Clinical Policy Title:	evinacumab-dgnb
Policy Number:	RxA.678
Drug(s) Applied:	Evkeeza™
Original Policy Date:	04/19/2021
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Evkeeza™ is an ANGPTL3 (angiopoietin-like 3) inhibitor indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH).

Limitations of Use:

- The safety and effectiveness of Evkeeza™ have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH).
- The effects of Evkeeza™ on cardiovascular morbidity and mortality have not been determined.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
evinacumab-dgnb (Evkeeza™)	homozygous familial hypercholesterolemia (HoFH)	15 mg/kg every 4 weeks	15 mg/kg IV every 4 weeks.

Dosage Forms

- Injection: 345 mg/2.3 mL (150 mg/mL) and 1,200 mg/8 mL (150 mg/mL) solution in single-dose vials.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the provisions of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Homozygous Familial Hypercholesterolemia (Hofh) (must meet all):

1. Diagnosis of homozygous familial hypercholesterolemia (Hofh) as determined by documented variant in two LDLR alleles or the presence of homozygous or compound heterozygous variants in ApoB or PCSK9;
2. Age ≥ 12 years;
3. Prescribed by or in consultation with a cardiologist, lipid specialist or endocrinologist;
4. Evkeeza™ is prescribed as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering

therapies, including maximally tolerated statin, ezetimibe, PCSK9 inhibitors, lomitapide, and apheresis;
5. Dose does not exceed 15 mg/kg IV every 4 weeks;
6. Patient has untreated LDL-C ≥500 mg/dL or treated LDL-C ≥250 mg/dL;
7. Patient has history of cutaneous or tendinous xanthomas before 10 years of age

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Homozygous Familial Hypercholesterolemia (Hofh) (must meet all):
1. Member is currently receiving the medication that has been authorized by RxAdvance or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Dose does not exceed 15 mg/kg IV every 4 weeks;

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
HoFH: Homozygous Familial Hypercholesterolemia
IV: Intra Venous
LDL-C: Low-Density Lipoprotein-Cholesterol
HeFH: Heterozygous Familial Hypercholesterolemia
PCSK9: Proprotein Convertase Subtilisin/Kexin Type 9
ANGPTL3: Angiopoietin-Like 3

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug name	Dosing Regimen	Dose Limit/Maximum Dose
Juxtapid™ (lomitapide mesylate)	Initial: 5 mg once daily; after ≥ 2 weeks of therapy, may increase to 10 mg once daily, as tolerated; then at ≥ 4-week intervals, may increase to 20 mg once daily, then to 40 mg once daily, and finally to a maximum dose of 60 mg/day as tolerated.	60 mg/day PO

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Evkeeza™ is contraindicated in patients with a history of serious hypersensitivity reaction to evinacumab-dgnb or to any of the excipients in Evkeeza™. Serious hypersensitivity reactions, including

anaphylaxis, have occurred.

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- Serious Hypersensitivity Reactions: If a serious hypersensitivity reaction occurs, discontinue Evkeeza™, treat according to standard-of-care and monitor until signs and symptoms resolve.
- Embryo-Fetal Toxicity: Advise patients who may become pregnant of the risk to a fetus. Consider obtaining a pregnancy test prior to initiating treatment with Evkeeza™. Advise patients who may become pregnant to use contraception during treatment and for at least 5 months following the last dose.

References

1. Pentsuk N, van der Laan JW. An interspecies comparison of placental antibody transfer: new insights into developmental toxicity testing of monoclonal antibodies. Birth Defects Res B Dev Reprod Toxicol. 2009;86(4):328-344. doi:10.1002/bdrb.20201. Accessed April 19, 2021.
2. Evkeeza™ prescribing information. Tarrytown, NY: Regeneron Pharmaceuticals Inc; February 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761181s000lbl.pdf. Accessed April 19, 2021.
3. Evkeeza™, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed April 19, 2021.
4. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated November 25, 2020. Accessed April 19, 2021.
5. Evkeeza™ is the first FDA-approved ANGPTL3 inhibitor and the latest example of the promise of Regeneron's development approach. Available at: https://www.biospace.com/article/releases/fda-approves-first-in-class-Evkeeza-evinacumab-dgnb-for-patients-with-ultra-rare-inherited-form-of-high-cholesterol/. Accessed April 19, 2021.
6. Evkeeza™, IPD Analytics Rx Insights_New Drug Review_Evkeeza_02 2021.pdf. Accessed with subscription at: https://www.ipdanalytics.com/. Accessed April 19, 2021.
7. Juxtapid™ prescribing information. Cambridge, MA: Aegerion Pharmaceuticals; December 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/203858s000lbl.pdf. Accessed April 19, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	04/19/2021	06/10/2021