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HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use RIASTAP® safely and effectively. See full prescribing information for RIASTAP.

RIASTAP, Fibrinogen Concentrate (Human)
Lyophilized Powder for Solution for Intravenous Injection
Initial U.S. Approval: 2009

----------RECENT MAJOR CHANGES----------
Dosage and Administration, Preparation and Reconstitution (2.2) xx/xxxx

----------INDICATIONS AND USAGE----------
RIASTAP, Fibrinogen Concentrate (Human) is a human blood coagulation factor indicated for the treatment of acute bleeding episodes in pediatric and adult patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. (1)

RIASTAP is not indicated for dysfibrinogenemia.

----------DOSAGE AND ADMINISTRATION----------
For intravenous use only.

- Dose (mg/kg body weight) =
  [Target level (mg/dL) - measured level (mg/dL)]
  1.7 (mg/dL per mg/kg body weight)
- Dose when fibrinogen level is unknown: 70 mg/kg body weight. (2.1)
- Monitoring of patient's fibrinogen level is recommended during treatment. A target fibrinogen level of 100 mg/dL should be maintained until hemostasis is obtained. (2.1)
- Injection rate should not exceed 5 mL per minute. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
- RIASTAP is available as a single-dose vial containing approximately 1 or 2 g lyophilized fibrinogen concentrate powder for reconstitution. (3)
- The actual fibrinogen potency for each lot is printed on the vial label and carton. (3)

----------CONTRAINDICATIONS ----------
Known anaphylactic or severe systemic reactions to human plasma-derived products (4)

----------WARNINGS AND PRECAUTIONS----------
- Monitor patients for early signs of anaphylaxis or hypersensitivity reactions and if necessary, discontinue administration and institute appropriate treatment. (5.1)
- Thrombotic events have been reported in patients receiving **RIASTAP**. Weigh the benefits of administration versus the risks of thrombosis. (5.2)
- Because **RIASTAP** is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. (5.3)

----------ADVERSE REACTIONS----------
- The most serious adverse reactions observed are thrombotic episodes (pulmonary embolism, myocardial infarction, deep vein thrombosis) and anaphylactic reactions. (6)
- The most common adverse reactions observed in clinical studies (frequency >1%) were fever and headache. (6)

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

----------USE IN SPECIFIC POPULATIONS----------
Pediatric: Shorter half-life and faster clearance than in adults has been observed. (8.4)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: xx/xxxx

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

RIASTAP®, Fibrinogen Concentrate (Human) is a human blood coagulation factor indicated for the treatment of acute bleeding episodes in pediatric and adult patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.

Limitation of Use
RIASTAP is not indicated for dysfibrinogenemia.

2 DOSAGE AND ADMINISTRATION

For intravenous use only.

2.1 Treatment of Congenital Fibrinogen Deficiency

RIASTAP dosing, duration of dosing and frequency of administration should be individualized based on the extent of bleeding, laboratory values, and the clinical condition of the patient.

RIASTAP dose when baseline fibrinogen level is known.
Dose should be individually calculated for each patient based on the target plasma fibrinogen level based on the type of bleeding, actual measured plasma fibrinogen level and body weight, using the following formula *[see Clinical Pharmacology (12.3)]*:

$$\frac{\text{[Target level (mg/dL) - measured level (mg/dL)]}}{\text{1.7 (mg/dL per mg/kg body weight)}}$$

RIASTAP dose when baseline fibrinogen level is not known.
If the patient's fibrinogen level is not known, the recommended dose is 70 mg per kg of body weight administered intravenously.

Monitor patient's fibrinogen level during treatment with RIASTAP. Maintain a target fibrinogen level of 100 mg/dL until hemostasis is obtained.

2.2 Preparation and Reconstitution

The procedures below are provided as general guidelines for preparation and reconstitution of RIASTAP.

Use aseptic technique when preparing and reconstituting RIASTAP.

