acute hypersensitivity reactions to Rhophylac or any of its components.

Rhophylac contains trace amounts of IgA (less than 5 mcg/mL) [see Description (11)]. Patients with known antibodies to IgA have a risk of developing potentially severe hypersensitivity and anaphylactic reactions. Rhophylac is contraindicated in patients with antibodies against IgA and a history of hypersensitivity reactions [see Contraindications (4)].

5.1.2 Interference with Laboratory Tests

The administration of Rh(D) immune globulin may affect the results of blood typing, the antibody screening test, and the direct antiglobulin (Coombs') test. Antepartum administration of Rh(D) immune globulin to the mother can also affect these tests in the newborn infant.

Rhophylac can contain antibodies to other Rh antigens (e.g., anti-C antibodies), which might be detected by sensitive serological tests following administration.

5.1.3 Transmissible Infectious Agents

Because Rhophylac is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. The risk of infectious agent transmission has been reduced by screening plasma donors for prior exposure to certain viruses, testing for the presence of certain current virus infections, and including virus inactivation/removal steps in the manufacturing process for Rhophylac.

Report any infections thought to be possibly transmitted by Rhophylac to CSL Behring Pharmacovigilance at 1-866-915-6958.

5.2 ITP

5.2.1 Intravascular Hemolysis

Serious intravascular hemolysis has occurred in a clinical study with Rhophylac. All cases resolved completely. However, as reported in the literature, some Rh(D)-positive patients treated with Rh(D) Immune Globulin Intravenous (Human) for ITP developed clinically compromising anemia, acute renal insufficiency, and, very rarely, disseminated intravascular coagulation (DIC) and death.\(^{1}\) Note: This warning does not apply to Rh(D)-negative patients treated for the suppression of Rh isoimmunization.

Monitor patients in a healthcare setting for at least 8 hours after administration of Rhophylac. Perform a hemoglobinuria test at baseline, 2 hours and 4 hours after administration, and prior to the end of the monitoring period.

Alert patients to, and monitor them for, the signs and symptoms of intravascular hemolysis, including back pain, shaking chills, fever, and discolored urine or hematuria. Absence of these signs and/or symptoms of intravascular hemolysis within 8 hours do not indicate intravascular hemolysis cannot occur subsequently. If signs and/or symptoms of intravascular hemolysis are present or suspected after Rhophylac administration, perform post-treatment laboratory tests, including plasma hemoglobin, haptoglobin, LDH, and plasma bilirubin (direct and indirect). DIC may be difficult to detect in the ITP population; the diagnosis is dependent mainly on laboratory testing.

If patients who develop hemolysis with clinically compromising anemia after receiving Rhophylac are to be transfused, Rh(D)-negative packed RBCs should be used to avoid exacerbating ongoing hemolysis.

5.2.2 Pre-existing Anemia

The safety of Rhophylac in the treatment of ITP has not been established in patients with pre-existing anemia. Rhophylac may increase the severity of anemia.

6 ADVERSE REACTIONS

The most serious adverse reactions in patients receiving Rh(D) Immune Globulin Intravenous (Human) have been observed in the treatment of ITP and include intravascular hemolysis, clinically compromising anemia, acute renal insufficiency, and, very rarely, DIC and death [see Boxed Warning, and Warnings and Precautions (5.3.1)].\(^{1}\)

The most common adverse reactions observed in the use of Rhophylac for suppression of Rh isoimmunization (≥0.5% of subjects) are nausea, dizziness, headache, injection-site pain, and malaise. The most common adverse reactions observed in the treatment of ITP (>14% of subjects) are chills, pyrexia/increased body temperature, and headache. Hemolysis (manifested by an increase in bilirubin, a decrease in hemoglobin, or a decrease in haptoglobin) was also observed.

6.1 Clinical Studies Experience

Because clinical studies are conducted under different protocols and widely varying conditions, adverse reaction rates observed cannot be directly compared to rates in other clinical trials and may not reflect the rates observed in practice.

