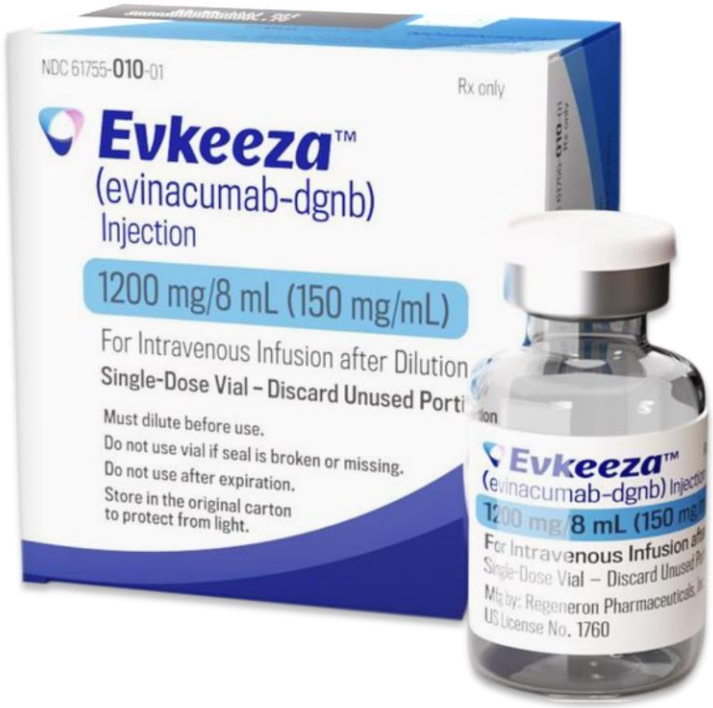
Evkeeza (evinacumab-dgnb)



NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Evkeeza
- **Generic name:** Evinacumab-dgnb
- **Pharmacologic class:** Angiopoietin-like 3 (ANGPTL3) inhibitor
- **Strength and Formulation:** 150mg/mL; soln for IV infusion after dilution; preservative-free
- **Manufacturer:** Regeneron Pharmaceuticals
- **How supplied:** Single-dose vials (2.3mL, 8mL)—1
- **Legal Classification:** Rx

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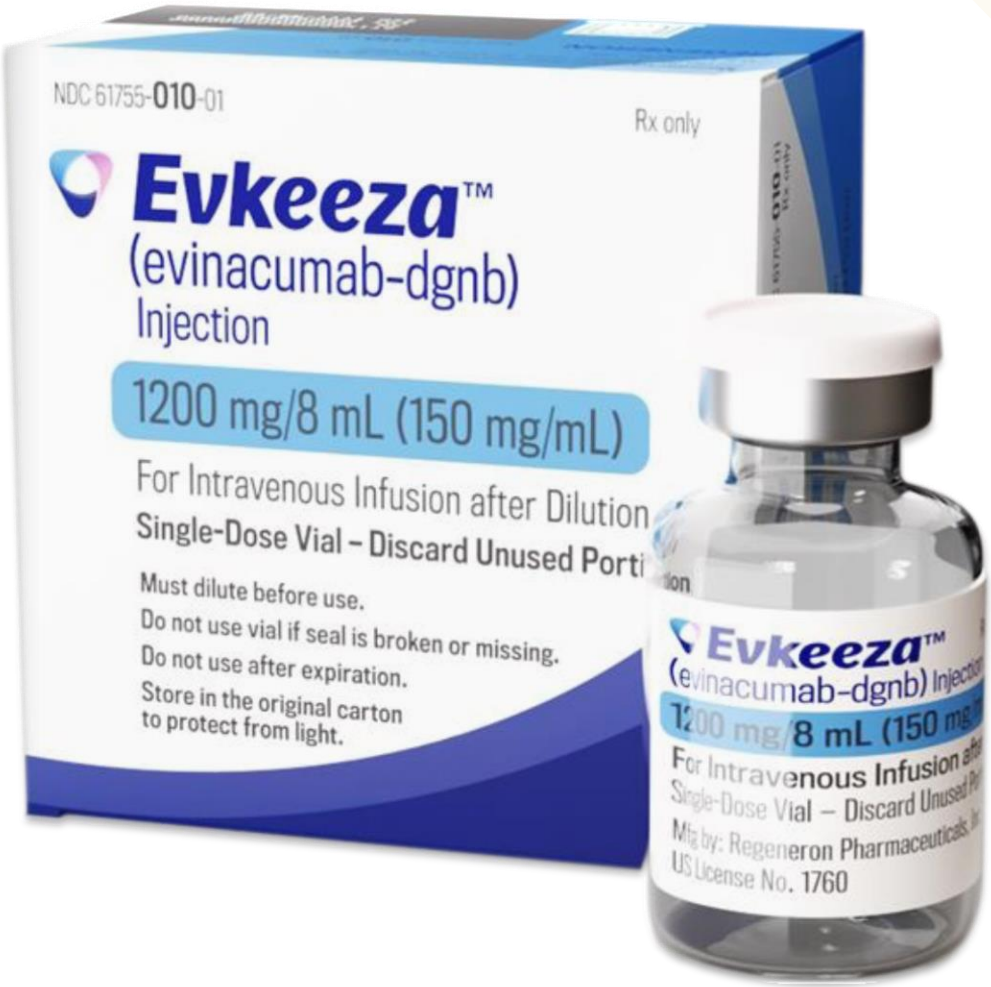
Evkeeza