Reconstitute RIASTAP at room temperature as follows:

1. Remove the cap from the product vial to expose the central portion of the rubber stopper.

2. Clean the surface of the rubber stopper with an antiseptic solution and allow it to dry.

3. Using an appropriate transfer device or syringe, transfer 50 mL (for 1 g dose vial) or 100 mL (for 2 g dose vial) of Sterile Water for Injection into the product vial.

4. Gently swirl the product vial to ensure the product is fully dissolved. **Do not shake the vial.**

After reconstitution, the RIASTAP solution should be colorless and clear to slightly opalescent. Inspect visually for particulate matter and discoloration prior to administration. Do not use if the solution is cloudy or contains particulates. Discard partially used vials.

RIASTAP is stable for 8 hours after reconstitution when stored at 20-25ºC; administer within this time period.

Before administration, filter reconstituted RIASTAP solution with a 17-micron filter (not supplied) into an appropriate syringe.

2.3 Administration

Do not mix RIASTAP with other medicinal products or intravenous solutions. Administer through a separate injection site.

Use aseptic technique when administering RIASTAP.

Administer RIASTAP at room temperature by slow intravenous injection at a rate not exceeding 5 mL per minute.

3 DOSAGE FORMS AND STRENGTHS

RIASTAP 1 g dose vial
RIASTAP is available as a single-dose vial containing approximately 1 g lyophilized fibrinogen concentrate powder for reconstitution with 50 mL of Sterile Water for Injection.

RIASTAP 2 g dose vial
RIASTAP is available as a single-dose vial containing approximately 2 g lyophilized fibrinogen concentrate powder for reconstitution with 100 mL of Sterile Water for Injection.

The actual fibrinogen potency for each lot is printed on the vial label and carton.

4 CONTRAINDICATIONS

RIASTAP is contraindicated in patients with known anaphylactic or severe systemic reactions to human plasma-derived products.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Allergic reactions may occur. If signs or symptoms of anaphylaxis or hypersensitivity reactions (including hives, generalized urticaria, tightness of the chest, wheezing, hypotension) occur, immediately discontinue administration *[see Patient Counseling Information (17)]*. The treatment required depends on the nature and severity of the reaction.

5.2 Thrombosis

Thrombosis may occur spontaneously in patients with congenital fibrinogen deficiency with or without the use of fibrinogen replacement therapy.[1] Thromboembolic events have been reported in patients treated with RIASTAP. Weigh the benefits of RIASTAP administration versus the risk of thrombosis. Monitor patients receiving RIASTAP for signs and symptoms of thrombosis *[see Patient Counseling Information (17)]*.

5.3 Transmissible Infectious Agents

Because RIASTAP is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by a process demonstrated to inactivate and/or remove certain viruses during manufacturing *[see Description (11)]*. Despite these measures, such products may still potentially transmit disease. There is also the possibility that unknown infectious agents may be present in such products *[see Patient Counseling Information (17)]*. All infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to CSL Behring Pharmacovigilance at 1-866-915-6958.

6 ADVERSE REACTIONS

The most serious adverse reactions reported in clinical studies or through postmarketing surveillance following RIASTAP treatment are thromboembolic episodes, including myocardial infarction, pulmonary embolism, deep vein thrombosis, arterial thrombosis, and allergic-anaphylactic reactions.

The most common adverse reactions observed in more than one subject in clinical trials (frequency >1%) were fever and headache.

6.1 Clinical Trials Experience

Because clinical trials are conducted under 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.

The safety and efficacy of fibrinogen concentrate (human) for routine prophylaxis, treatment of bleeding or surgery in subjects with congenital fibrinogen deficiency was evaluated in a retrospective, multicenter trial with a prospective one-year follow-up period. Twenty-two subjects between 2 to 78 years with a mean age of 34 years were enrolled, with treatment recorded during the retrospective period from an age of less than 1 year. Thirteen of the 22 (59.1%) subjects were female, 21 (95.5%) subjects were white, and 1 (4.5%) subject Asian *[see Clinical Studies (14)]*.