6.2 Postmarketing Experience

Serious adverse reactions (SARs) were reported in 4 (4.1%) subjects. SARs were intravascular hemolytic reaction (hypotension, nausea, chills and headache, and a decrease in haptoglobin and hemoglobin) in two subjects; headache, dizziness, nausea, pallor, shivering, and weakness requiring hospitalization in one subject; and an increase in blood pressure and severe headache in one subject. All four subjects recovered completely.

6.3 Suppression of Rh Isoimmunization

Hypersensitivity reactions, including rare cases of anaphylactic shock or anaphylactoid reactions, headache, dizziness, vertigo, hypotension, tachycardia, dyspnea, nausea, vomiting, rash, erythema, pruritus, chills, pyrexia, malaise, diarrhea and back pain have been reported. Transient injection-site irritation and pain have been observed following intramuscular administration.

There have been reports of lack of effect in patients with a body mass index ≥30 when administered via the intramuscular route was attempted [see Dosing and Administration (2.2)].

Suppression of Rh Isoimmunization

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Hypersensitivity reactions, including rare cases of anaphylactic shock or anaphylactoid reactions, headache, dizziness, vertigo, hypotension, tachycardia, dyspnea, nausea, vomiting, rash, erythema, pruritus, chills, pyrexia, malaise, diarrhea and back pain have been reported. Transient injection-site irritation and pain have been observed following intramuscular administration.

7 DRUG INTERACTIONS

7.1 Live Virus Vaccines

Passive transfer of antibodies may transiently impair the immune response to live attenuated virus vaccines such as measles, mumps, rubella, and varicella [see Patient Counseling Information (17.1)]. Do not immunize with live vaccines within 3 months after the final dose of Rhophylac. If Rhophylac is administered within 14 days after administration of a live vaccine, the immune response to the vaccination may be inhibited.\(^{3}\)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with Rhophylac.

8.2 Suppression of Rh Isoimmunization

Rhophylac is used in pregnant women for the suppression of Rh isoimmunization. The available evidence suggests that Rhophylac does not harm the fetus or affect future
Rhophylac contains a maximum of 30 mg/mL of human plasma proteins, 10 mg/mL of which is human albumin added as a stabilizer. Prior to the addition of the stabilizer, Rhophylac has a purity greater than 95% IgG. Rhophylac contains less than 5 mcg/mL of IgA, which is the limit of detection. Additional excipients are approximately 20 mg/mL of glycine and up to 0.25 M of sodium chloride. Rhophylac contains no preservative. Human albumin is manufactured from pooled plasma of US donors by cold ethanol fractionation, followed by pasteurization.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of which Rh(D) immune globulin suppresses immunization to Rh(D)-positive RBCs is not completely known. In a clinical study of Rh(D)-negative healthy male volunteers, both the intravenous and intramuscular administration of a 1500 IU (300 mcg) dose of Rhophylac 24 hours after injection of 15 mL of Rh(D)-positive RBCs resulted in an effective clearance of Rh(D)-positive RBCs. On average, 99% of injected RBCs were cleared within 12 hours following intravenous administration and within 144 hours following intramuscular administration.

ITP

Rhophylac has been shown to increase platelet counts and to reduce bleeding in non-splenectomized Rh(D)-positive subjects with chronic ITP. The mechanism of action is thought to involve the formation of Rh(D) immune globulin RBC complexes, which are preferentially removed by the reticuloendothelial system, particularly the spleen. This results in Fc receptor blockade, thus sparing antibody-coated platelets.

12.2 Pharmacokinetics

Suppression of Rh Isoimmunization

In a clinical study comparing the pharmacokinetics of intravenous versus intramuscular administration, 15 Rh(D)-negative pregnant women received a single 1500 IU (300 mcg) dose of Rhophylac at Week 28 of gestation.

Following intravenous administration, peak serum levels of Rh(D) immune globulin ranged from 62 to 84 ng/mL after 1 day (i.e., the time the first blood sample was taken following the antepartum dose). Mean systemic clearance was 0.20 ± 0.03 mL/min, and half-life was 16 ± 4 days. Following intramuscular administration, peak serum levels ranged from 7 to 46 ng/mL and were achieved between 2 and 7 days. Mean apparent clearance was 0.29 ± 0.12 mL/min, and half-life was 18 ± 5 days. The absolute bioavailability of Rhophylac was 69%.