NDC 61755-010-01
Rx only
Evkeeza™
(evinacumab-dgnb)
Injection
1200 mg/8 mL (150 mg/mL)
For Intravenous Infusion after Dilution
Single-Dose Vial – Discard Unused Porti
Must dilute before use.
Do not use vial if seal is broken or missing.
Do not use after expiration.
Store in the original carton
to protect from light.
Evkeeza™
(evinacumab-dgnb) Injection
8 mL (150 mg
For Intravenous Infusion
Single-Dose Vial – Discard Unused
Mfg by: Regeneron Pharmaceuticals,
US License No. 1760

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Indication

- 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.

Dosage and Administration

- Administer diluted solution by intravenous (IV) infusion over 60 minutes.
- Rate of infusion may be slowed, interrupted or discontinued if patient develops adverse reactions, including infusion or hypersensitivity reactions.
- ≥12 years: **15mg/kg once monthly** (every 4 weeks).
- Assess LDL-C when clinically appropriate, may be measured as early as 2 weeks after initiation.
- May be administered without regard to timing of lipoprotein apheresis.

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Considerations for Specific Populations

- **Pregnancy:** may cause fetal harm based on data from animal reproduction studies; available human data are insufficient to assess for drug-associated risk.
  - *Pregnancy exposure registry*: (833) 385-3392.
- **Nursing mothers:** No data on presence of evinacumab-dgnb in human or animal milk; consider benefits of breastfeeding along with mother's clinical need for Evkeeza and any potential adverse effects.
- **Pediatric**: <12 years: not established.
- **Geriatrics**: Clinical studies did not include sufficient numbers to determine difference from younger adult patients.

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Contraindications

- Patients with a history of serious hypersensitivity reaction to evinacumab-dgnb or to any of the excipients in Evkeeza.

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Warnings and Precautions

- Discontinue if signs or symptoms of serious **hypersensitivity reactions** occur.
  - Treat appropriately according to standard of care, and monitor until signs and symptoms resolve.
- **Embryo-fetal toxicity**: may cause fetal harm.
  - Consider obtaining a pregnancy test prior to initiation.
  - Advise patients who may become pregnant to use effective contraception during treatment and for at least 5 months after the last dose.

