BIOHUI®
博晖生物

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Instructions of Human Prothrombin Complex

Please read the instructions carefully and use the product under the guidance of a physician

Warning: Since the source plasma comes from human blood, although the source plasma has been screened for relevant pathogens and measures to remove and inactivate viruses have been taken in the manufacturing process, theoretically, there is still a potential risk of transmitting certain known and unknown pathogens, and the pros and cons shall be weighed when used clinically.

【Drug Name】
Generic Name: Human Prothrombin Complex
English Name: Human Prothrombin Complex
Chinese Pinyin: Ren Ningxuemeiyuan Fuhewu

【Ingredients】
The active ingredients of the product are human coagulation factors Ⅱ, Ⅶ, Ⅸ and X. The excipients are sodium heparin, glycine and sodium citrate.

【Appearance】
The product shall be white or gray-green loose constitution. After reconstitution, it shall be a colorless, light yellow, light blue or yellow-green clear liquid, with slight opalescence.

【Indications】
The product is mainly used for the treatment of congenital and acquired coagulation factor Ⅱ, Ⅶ, Ⅸ and X deficiencies (single or combined deficiencies), including:
1.Coagulation factor Ⅸ deficiency (hemophilia B), and coagulation factor Ⅱ, Ⅶ, and X deficiencies;
2.Anticoagulant overdose and vitamin K deficiency;
3.Correction of the coagulation dysfunction in patients with blood coagulation system disturbance caused by liver diseases, or with hemorrhage caused by liver diseases;
4.Patients scheduled for surgery with prolonged prothrombin time due to various reasons, but it may be ineffective in patients with blood coagulation factor V deficiency.
5.Treatment of haemorrhage symptoms in patients with hemophilia A who have developed factor Ⅶ inhibitors;
6.Reversal of coumarin anticoagulant-induced hemorrhage.

【Strength】
300IU/vial, 20ml volume after reconstitution. Each vial contains Human Coagulation Factors Ⅸ 300IU, Ⅱ 300IU, Ⅷ 300IU, and X 300IU.

【Usage and Dosage】
1.The product is intended for intravenous infusion and shall be administered under the strict supervision of a clinician.
2.Pre-warm the product and sterile water for injection or 5% glucose injection to 20 to 25℃ before use, inject the pre-warmed sterile water for injection or 5% glucose injection as per the labeled volume on the bottle, and rotate it gently until the product is completely dissolved (be careful not to create too much foam). It can also be diluted to 50 to 100ml with sodium chloride injection or 5% glucose injection.
3.Intravenous drip with a blood transfusion apparatus with a strainer device. The infusion rate shall be slow at first, about 15 drops/min. After 15 minutes, the infusion rate shall be increased slightly (40-60 drops/min), and the infusion shall be finished within 30-60 minutes.
4.The physician shall always pay attention to the use of the product during the infusion. If clinical symptoms and physical signs of disseminated intravascular coagulation or thrombosis are found, the physician must stop using the product immediately. Besides, heparin antagonists shall be used.
Dosage:
1.The dosage varies with the degree of factor deficiency. Generally, 10-20 IU per kg of body weight shall be infused, then the dosage can be reduced as appropriate at 24-hour intervals for patients with coagulation factor Ⅸ deficiency, at 24-48 hour intervals for patients with coagulation factor Ⅱ and coagulation factor X deficiency, and at 6-8 hour intervals for patients with coagulation factor Ⅶ deficiency. This will generally last for 2-3 days.
2.In the case of large blood loss or major surgery, the dose can be appropriately increased according to the conditions.
3.If a patient with prolonged prothrombin time is scheduled to receive splenectomy, the product shall be used before the operation. Whether to use the product during and after the operation shall be based on the patient's condition.

