Coagulation Factor X Medical Drug Criteria Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
11-01-2024

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Coagadex® (coagulation Factor X [human]) Lyophilized powder for solution for intravenous injection	• Adults and children with hereditary Factor X deficiency for: ○ Routine prophylaxis to reduce the frequency of bleeding episodes ○ On-demand treatment and control of bleeding episodes ○ Perioperative management of bleeding in patients with mild and moderate hereditary Factor X deficiency Limitation of Use: Perioperative management of bleeding in major surgery in patients with severe hereditary Factor X deficiency has not been studied		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Hereditary Factor X deficiency	Factor X (FX), or Stuart-Prower factor, deficiency was first identified in the 1950s in the US and England in two patients. The incidence of FX deficiency is estimated at 1 in 500,000 to 1 in a million. Inheritance is autosomal recessive, meaning females and males can equally be affected. The factor X protein plays an important role in activating the enzymes that help to form a clot. It needs vitamin K for synthesis, which is produced by the liver.(2) People with mild FX deficiency experience easy bruising, nose or mouth bleeds, and bleeding after trauma or surgery. Symptoms for patients with severe FX deficiency include excessive umbilical cord bleeding, joint bleeds, intramuscular bleeds, and a high risk of intracranial hemorrhage in the first weeks of life.(2) Women with FX deficiency may additionally exhibit menorrhagia, or heavy menstrual bleeding. Pregnant women with FX may experience first trimester miscarriage or post-partum hemorrhage and should receive consultation by a hematologist and obstetrician prior to delivery.(2) Diagnosis is made through family history, prothrombin time (PT) test, partial thromboplastin time (PTT) or activated partial thromboplastin time (APTT) test. Diagnosis can be confirmed by a FX assay.(2) Factor X deficiency produces a variable bleeding tendency; patient with severe Factor X deficiency tend to have the most clinically significant bleeding symptoms observed in rare coagulation disorders. Factor X deficiency has been classified into 3 groups: severe (Factor X level less than 1%), moderate (Factor X level 1 -5%), and mild

	(Factor X level 6-10%). Factor X levels above 20% are infrequently associated with bleeding, and heterozygotes are usually asymptomatic.(3) Because Factor X is synthesized in the liver, liver disease may result in decreased Factor X levels. Vitamin K deficiency and warfarin use also result in decreased levels of Factor X.(3) For minor bleeding symptoms, topical and antifibrinolytic agents may be adequate. Topical powders for nosebleeds may be helpful in the treatment of epistaxis, and fibrin glue preparations can be used at surgical sites to achieve local hemostasis. Aminocaproic acid can be used as a mouthwash or taken orally for oral bleeding or recurrent epistaxis. Aminocaproic acid is also reported to be effective in the treatment of idiopathic menorrhagia and is used with generally good results in women with bleeding disorders. Tranexamic acid is a better tolerated and more potent antifibrinolytic agent that also can be used. (3) The National Hemophilia Foundation Medical and Scientific Advisory Council (MASAC) recommends that patients who use on-demand therapy or who infrequently infuse have doses of product available at home to allow for safe patient care; this will provide care in an emergency, as local healthcare facilities cannot be relied upon to stock the appropriate replacement products for these patients. Patients treated on prophylaxis require extra doses at home to treat breakthrough bleeding episodes. These doses should not be subtracted from the calculated monthly doses designated for prophylaxis and should be replaced as utilized. Patients and family members are encouraged to track expiration dates of product on a monthly basis, and doses that are about to expire should be utilized first to prevent waste.(4)
Efficacy	Coagadex temporarily replaces the missing Factor X needed for effective hemostasis. Factor X is an inactive zymogen, which can be activated by Factor IXa (via the intrinsic pathway) or by Factor VIIa (via the extrinsic pathway). Factor X is converted from its inactive form to the active form (Factor Xa) by the cleavage of a 52-residue peptide from the heavy chain. Factor Xa associates with Factor Va on a phospholipid surface to form the prothrombinase complex, which activates prothrombin to thrombin in the presence of calcium ions.(1) The pharmacokinetics, safety, and efficacy of Coagadex was evaluated in a multicenter, open-label, non-randomized clinical trial in 16 patients with moderate to severe hereditary Factor X deficiency. In this study Coagadex was used to treat spontaneous, traumatic, and menorrhagic bleeding episodes. If hemostasis was not achieved with a single dose of Coagadex, additional doses could be given until the bleed stopped. The patients could also continue with treatment after the bleed had stopped to reduce the risk of recurrence of a given bleed.(1) The efficacy of Coagadex in 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. This rating scale was based on the number of infusions required to treat the bleed and the interval between infusions, and differed for each type of bleed (overt, covert, or menorrhagic). Coagadex was considered to be good or excellent in treating 98% of bleeding episodes. Of the 187 bleeding episodes in the efficacy analysis, 155 bleeds were treated with one infusion, 28 bleeds with two infusions, 3 bleeds with three infusions, and 1 bleed with four infusions.(1) The safety and efficacy of Coagadex for perioperative management was evaluated in five patients who underwent a total of seven surgical procedures. For all surgical procedures, Coagadex was assessed as excellent (no post-operative bleeding, no requirement of blood transfusions, and blood loss was no more than "as expected") in controlling blood loss during and after surgery. For major surgeries a range of 2 to 15 infusions was required to control blood loss during and after surgery and for minor surgeries a range of 1 to 4 infusions was required.(1)