The adverse reactions reported in the retrospective period were visual impairment, chest discomfort, chest pain, cough, wheezing, flushing, and venous thrombosis of the limb [1 event each] and dyspnea [2 events]. No adverse reactions were found in the prospective period.

6.2 Postmarketing Experience

Because postmarketing reporting of adverse reactions is voluntary and from a population of uncertain size, it is not always possible to reliably estimate the frequency of these reactions or establish a causal relationship to product exposure.

The following adverse reactions, identified by system organ class, have shown a possible causal relationship with RIASTAP.

- *Allergic-anaphylactic reactions:* anaphylaxis, dyspnea, rash
- *Cardiovascular:* thromboembolic complications such as myocardial infarction, pulmonary embolism, and deep vein thrombosis *[see Warnings and Precautions (5.2)]*
- *General/Body as a Whole:* chills, nausea, vomiting

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no studies of RIASTAP use in pregnant women. Animal reproduction studies have not been conducted with RIASTAP. It is not known whether RIASTAP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of RIASTAP in human milk, its effects on the breastfed infant, or its effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for RIASTAP and any potential adverse effects on the breastfed infant from RIASTAP or from the underlying maternal condition.

8.4 Pediatric Use

RIASTAP studies have included subjects below the age of 16 years. In the pharmacokinetic study *[see Clinical Pharmacology (12.3)]*, 2 children aged 8 and 11 years and 3 adolescents aged 12, 14 and 16 years were studied. Subjects <16 years of age (n = 4) had shorter half-life (69.9 ± 8.5 h) and faster clearance (0.7 ± 0.1 mL/h/kg) compared with adults (half-life: 82.3 ± 20.0 h, clearance: 0.53 ± 0.1 mL/h/kg. The number of subjects <16 years of age in this study limits statistical interpretation.

A multicenter, non-interventional, retrospective cohort study with a prospective observational 12-month follow-up period was conducted to investigate the safety and efficacy of RIASTAP *[see Clinical Studies (14)]*. In this study, 11 of 22 subjects below 16 years were enrolled. Seven patients were 6 years or younger at first recorded treatment with fibrinogen concentrate (human), starting from an age of <1 year. Fibrinogen concentrate (human) was administered for prophylaxis as well as for treatment of bleeding events and for perioperative use. Ten patients younger than 18 years of age experienced bleeding events; hemostatic efficacy of fibrinogen concentrate (human) was rated as "effective" in all cases. Six patients underwent 7 surgeries and hemostatic efficacy was rated as "effective" in all cases.

8.5 Geriatric Use

The safety and efficacy of RIASTAP in the geriatric population has not been studied. There were an insufficient number of subjects in this age group to determine whether they respond differently from younger subjects.

11 DESCRIPTION

RIASTAP is a sterile, heat-treated, lyophilized fibrinogen (coagulation factor I) concentrate powder manufactured from pooled human plasma.

Fibrinogen (factor I) is a soluble plasma glycoprotein with a molecular weight of about 340 kDa. The native molecule is a dimer and consists of three pairs of polypeptide chains (Aα, Bβ and γ). Fibrinogen is a physiological substrate of three enzymes: thrombin, factor XIIIa, and plasmin.

Each RIASTAP 1 g dose vial contains 900 to 1300 mg fibrinogen, 400 to 700 mg human albumin, 375 to 660 mg L-arginine hydrochloride, 200 to 350 mg sodium chloride and 50 to 100 mg sodium citrate.

Each RIASTAP 2 g dose vial contains 1800 to 2600 mg fibrinogen, 800 to 1400 mg human albumin, 750 to 1320 mg L-arginine hydrochloride, 400 to 700 mg sodium chloride and 100 to 200 mg sodium citrate.

Sodium hydroxide and hydrochloric acid may have been used to adjust the pH. The pH of the reconstituted RIASTAP is in a range of 6.5 to 7.5.

