FACTOR 9 - COMPLEX HEAT - TREATED INJECTION 500 IU VIAL

Class: Antihemophilic Agent

Indications: Prevention and control of bleeding in patients with factor IX deficiency (hemophilia B or Christmas disease).

Unlabeled

Emergent correction of warfarin-induced coagulopathy (with clinically significant bleeding); **Note:** Products contain low or nontherapeutic levels of factor VII component; use of fresh frozen plasma (FFP) should be considered

Available dosage form in the hospital:

-FACTOR 9 - COMPLEX HEAT - TREATED INJECTION 500 IU VIAL

Dosage:

Note: Factor IX complex (Human) [Factors II, IX, X] (Bebulin, Profilnine) contains low or nontherapeutic levels of factor VII component and should not be confused with Prothrombin Complex Concentrate (Human) [(Factors II, VII, IX, X), Protein C, Protein S] (Kcentra, Octaplex)) which contains therapeutic levels of factor VII.

Dosage is expressed in units of factor IX activity and must be individualized based on severity of factor IX deficiency, extent and location of bleeding, and clinical status of patient. When multiple doses are required, administer at 24-hour intervals unless otherwise specified. Administer I.V. only:

-Formula for units required to raise blood level %:

-Bebulin® VH: In general, factor IX 1 unit/kg will increase the plasma factor IX level by 0.8%

**Number of Factor IX units required = body weight (kg) x desired factor IX increase (as %) x 1.2 units/kg

-Profilnine® SD: In general, factor IX 1 unit/kg will increase the plasma factor IX level by 1%:

**Number of factor IX units required = bodyweight (kg) x desired factor IX increase (as %) x 1 unit/kg

- For example, to increase factor IX level to 25% of normal in a 70 kg patient: Number of factor IX units needed = 70 kg x 25 x 1 unit/kg = 1750 units

-As a general rule, the level of factor IX required for treatment of different conditions is listed below:

-Hemorrhage: I.V.:

-Minor bleeding (early hemarthrosis, minor epistaxis, gingival bleeding, mild hematuria):

-Bebulin® VH: Raise factor IX level to 20% of normal [typical initial dose: 25-35 units/kg]; generally a single dose is sufficient.

-Profilnine® SD: Mild-to-moderate bleeding: Raise factor IX level to 20% to 30% of normal.

-Moderate bleeding (severe joint bleeding, early hematoma, major open bleeding, minor trauma, minor hemoptysis, hematemesis, melena, major hematuria):

-Bebulin® VH: Raise factor IX level to 40% of normal [typical initial dose: 40-55 units/kg]; average duration of treatment is 2 days or until adequate wound healing.

-Profilnine® SD: Mild-to-moderate bleeding: raise factor IX level to 20% to 30% of normal.

-Major bleeding (severe hematoma, major trauma, severe hemoptysis, hematemesis, melena):

-Bebulin® VH: Raise factor IX level to ≥60% of normal [typical initial dose: 60-70 units/kg]; average duration of treatment is 2-3 days or until adequate wound healing. Do not raise >60% in patients who may be predisposed to thrombosis.

-Profilnine® SD: Raise factor IX level to 30% to 50% of normal.

-Surgical procedures: I.V.:

1.Dental surgery:

-Bebulin® VH: Raise factor IX level to 40% to 60% of normal on day of surgery [typical dose: 50-60 units/kg]. One infusion, administered 1 hour prior to surgery, is generally sufficient for the extraction of one tooth; for the extraction of multiple teeth, replacement therapy may be required for up to 1 week (See dosing guidelines for *Minor Surgery*).

-Profilnine® SD: Raise factor IX level to 50% of normal immediately prior to procedure.

2.Minor surgery:

-Bebulin® VH: Raise factor IX level to 40% to 60% of normal on day of surgery [typical initial dose: 50-60 units/kg]. Decrease factor IX level from 40% of normal to 20% of normal during initial postoperative period (1-2 weeks or until adequate wound healing) [typical dose: 55 units/kg decreasing to 25 units/kg]. The preoperative dose should be given 1 hour prior to surgery. The average dosing interval may be every 12 hours initially, then every 24 hours later in the postoperative period.