Adverse Reactions

- **Most common (≥5%)**: Nasopharyngitis, influenza-like illness, dizziness, rhinorrhea, nausea.
- **Others**: Serious hypersensitivity reactions.

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Mechanism of Action

- **Evinacumab-dgnb** is a recombinant human monoclonal antibody that binds to and inhibits ANGPTL3, a member of the angiopoietin-like protein family that is expressed primarily in the liver and plays a role in the regulation of lipid metabolism by inhibiting lipoprotein lipase and endothelial lipase.
- This leads to reduction in LDL-C, high density lipoprotein cholesterol (HDL-C), and triglycerides (TG).

Mechanism of Action

- Evinacumab-dgnb reduces LDL-C independent of the presence of LDL receptor by promoting very low-density lipoprotein (VLDL) processing and clearance upstream of LDL formation.
- The blockade of ANGPTL3 lowers TG and HDL-C by rescuing lipoprotein lipase and endothelial lipase activities, respectively.

Clinical Trials

- Approval was based on the multicenter, double-blind, randomized, placebo-controlled ELIPSE-HoFH trial (ClinicalTrials.gov: NCT03399786) that evaluated the efficacy and safety of Evkeeza in 65 patients with HoFH.
- During the 24-week, double-blind treatment period, patients were randomly assigned 2:1 to receive either Evkeeza 15mg/kg IV every 4 weeks (n=43) or placebo (n=22).
- After the treatment period, 64 patients entered a 24-week open-label extension period in which all patients received Evkeeza 15mg/kg IV every 4 weeks.
- The **primary efficacy endpoint** was percent change in LDL-C from baseline to week 24.

Clinical Trials

- **Patient demographics**
  - Patients were on the following lipid-lowering therapies: statins (94%), ezetimibe (75%), PCSK9 inhibitor antibodies (77%), lomitapide (22%), and lipoprotein apheresis (34%).
  - Mean LDL-C at baseline: 255mg/dL.
  - Mean age at baseline: 42 years (range: 12 to 75); 12% were ≥65 years.
  - 54% Women; 3% Hispanic; 74% White; 15% Asian; 3% Black; 8% other or not reported.

Clinical Trials

- Results showed that patients treated with Evkeeza had a 47% reduction in LDL-C compared with a 2% increase for patients who received placebo (least squares mean treatment difference: -49%; 95% CI, -65, -33; *P* <.0001).
- Statistically significant reductions for Evkeeza vs placebo, respectively (*P* <.0001 for all):
  - Apolipoprotein B: -41% vs -5%
  - Non-HDL-C: -50% vs +2%
  - Total Cholesterol: -47% vs +1%
  - Triglycerides: -55% vs -5%

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Clinical Trials

- At week 24, the observed reduction in LDL-C with Evkeeza was similar across predefined subgroups, including age, sex, limited LDLR activity, concomitant treatment with lipoprotein apheresis, and concomitant background lipid-lowering medications.
- After 24 weeks of open-label Evkeeza treatment (week 24 to week 48), the observed LDL-C reduction from baseline was similar in patients who crossed over from placebo to Evkeeza and was maintained in patients who remained on Evkeeza for 48 weeks.

Clinical Trials

- In ELIPSE-HoFH, 1 pediatric patient received Evkeeza 15mg/kg IV every 4 weeks and 1 pediatric patient received placebo, as an adjunct to other lipid-lowering therapies.
  - At week 24, the percent change in LDL-C was -73% with Evkeeza vs +60% with placebo.

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Clinical Trials

- In an open-label extension study, 13 pediatric patients 12 to 17 years of age with HoFH received Evkeeza 15mg/kg IV every 4 weeks as an adjunct to other lipid-lowering therapies.
  - At week 24, the percent change in LDL-C was -52% in the 9 patients who completed treatment and had a lipid assessment.
  - Overall effect on lipid parameters was generally similar to that seen in adults.

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/evkeeza/