Viral Clearance

All plasma used in the manufacture of RIASTAP is tested using serological assays for hepatitis B surface antigen and for antibodies to Human Immunodeficiency Virus (HIV)-1/2 and Hepatitis C Virus (HCV). As an additional safety measure, the plasma is tested with Nucleic Acid Testing (NAT) for Hepatitis B Virus (HBV), HCV and HIV-1 and found to be non-reactive (negative). The plasma is also screened for Hepatitis A Virus (HAV) and Human Parvovirus B19 (B19V) by NAT. Only plasma that passed virus screening is used for production, and the limit for B19V in the fractionation pool is set not to exceed 10^4 IU of B19V DNA per mL.

RIASTAP is manufactured from cryoprecipitate into a glycine precipitate, which is then further purified by multiple precipitation/adsorption steps. The manufacturing process has been demonstrated to reduce the risk of virus transmission in an additive manner: cryoprecipitation, heat treatment (+60ºC for 20 hours in an aqueous solution), two subsequent glycine precipitation steps (initial and main glycine precipitation steps), and lyophilization. These steps have been validated independently in a series of in vitro experiments for their capacity to inactivate and/or remove both enveloped and non-enveloped viruses. The results of virus clearance validation studies for RIASTAP manufacturing process are summarized in Table 1.

Table 1. Cumulative (Log_{10}) Virus Reduction Factors for RIASTAP

Manufacturing Step	Virus Reduction Factor (log_{10})					
	Enveloped viruses				Non-enveloped viruses	
	HIV*	BVDV†	WNV‡	PRV§	HAV‖	CPV¶
Cryoprecipitation	n.d.	n.d.	n.d.	1.6	n.d.	1.9
Heat Treatment	≥5.7	≥9.1	≥8.3	5.4	5.9	1.4
Glycine precipitations (two subsequent steps)	3.9	2.1	n.d.	1.8	1.0	1.6
Lyophilization	n.d.	n.d.	n.d.	n.d.	1.7	n.d.
Cumulative virus reduction (log10)	**≥9.6**	**≥11.2**	**≥8.3**	**8.8**	**8.6**	**4.9**

Studies using human parvovirus B19, which are considered experimental in nature, have demonstrated a virus reduction factor of ≥4.5 log10 by heat treatment

* HIV, human immunodeficiency virus, a model for HIV-1 and HIV-2

† BVDV, bovine viral diarrhea virus, a model for Hepatitis C virus (HCV) and West Nile Virus (WNV)

‡ WNV, West Nile virus

§ PRV, Pseudorabies virus, a model for large enveloped DNA viruses

‖ HAV, Hepatitis A virus

¶ CPV, canine parvovirus, a model for B19V

n.d. not determined

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

During the coagulation process, thrombin cleaves the Aα and Bβ chains releasing fibrinopeptides A and B (FPA and FPB, respectively).[2] FPA is separated rapidly and the remaining molecule is a soluble fibrin monomer (fibrin I). The slower removal of FPB results in formation of fibrin II that is capable of polymerization that occurs by aggregation of fibrin monomers.[2] The resulting fibrin is stabilized in the presence of calcium ions and by activated factor XIII, which acts as a transglutaminase. Factor XIIIa-induced cross-linking of fibrin polymers renders the fibrin clot more elastic and more resistant to fibrinolysis.[3] Cross-linked fibrin is the end result of the coagulation cascade, and provides tensile strength to a primary hemostatic platelet plug and structure to the vessel wall.

12.2 Pharmacodynamic Action

Administration of RIASTAP to patients with congenital fibrinogen deficiency replaces missing or low levels of coagulation factor. Normal levels are in the range of 200 to 450 mg/dL.[4]

12.3 Pharmacokinetics

A prospective, open label, uncontrolled, multicenter pharmacokinetic study was conducted in 5 females and 9 males with congenital fibrinogen deficiency (afibrinogenemia), ranging in age from 8 to 61 years (2 children, 3 adolescents, 9 adults). Each subject received a single intravenous dose of 70 mg/kg RIASTAP. Blood samples were collected to determine fibrinogen activity at

baseline and up to 14 days after infusion. The pharmacokinetic parameters of RIASTAP are summarized in Table 2.