Regardless of the route of administration, Rh(D) immune globulin titers were detected in all women up to at least 9 weeks following administration of Rhophylac.

ITP

Pharmacokinetic studies with Rhophylac were not performed in Rh(D)-positive subjects with ITP. Rh(D) immune globulin binds rapidly to Rh(D)-positive erythrocytes.

14 CLINICAL STUDIES

14.1 Suppression of Rh Isoimmunization

In two clinical studies, 447 Rh(D)-negative pregnant women received a 1500 IU (300 mcg) dose of Rhophylac during Week 28 of gestation. The women who gave birth to an Rh(D)-positive baby received a second 1500 IU (300 mcg) dose within 72 hours of birth.

- Study 1 (Pharmacokinetic Study) – Eight of the women who participated in the pharmacokinetic study [see Clinical Pharmacology (12.3)] gave birth to an Rh(D)-positive baby and received the postpartum dose of 1500 IU (300 mcg) of Rhophylac. Antibody tests performed 6 to 8 months later were negative for all women. This suggests that no Rh(D) immunization occurred.

- Study 2 (Pivotal Study) – In an open-label, single-arm clinical study at 22 centers in the US and United Kingdom, 432 pregnant women received the antepartum dose of 1500 IU (300 mcg) of Rhophylac either as an intravenous or intramuscular injection (two randomized groups of 216 women each). Subjects received an additional 1500 IU (300 mcg) dose if an obstetric complication occurred between the routine antepartum dose and birth or if extensive fetomaternal hemorrhage was measured after birth. Of the 270 women who gave birth to an Rh(D)-positive baby, 248 women were evaluated for Rh(D) immunization 6 to 11.5 months postpartum. None of these women developed antibodies against the Rh(D) antigen.

14.2 ITP

In an open-label, single-arm, multicenter study, 98 Rh(D)-positive adult subjects with chronic ITP and a platelet count of 30 x 10^9/L or less were treated with Rhophylac. Subjects received a single intravenous dose of 250 IU (50 mcg) per kg body weight. The primary efficacy endpoint was the response rate defined as achieving a platelet count ≥30 x 10^9/L as well as an increase of >20 x 10^9/L within 15 days after treatment with Rhophylac. Secondary efficacy endpoints included the response rate defined as an increase in platelet counts to ≥50 x 10^9/L within 15 days after treatment and, in subjects who had bleeding at baseline, the regression of hemorrhage defined as any decrease from baseline in the severity of overall bleeding status. Table 4 presents the primary response rates for the intent-to-treat (ITT) and per-protocol (PP) populations.
Table 4: Primary Response Rates (ITT and PP Populations)

<table>
<thead>
<tr>
<th>Analysis Population</th>
<th>No. Subjects</th>
<th>No. Responders</th>
<th>Primary Response Rate at Day 15 % Responders</th>
<th>95% Confidence Interval (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT</td>
<td>98</td>
<td>65</td>
<td>66.3%</td>
<td>56.5%, 74.9%</td>
</tr>
<tr>
<td>PP</td>
<td>92</td>
<td>62</td>
<td>67.4%</td>
<td>57.3%, 76.1%</td>
</tr>
</tbody>
</table>

The primary efficacy response rate (ITT population) demonstrated a clinically relevant response to treatment, i.e., the lower bound of the 95% confidence interval (CI) was greater than the predefined response rate of 50%. The median time to platelet response was 3 days, and the median duration of platelet response was 22 days.

