IOWA | Health and Human Services

Iowa PDL New Drug Review

Proprietary Name: Andembry®
Common Name: garadacimab-gxii
PDL Category: Hereditary Angioedema Agents

Pharmacology/Usage: Garadacimab-gxii, the active ingredient of Andembry®, is an activated Factor XII (FXIIa) inhibitor. It is a recombinant, fully human, monoclonal antibody (IgG4/λ-light chain) produced in Chinese Hamster Ovary (CHO) cells. Garadacimab-gxii binds to the catalytic domain of activated Factor XII and inhibits its catalytic activity. FXII is the first factor activated in the contact activation pathway and initiates the inflammatory bradykinin-producing kallikrein-kinin system. The inhibition of FXIIa decreases the activation of pre-kallikrein to kallikrein and the generation of bradykinin, which is associated with inflammation and swelling in HAE attacks, thus reducing the cascade of events leading to an HAE attack.

Indication: For prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years and older.

There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use in pregnant women to assess for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Monoclonal antibodies are transported across the placenta during the third trimester of pregnancy; thus, potential effects on a fetus are likely to be greater during the third trimester of pregnancy. The safety and efficacy of use in the pediatric population younger than 12 years of age have not been established.

Dosage Form: Preservative-free solution for Injection, available as:

- 200mg/1.2ml of solution in a single-dose prefilled autoinjector.
- 200mg/1.2ml (167mg/ml) of solution in a single-dose prefilled syringe with needle safety device.

Prior to administration, remove from the refrigerator and allow to sit for 30 minutes at room temperature before use.

Recommended Dosage: The recommended dosage is an initial loading dose of 400mg (two injections of 200mg) administered subcutaneously (SC) on the first day of treatment, followed by a maintenance dosage of 200mg administered SC QM. Administer SC into the thigh or abdomen ensuring to stay 1 inch away from the navel. The upper arm can also be used if a caregiver administers the injection. If a dose is missed, administer the dose as soon as possible.

Andembry® is for SC use only and is intended for self-administration or administration by a caregiver. Prior to initiation of treatment, train patients/caregivers on proper preparation and SC administration technique.

Drug Interactions: Andembry® can prolong activated partial thromboplastin time (aPTT) due to an interaction of garadacimab-gxii with the aPTT assay. The reagents used in the aPTT laboratory test initiate intrinsic coagulation through the activation of FXII in the contact system; thus, inhibition of plasma FXIIa by Andembry® can prolong aPTT in this assay.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Andembry®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.* The most frequently reported adverse events included nasopharyngitis (9%) and abdominal pain (8%).

Contraindications: There are no contraindications listed with this product.

Manufacturer: CSL Behring

Analysis: The efficacy of Andembry® for prophylaxis to prevent HAE attacks was assessed in a multicenter, randomized, double-blind, placebo-controlled, parallel-group study (VANGUARD) that was of 6 months duration. This study enrolled adult and pediatric patients 12 years of age and older (N=64) with Type I or Type II HAE who experienced at least 2 investigator-confirmed HAE attacks over a 2-month period prior to treatment with Andembry® or placebo. Patients were required to discontinue other prophylactic HAE medications prior to entry into the study; however, all patients were allowed to use on-demand medications for the treatment of HAE attacks during the study. Patients in the study were mostly females (59%), White (86%), were >17 years (91%), and had C1-INH HAE Type 1 (88%). In addition, 33% had prior HAE prophylaxis. The baseline HAE attack rate of 1 to <3 attacks was 41% while ≥3 attacks was 59%.

The primary endpoint was the monthly HAE attack rate at 6 months (number of investigator-confirmed HAE attacks per month). Results suggested that the least squares mean for the monthly HAE attack rate was lower with Andembry® as compared with placebo. Results are presented in the table below, which was adapted from the prescribing information.

Rate of monthly HAE attack	Andembry® (N=39)	Placebo (N=25)
Least squares (LS) mean	0.22	2.07
Percent reduction relative to placebo	89.2	
p-value	<0.001	

The monthly rate of HAE attacks needing on-demand therapy and the monthly rate of moderate or severe HAE attacks were assessed as secondary endpoints. There was a 91.2% reduction with Andembry® relative to placebo in the monthly rate of HAE attacks requiring on-demand therapy and a 93.6% reduction with Andembry® relative to placebo in the monthly rate of moderate or severe HAE attacks.

Additional secondary endpoints assessed the proportion of patients with a ≥50, ≥70%, ≥90%, and 100% (attack-free) reduction in monthly HAE attack rate from the first dose through the end of the 6-month treatment period compared to the 2-month period prior to treatment. The proportion of patients with a ≥50, ≥70%, ≥90%, and 100% reduction was 95%, 92%, 74%, and 62% on Andembry® as compared with 33%, 17%, 8%, and 0% on placebo, respectively.

Place in Therapy: Andembry® is an activated Factor XII (FXIIa) inhibitor (monoclonal antibody) indicated for prophylaxis to prevent attacks of HAE in adult and pediatric patients aged 12 years and older. It is for subcutaneous use only, intended to be self-administered by the patient or administered by a caregiver. Its efficacy was assessed in a double-blind, randomized, placebo-controlled trial that included patients with Type I or Type II HAE who experienced at least 2 investigator-confirmed HAE attacks over a 2-month period prior to randomized treatment. The primary endpoint was the monthly HAE attack rate at 6 months and results suggested that the least squares mean for the monthly HAE attack rate was significantly lower with Andembry® as compared with placebo. Per one

noted reference source, plasma-derived C1 INH, lanadelumab, berotralstat, or garadacimab-gxii are recommended rather than other treatments for long-term prophylaxis in patients with severe disease.[2]

Summary

There is no evidence to suggest that Andembry® is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Andembry® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

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

References

[1] Andembry [package insert]. Kankakee, IL: CSL Behring LLC; 2025.
[2] UpToDate online. Hereditary angioedema (due to C1 inhibitor deficiency): General care and long-term prophylaxis. Accessed September 2025.