No statistically relevant difference in fibrinogen activity was observed between males and females. Subjects <16 years of age (n=4) had shorter half-life (69.9 ± 8.54 h) and faster clearance (0.73 ± 0.14 mL/h/kg) compared with subjects ≥16 years of age (half-life of 82.3 ± 20.04 h and clearance of 0.53 ± 0.07 mL/h/kg). The number of subjects <16 years of age in this study limits statistical interpretation.

The incremental in vivo recovery (IVR) was determined from levels obtained up to 4 hours post-infusion. The median incremental IVR was 1.7 mg/dL (range 1.30 – 2.73 mg/dL) increase per mg/kg. The median in vivo recovery indicates that a dose of 70 mg/kg will increase fibrinogen plasma concentration in patients by approximately 120 mg/dL.

The pharmacokinetic analysis using fibrinogen antigen data (ELISA) was concordant with the fibrinogen activity (Clauss assay).

Table 2. Pharmacokinetic Parameters (n=14) for Fibrinogen Activity

Parameters	**Mean ± SD (range)**
Half-life [h]	78.7 ± 18.13 (55.73-117.26)
C_{max} [mg/dL]	140 ± 27 (100-210)
AUC for dose of 70 mg/kg [mg*h/mL]	124.3 ± 24.16 (81.73-156.40)
Clearance [mL/h/kg]	0.59 ± 0.13 (0.45-0.86)
Mean residence time [h]	92.8 ± 20.11 (66.14-126.44)
Volume of distribution at steady state [mL/kg]	52.7 ± 7.48 (36.22-67.67)

h: hours

14 CLINICAL STUDIES

The efficacy of RIASTAP is based on maximum clot firmness, a measure of clot structural integrity that reflects the underlying effectiveness of the fibrinogen present to form a fibrin clot. A pharmacokinetic study evaluated single-dose PK *[see Clinical Pharmacology (12.3)]* and maximum clot firmness (MCF) in subjects with afibrinogenemia. MCF was determined by thromboelastometry (ROTEM) testing and was used to demonstrate functional activity of replacement fibrinogen when a fixed dose of RIASTAP was administered. Clot firmness is a functional parameter that depends on activation of coagulation, fibrinogen content of the sample and polymerization/crosslinking of the fibrin network. Thromboelastometry has been shown to be a functional marker for assessment of fibrinogen content and for effects of fibrinogen supplementation on clinical efficacy.[5]

For each subject, MCF was determined before (baseline) and one hour after single dose administration of RIASTAP. RIASTAP was found to be effective in increasing clot firmness in subjects with congenital fibrinogen deficiency (afibrinogenemia) as measured by thromboelastometry. The study results demonstrated that MCF values were significantly higher after administration of RIASTAP than at baseline (see Table 3). Mean change from pre-infusion to 1 hour post-infusion was 8.9 mm in the primary analysis (9.9 mm for subjects <16years old and 8.5 mm for subjects ≥16 to <65 years old). Mean change in MCF values closely approximated levels expected from adding known amounts of fibrinogen to plasma in vitro.[6]

Table 3. MCF [mm] (ITT population)

Time point	n	Mean ± SD	Median (range)
Pre-infusion	13	0 ± 0	0 (0-0)
1 hour post-infusion	13	10.3 ± 2.7	10.0 (6.5-16.5)
Mean change (primary analysis)*	15†	8.9 ± 4.4	9.5 (0-16.5)

MCF = maximum clot firmness; mm = millimeter; ITT = intention-to-treat.
* p-value was <0.0001.
† The mean change was set to 0 for 2 subjects with missing MCF data.

A multicenter, non-interventional, retrospective cohort study with a prospective observational 12-month follow-up period was conducted to investigate the safety and efficacy of RIASTAP for the treatment of acute bleeding events, routine prophylaxis, and perioperative hemostasis in subjects with congenital fibrinogen deficiency.

A total of 22 subjects were enrolled. Eleven of the 22 subjects enrolled were 16 years of age or younger and 11 subjects were 18 years of age or older at the time of first recorded treatment, which was documented in the retrospective period prior to enrollment.