Table 5: Response Rates By Baseline Platelet Count (ITT Population)

<table>
<thead>
<tr>
<th>Baseline Platelet count (x 10^9/L)</th>
<th>Total No. Subjects</th>
<th>No. (%) Subjects Achieving a Platelet Count of ≥30 x 10^9/L and an Increase of &gt;20 x 10^9/L</th>
<th>No. (%) Subjects With an Increase in Platelet Counts to ≥50 x 10^9/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤10</td>
<td>38</td>
<td>15 (39.5)</td>
<td>10 (26.3)</td>
</tr>
<tr>
<td>&gt;10 to 20</td>
<td>28</td>
<td>22 (78.6)</td>
<td>17 (60.7)</td>
</tr>
<tr>
<td>&gt;20 to 30</td>
<td>27</td>
<td>24 (88.9)</td>
<td>22 (81.5)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>5</td>
<td>4 (80.0)</td>
<td>5 (100.0)</td>
</tr>
<tr>
<td>Overall (all subjects)</td>
<td>98</td>
<td>65 (66.3)</td>
<td>54 (55.1)</td>
</tr>
</tbody>
</table>

* Reflects subjects with a platelet count of ≥30 x 10^9/L at screening but >30 x 10^9/L immediately before treatment.

During the study, an overall regression of hemorrhage was seen in 44 (88%, 95% CI: 76% to 94%) of the 50 subjects with bleeding at baseline. The percentage of subjects showing a regression of hemorrhage increased from 20% at Day 2 to 64% at Day 15. There was no evidence of an association between the overall hemorrhage regression rate and baseline platelet count.

Approximately half of the 98 subjects in the ITT population had evidence of bleeding at baseline. Post-baseline, the percentage of subjects without bleeding increased to a maximum of 70.4% at Day 8.

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

- Rhophylac 1500 IU (300 mcg) is supplied in packages of one or ten (10) prefilled, ready-to-use, glass syringes, each containing 2 mL liquid for injection. Each syringe is accompanied by a SafetyGlide™ needle for intravenous or intramuscular use.

Each product presentation includes a package insert and the following components:

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Carton NDC Number</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>1500 IU (300 mcg)</td>
<td>44206-300-01</td>
<td>Single-use, prefilled 2 mL syringe (NDC 44206-300-90)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SafetyGlide needle</td>
</tr>
<tr>
<td>1500 IU (300 mcg) Multipack</td>
<td>44206-300-10</td>
<td>Ten single-use, prefilled 2 mL syringes (NDC 44206-300-90)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ten SafetyGlide needles</td>
</tr>
</tbody>
</table>

16.2 Storage and Handling

- DO NOT FREEZE.
- Rhophylac contains no preservatives; do not store at room temperature.
- Store at 2 to 8°C (36 to 46°F) for a shelf life of 36 months from the date of manufacture, as indicated by the expiration date printed on the outer carton and syringe label.
- Keep Rhophylac in its original carton to protect it from light.
- The prefilled Rhophylac syringe is not made with natural rubber latex.

17 PATIENT COUNSELING INFORMATION

Both Indications

- Inform patients to immediately report the following signs and symptoms to their physician: hives, chest tightness, wheezing, hypotension, and anaphylaxis [see Warnings and Precautions (5.1.3)].
- Inform patients that Rhophylac is made from human blood and may contain infectious agents that can cause disease (e.g., viruses and, theoretically, the CJD agent). Explain that the risk Rhophylac may transmit an infectious agent has been reduced by screening all plasma donors, by testing the donated plasma for certain viruses, and by inactivating and/or removing certain viruses during manufacturing. Advise patients to report any symptoms that concern them and that may be related to viral infections [see Warnings and Precautions (5.1.3)].

- Inform patients that Rhophylac may interfere with the response to live virus vaccines (e.g., measles, mumps, rubella, and varicella), and instruct them to notify their healthcare professional of this potential interaction when they are receiving vaccinations.

Suppression of Rh Isoimmunization

- Inform patients receiving the antepartum dose of Rhophylac for suppression of Rh isoimmunization that they will need a second dose within 72 hours of birth if the baby’s blood type is Rh-positive.

ITP

- Instruct patients being treated with Rhophylac for ITP to immediately report symptoms of intravascular hemolysis, including back pain, shaking chills, fever, discolored urine, decreased urine output, sudden weight gain, edema, and/or shortness of breath [see Warnings and Precautions (5.2.1)].