-Profilnine® SD: Raise factor IX level to 30% to 50% of normal for at least 1 week following surgery.

3.Major surgery:

-Bebulin® VH: Raise factor IX level to ≥60% of normal on day of surgery [typical initial dose: 70-95 units/kg]; do not raise >60% in patients who may be predisposed to thrombosis. Decrease factor IX level from 60% of normal to 20% of normal during initial postoperative period (1-2 weeks) [typical dose: 70 units/kg decreasing to 35 units/kg]; further decrease to maintain a factor IX level of 20% of normal during late postoperative period (≥3 weeks) and continuing until adequate wound healing is achieved [typical dose: 35 units/kg decreasing to 25 units/kg]. The preoperative dose should be given 1 hour prior to surgery. The average dosing interval may be every 12 hours initially, then every 24 hours later in the postoperative period.

-Profilnine® SD: Raise Factor IX level to 30% to 50% of normal for at least 1 week following surgery.

-Hemorrhage: I.V.:

Long-term prophylactic treatment: Bebulin® VH: 20-30 units/kg once or twice a week may reduce frequency of spontaneous hemorrhage; dosing regimen should be individualized.

-Warfarin associated hemorrhage (unlabeled use): I.V.: **Note:** Products contain low or nontherapeutic levels of factor VII component; therefore, additional fresh frozen plasma (FFP) or factor VIIa may be considered (Masotti, 2011). When immediate INR reversal is required, concomitant use of 1-2 units of FFP should be considered to ensure acute INR reversal (Baker, 2004; Chong, 2010; Holland, 2009). Administer vitamin K (phytonadione) 5-10 mg by slow I.V. infusion (Guyatt, 2012); vitamin K may be repeated every 12 hours if INR is persistently elevated.

Adjusted-dose regimen, weight based (Chong, 2010): Profilnine® SD:

- INR <5: 30 units/kg
- INR >5 (emergent): 50 units/kg

Note: If after administration, INR remains >1.2 consider repeating dose and administering more FFP until INR <1.2

**The following 2 methods have also been suggested, but are not product specific:

Adjusted-dose regimen, weight based (Liumbruno, 2009):

- INR <2.0: 20 units/kg
- INR 2.0-4.0: 30 units/kg
- INR >4.0: 50 units/kg

Note: If after administration, INR remains >1.5 consider repeating dose appropriate for INR.

May also determine dose based on presenting INR and estimated functional prothrombin complex (PC) expressed as percentage of normal plasma levels (see table; Masotti, 2011):

Units needed to be infused = (**target** % of functional PC to be reached – **current** estimated % of functional PC) x kg of body weight

Example:

Patient (weight: 70 kg) presents with INR of 4.5 which corresponds to an **estimated % functional PC** of 10% (see table). Target INR of 1.4 corresponds to an **estimated target % functional PC** of 40%.

Units needed to be infused = (40 - 10) x 70 kg = 2100 units

Conversion of the INR to Estimated Functional Prothrombin Complex (PC)

INR Value	Estimated Functional PC
≥5.0	5%
4-4.9	10%
2.6-3.2	15%
2.2-2.5	20%
1.9-2.1	25%
1.7-1.8	30%
1.4-1.6	40%
1.0-1.3	100%

Geriatric

Refer to adult dosing.

Renal Impairment:

No dosage adjustment provided in manufacturer's labeling.

Hepatic Impairment:

No dosage adjustment provided in manufacturer's labeling; use with caution.

Common side effect:

As with other plasma preparations, reactions manifested by chills and fever may occasionally be seen, particularly when large doses of Factor IX Complex, Heat Treated are administered. A rate of infusion that is too rapid may cause headache, flushing, and changes in pulse rate and blood pressure. In such instances, stopping the infusion allows the symptoms to disappear promptly. With all but the most reactive individuals, the infusion may be resumed at a slower rate. The risk of thrombosis is present with the administration of Factor IX Complex, Heat Treated.

Pregnancy Risk Factor: C