In the retrospective period, the hemostatic efficacy was rated by the investigator as “effective” for 97% of the acute bleeding events and for 97.5% of the bleeding events during surgery, and prophylactic use of RIASTAP was associated to a low median ABR of 1.43 bleeding events per year. The efficacy during the prospective period was consistent with that observed for the retrospective period: hemostatic efficacy was rated by the investigator as “effective” for 100% of bleeding events and during surgery, and the median ABR was also low at 1.26 bleeding events per year during routine prophylaxis with RIASTAP.

15 REFERENCES

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2. Kreuz W, Meili E, Peter-Salonen K, *et al.* Pharmacokinetic properties of a pasteurized fibrinogen concentrate. *Transfusion and Apheresis Science* 2005; 32:239-46.
3. Colman R, Clowes A, George J, *et al.* Overview of Hemostasis. In: *Hemostasis and Thrombosis: Basic Principles and Clinical Practice* (5th ed.). Colman R, Clowes A, George J, Goldhaber S, Marder VJ (eds.). Lippincott Williams & Wilkins, Philadelphia 2006:11-14.
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5. Fries D, Innerhofer P, Reif C, *et al.* The Effect of Fibrinogen Substitution on Reversal of Dilutional Coagulopathy: An In Vitro Model. *Anesth Analg* 2006; 102:347-351.

6. Kalina U, Stöhr HA, Bickhard H, *et. al*. Rotational thromboelastography for monitoring of fibrinogen concentrate therapy in fibrinogen deficiency. *Blood Coagulation and Fibrinolysis*. 2008; 19:777-783.

16 HOW SUPPLIED/STORAGE AND HANDLING

- RIASTAP is supplied in a single-dose vial.
- Each carton contains one vial of RIASTAP.
- Components are not made with natural rubber latex.
- RIASTAP contains no preservative.
- The actual potency of fibrinogen concentrate in milligram (mg) is stated on each RIASTAP vial label and carton.

The product presentation includes a package insert and the following component:

Table 4. How Supplied

Presentation	Carton NDC Number	Component	Color coding
1 g dose vial	63833-891-51	RIASTAP in a single-dose vial (NDC 63833-891-90)	red
2 g dose vial	63833-892-51	RIASTAP in a single-dose vial (NDC 63833-892-90)	green

- When stored at temperatures of 2-8°C (36-46°F), RIASTAP is stable for the period indicated by the expiration date on the carton and vial label (up to 60 months). Do not use RIASTAP beyond the expiration date.
- Keep RIASTAP in its original carton until ready to use.
- Do not freeze. Protect from light.
- Discard partially used vials.

17 PATIENT COUNSELING INFORMATION

- **Allergic Reactions**
  Inform patients of the early signs of allergic or hypersensitivity reactions to RIASTAP, including hives, chest tightness, wheezing, hypotension, and anaphylaxis. Advise them to notify their physician immediately if they experience any of these symptoms *[see Warnings and Precautions (5.1)]*.

- **Thrombosis**
  Inform patients that thrombosis with or without embolization has been reported with the use of RIASTAP. Any symptoms of thrombotic events such as unexplained pleuritic, chest and/or leg pain or edema, hemoptysis, dyspnea, tachypnea or unexplained neurologic symptoms should be reported to their physician immediately *[see Warnings and Precautions (5.2)]*.

- **Transmissible Infectious Agents**
  Inform patients that RIASTAP is made from human plasma (part of the blood) and may carry a risk of transmitting infectious agents e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. Explain that the risk of transmitting an infection agent using RIASTAP has been reduced by screening plasma donors, testing the donated plasma for certain virus infections, and incorporating a process demonstrated to inactivate and/or remove certain viruses during manufacturing. Symptoms of possible virus infection include headache, fever, nausea, vomiting, weakness, malaise, diarrhea, or, in the case of hepatitis, jaundice *[see Warnings and Precautions (5.3)]*.

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