PDL DRUG REVIEW

Proprietary Name: Coagadex®
Common Name: Coagulation Factor X (Human)
PDL Category: Antihemophilic Agents

Summary

Pharmacology/Usage: Coagadex® is a plasma-derived, concentrate of human coagulation Factor X, with sucrose as a stabilizer. It does not contain added biological agents such as heparin, albumin, or anti-thrombin; however, it is manufactured from plasma from healthy US donors who have passed viral screening tests. All plasma donors are screened for antibody to HIV-1/2 and hepatitis C virus, as well as hepatitis B surface antigen. There are 3 processing steps designed to inactivate or remove viruses: Solvent/detergent treatment targeted to inactivate enveloped viruses; a 15-nm filtration step designed to remove small viruses including non-enveloped viruses; and terminal dry-heat treatment at 80°C for 72 hours in the final container to inactivate enveloped and non-enveloped viruses.

Coagadex® temporarily replaces the missing Factor X needed for effective hemostasis.

Indication: For adults and children ≥12 years of age with hereditary Factor X deficiency for: On-demand treatment and control of bleeding episodes AND perioperative management of bleeding in patients with mild hereditary Factor X deficiency. A limitation of use is that perioperative management of bleeding in major surgery in patients with moderate and severe hereditary Factor X deficiency has not been studied.

While there is no pregnancy category with this class, the risk summary indicates there are no data with Coagadex® use in pregnant women to inform on drug-associated risk. In addition, animal reproduction studies have not been conducted. It is not known if Coagadex® can cause fetal harm if administered to a pregnant woman. It is recommended that Coagadex® be given to a pregnant woman only if clearly needed. The safety and efficacy of use have not been established in children <12 years of age.

Dosage Forms: Lyophilized powder for reconstitution in single-use vials containing nominally (approximately) 250IU or 500IU of Factor X activity; the exact potency/content is listed on the vial label. When reconstituted with sterile water, the final concentration is about 100IU/ml. For intravenous administration only.

Recommended Dosage: The dose and duration of treatment should be individualized and depends on the severity of Factor X deficiency, location, extent of bleeding, and the patient's clinical condition. It is recommended to not give more than 60IU/kg daily. The dose to achieve an *in vivo* peak increase in Factor X level may be calculated using the following formula: Dose (IU) = body weight (kg) X desired Factor X Rise (IU/dl) X 0.5. (The desired Factor X rise is the difference between the patient's plasma Factor X level and the desired level. The dosing formula is based on the observed recovery of 2IU/dl per IU/kg.

For on-demand treatment and control of bleeding episodes: Infuse 25IU/kg when the first sign of bleeding occurs. Repeat at intervals of 24 hours until the bleed stops. *Perioperative management of bleeding:* It is recommended to measure post-infusion plasma Factor X levels for patients before and after surgery. With pre-surgery, calculate the dose of Coagadex® to raise plasma Factor X levels to 70-90IU/dl using the formula above. For post-surgery, repeat dose as needed to maintain plasma Factor X levels at a minimum of 50IU/dl until there is no longer a risk of bleeding due to surgery.

It is recommended to monitor for the following: plasma Factor X activity by performing a validated test to confirm that adequate Factor C levels have been achieved and maintained; AND for the development of Factor X inhibitors.

Drug Interactions: Drug interaction studies have not been performed; however, it is recommended to use Coagadex® with caution in patients who are receiving other plasma products that may contain Factor X.

Common Adverse Drug Reactions: *There was no placebo data to compare with Coagadex®.* The most frequently reported adverse events included infusion site erythema (2 reports in 1 subject; 5.6%), fatigue (2 reports in 1 subject; 5.6%), back pain (1 report; 5.6%), and infusion site pain (1 report; 5.6%).

The formation of neutralizing antibodies (inhibitors) to Factor X may occur with Coagadex® use. It is therefore recommended to monitor patients treated for the development of inhibitors by observation and laboratory tests.

As Coagadex® is manufactured from human blood, the risk of transmitting infectious agents (e.g. viruses, the variant Creutzfeldt-Jacob disease agent, or unknown infectious agents) is possible. While a screening process is in place to help reduce the transmission, the product still may potentially transmit diseases. Any infection should be reported to the prescribing healthcare provider.

Contraindications: In patients with have had life-threatening hypersensitivity reactions to Coagadex® or any of the components

Manufacturer: Bio Products Laboratory USA, Inc

Analysis: A small (N=16) multicenter, open-label, non-randomized trial was performed to assess the safety and efficacy of Coagadex® when used in patients with moderate to severe hereditary Factor X deficiency to treat spontaneous, traumatic, and menorrhagic bleeding episodes. Additional doses of Coagadex® could be given if hemostasis was not achieved after the first dose. In addition, patients could continue treatment after the bleed stopped to reduce the risk of recurrence of a given bleed. Included patients were 12-58 years of age. The efficacy for treating bleeding episodes was assessed by the subject and/or investigator for each new bleeding episode, using a bleed-specific ordinal rating scale of excellent, good, poor, and unassessable. The rating scale was based on the number of infusions needed to treat the bleed and the intervals between infusions.

There were 208 bleeds treated with Coagadex®. Of these, 187 bleeding episodes in 15 subjects were assessed for efficacy. Ninety eight (53%) were major bleeding episodes and 88 (47%) were minor bleeds. Coagadex® was considered to be good (7%) or excellent (91%) in treating 98% of bleeding episodes. Four bleeding episodes in two subjects were considered treatment failures. Of the 187 bleeding episodes, 155 bleeds were treated with one infusion, 28 bleeds were treated with 2 infusions, 3 bleeds were treated with 3 infusions, and 1 bleed with 4 infusions.

The safety and efficacy of Coagadex® treatment for perioperative management was assessed in 5 subjects aged 14-59 years who underwent a total of 7 surgical procedures. For all surgical procedures, Coagadex® was assessed as excellent in controlling blood loss during and after surgery (thus no post-op bleeding, no requirement of blood transfusions, and blood loss was no more than 'as expected'). For major surgeries, there was a median of 13 infusions required to maintain hemostasis. For minor surgeries, there was a median of 2.5 infusions needed to maintain hemostasis.

Place in Therapy: Generally, Factor X disorder is treated with fresh-frozen plasma or plasma-derived prothrombin complex concentrates. Coagadex® is the first FDA approved Factor X concentrate for hereditary Factor X deficiency that has been subject to a highly intense purification process.[2]

It is recommended that Coagadex® be added to the RDL as Non-Recommended. It should only be utilized in very specific clinical circumstances per its approved indication.

PDL Placement:
☐ **Recommended**
☒ **Non-Recommended**

References

[1] Coagadex [package insert]. Durham, NC: Bio Products Lab USA, Inc; 2015.
[2] FDA News Release. FDA approves first Factor X concentrate to treat patients with rare hereditary bleeding disorder. Website: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm468038.htm. Accessed January 2016.