	In a multicenter, open-label, non-randomized clinical trial, the use of Coagadex in routine prophylaxis of bleeding episodes was evaluated in nine children aged less than 12 years of age. Eight subjects had severe FX deficiency and the other 4 had moderate deficiency. After first dose of Coagadex 50 IU/kg, given at a rate not exceeding 3 mL/minute, all subjects underwent a 30-minute post-dose incremental recover assessment. Routine prophylaxis was started on Day 2 or 3 with unit doses of 40-50 IU/kg and during the first 6 weeks trough levels of Factor X were measured to adjust the dosage regimen to maintain a trough level of at least 5 IU/dL. At the end of the study (at least 6 months and at least 50 exposure days) a repeat 30-minute incremental recovery was performed. Investigators' assessment following 6 months of routine prophylaxis was rated excellent in all 9 subjects; excellent was defined as "no minor or major bleeds occurred during the study period" or "lower frequency of bleeds than expected, given the subject's medical/treatment history".(1)
Safety	Coagadex is contraindicated in patients who have had life-threatening hypersensitivity reactions to Coagadex or any of the components.(1) Drug interaction studies have not been performed with Coagadex. Based on the mechanism of action, Coagadex is likely to be counteracted by direct and indirect Factor Xa inhibitors.(1)

REFERENCES

Number	Reference
1	Coagadex Prescribing Information. Bio Products Laboratory USA. November 2020.
2	National Hemophilia Foundation. Bleeding Disorders, Types of Bleeding Disorders, Other Factor Deficiencies, Factor X. Accessed at https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Other-Factor-Deficiencies/Factor-X.
3	Brown DL, Kouides PA. Diagnosis and treatment of inherited Factor X deficiency. Haemophilia. 2008;14, 1176-1182.
4	National Hemophilia Foundation MASAC Recommendations number 242. Recommendations Regarding Doses of Clotting Factor Concentrate in the Home. June 2016.
5	Reference no longer used

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
J7175	Coagadex	coagulation factor x (human) for inj	250 UNIT ; 500 UNIT	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Coagadex	coagulation factor x (human) for inj	250 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Coagadex	coagulation factor x (human) for inj	250 UNIT	Commercial ; HIM ; ResultsRx
Coagadex	coagulation factor x (human) for inj	500 UNIT	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
Coagadex (coagulation Factor X ([human])

   1. The patient has been treated with the requested agent for the requested use (e.g., prophylaxis, on-demand) within the past 90 days **OR**
   2. The prescriber states the patient has been treated with the requested agent for the requested use (e.g., prophylaxis, on-demand) within the past 90 days AND is at risk if therapy is changed **OR**

   B. The patient has a diagnosis of hereditary Factor X deficiency AND ONE of the following:
      1. The patient is currently experiencing a bleed AND BOTH of the following:
         A. The patient is out of medication **AND**
         B. The patient needs to receive a ONE TIME emergency supply of medication **OR**
      2. The requested agent will be used for prophylaxis treatment AND ONE of the following:
         A. The patient has severe or moderate Factor X deficiency (Factor X level less than or equal to 5%) **OR**
         B. The patient has mild Factor X deficiency (Factor X level 6-10%) AND there is support for prophylaxis use of the requested agent (medical records required) **OR**
      3. The requested agent will be used as on-demand treatment to control bleeding episodes AND BOTH of the following:
         A. The prescriber has communicated with the patient (via any means) and has verified that the patient does NOT have more than 5 on-demand doses on hand **AND**
         B. ONE of the following:
            1. The patient has tried and had an inadequate response to aminocaproic acid or tranexamic acid **OR**
            2. The patient has an intolerance or hypersensitivity to aminocaproic acid or tranexamic acid **OR**
            3. The patient has an FDA labeled contraindication to BOTH aminocaproic acid AND tranexamic acid **OR**
            4. There is support for the use of the requested agent over BOTH aminocaproic acid AND tranexamic acid **OR**
      4. The requested agent will be used as perioperative management of bleeding AND BOTH of the following:
         A. The patient has mild (Factor X level 6-10%) or moderate (Factor X level 1-5%) hereditary Factor X deficiency **AND**
         B. ONE of the following:
            1. The patient has tried and had an inadequate response to aminocaproic acid or tranexamic acid **OR**

Module	Clinical Criteria for Approval
	2. The patient has an intolerance or hypersensitivity to aminocaproic acid or tranexamic acid **OR** 3. The patient has an FDA labeled contraindication to BOTH aminocaproic acid AND tranexamic acid **OR** 4. There is support for the use of the requested agent over BOTH aminocaproic acid AND tranexamic acid **AND** 2. The prescriber is a specialist (e.g., hematologist) in the area of the patient's diagnosis or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient does NOT have liver disease **AND** 4. The patient does NOT have vitamin K deficiency **AND** 5. The patient will NOT be using the requested agent in combination with an indirect or direct Factor Xa inhibitor [e.g., apixaban (Eliquis), dalteparin (Fragmin), edoxaban (Savaysa), enoxaparin (Lovenox), fondaparinux (Arixtra), rivaroxaban (Xarelto) or warfarin (Coumadin)] **AND** 6. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 7. ONE of the following: A. The requested quantity (dose) does NOT exceed the program quantity limit defined by BOTH of the following: 1. The requested quantity (dose) is within the FDA labeled dosing **AND** 2. The requested quantity (number of doses) is appropriate based on intended use (e.g., on-demand, perioperative management of bleeding, prophylaxis) **OR** B. There is support for exceeding the appropriate quantity limit based on the FDA labeled dosing and/or intended use (medical records required) **Length of Approval:** One time emergency use: 1 time Perioperative management of bleeding: 1 time per request On-demand treatment: 3 months Prophylaxis treatment: 12 months