【Adverse Reactions】
The monitoring data of adverse reactions have yet to be collected.
1.Rapid infusion can cause fever, flushing, headache, and other side effects. The above symptoms will disappear by slowing down or stopping the infusion.
2.A few patients will have allergic reactions such as facial flushing, eyelid edema, rash and tachypnea, and even a drop of blood pressure or anaphylactic shock in severe cases.
3.This product contains erythrocyte lectin (anti-A, anti-B). Sometimes hemolysis can occur when patients with A, B,

or AB blood type are infused with high doses.
4.Disseminated intravascular coagulation (DIC), deep vein thrombosis (DVT), and pulmonary embolism (PE) have occasionally been reported due to massive infusion. Patients with a history of thrombosis shall weigh the advantages and disadvantages and use this product with caution when undergoing surgery.

[Contraindications]

1.The indications must be strictly controlled, and the product shall be prohibited for those allergic to it.
2.The product shall be contraindicated in patients with a history of heparin allergy or with heparin-induced thrombocytopenia.

[Precautions]

1.Before using the product, it shall be confirmed whether the patients have coagulation factor II, VII, IX, and/or X deficiencies except for patients with liver hemorrhage. The product shall be used with caution in patients with coronary heart disease, myocardial infarction, severe liver disease and surgical operations who have a tendency to thrombosis or disseminated intravascular coagulation (DIC).
2.This product shall only be used for i.v. injection.
3.The product shall not be used in case of vial cracks, expiration, or the presence of precipitate that cannot be shaken apart after the dissolution of the product. Do not use the product if the vacuum level in the vial has been compromised.
4.During the i.v. drop, the physician shall always pay attention to the useof the product. If clinical symptoms and physical signs of disseminated intravascular coagulation or thrombosis are found, the physician must stop using the product immediately. Besides, heparin antagonists shall be used. The product contains heparin with half the potency of coagulation factor IX, which can reduce the risk of thrombosis. However, once any suspicious situation is found, the dosage shall be greatly reduced, even if the patient's condition does not allow complete discontinuation.
5.The activated partial thromboplastin time, fibrinogen, platelet and prothrombin time shall be monitored regularly during medication to detect complications early, such as intravascular coagulation.
6.Once the vial is opened, the product shall be used immediately (generally within 3 hours), and the remainder cannot be kept for reuse.
7.Since virus inactivation through dry heat method is used to the lyopbilized product, it may cause decreased biological activity and immunogenicity changes in human prothrombin complex. It is suggested that the product shall be used only when there are no other effective treatment methods and it is really necessary to supplement prothrombin complex after weighing the advantages and disadvantages.
[Use in Pregnant and Lactating Women]
The product shall be used with caution. If necessary, the product shall be used under doctors' guidance and close observation.

[Pediatric Use]

No specific experimental study has been conducted, and there are no systematic and reliable literature references. Infants and children are more sensitive to this product than adults and are susceptible to thrombotic comorbidities. It is advisable to use the product with caution.

[Geriatric Use]

The physiological function of the elderly is generally reduced, so the drug shall be used carefully according to the state of the patient.

[Drug Interactions]

It shall not be used in combination with other drugs.

[Overdose]

There is a risk of thrombosis.

[Toxicology]

The product contains vitamin K-dependent coagulation factors II, VII, IX, X synthesized in the liver. Deficiency of vitamin K and severe liver disease can cause deficiency of the four factors. The deficiency of any of these factors can lead to coagulation disorder. Infusion of this product can increase the concentration of coagulation factors II, VII, IX and X in the blood.

[Pharmacokinetics]

Pharmacokinetic studies have not been conducted on this product. The biological half-life of human coagulation factor IX is 18-24 hours according to domestic and international data.

[Storage]

Store and transport away from light at 2-8 °C.

[Packaging]

Medium borosilicate glass molded injection vial 50ml (lyophilized) and chlorinated rubber stopper for freeze-dried sterile powder for injection. 1 set/box. 1 set contains 1 vial of Human Prothrombin Complex and 1 vial of sterile water for injection.

[Shelf Life]

36 months.

[Executive Standards]

YBS00162020

[Approval No.]

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[Marketing Authorization Holder]

Bohui Biopharmaceutical (Hebei) Co., Ltd.

[Manufacturer]

Name: Bohui Biopharmaceutical (Hebei) Co., Ltd.
Address: No. 6 Qingshan Road, Luquan Lvdao Torch Development Zone, Shijiazhuang City
Post code: 050200
Tel: 0311-83935518