Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Evinacumab

Evidence Summary

Evinacumab is the first-in-class ANGPTL3 targeting antibody which reduces LDL-C and triglycerides. It shows good safety in trials. To date, it's approved for a rare inherited form of hypercholesterolemia.

Neuroprotective Benefit: Evinacumab has not been tested for neuroprotection.

Aging and related health concerns: Evinacumab reduces levels of atherogenic lipid classes, such as LDL-C, in a distinct manner from other lipid-lowering agents. It remains to be determined whether this will translate to a reduction in cardiovascular risk.

Safety: Evinacumab is generally well-tolerated. Reported cases of liver enzyme elevations in trials were relatively low. Commonly reported adverse events include fatigue, dizziness, and nasal-respiratory infections. It may also induce fetal abnormalities.

Availability: Rx	**Dose**: 15 mg/kg every 4 weeks via i.v. administration is the recommended dose for patients with homozygous familial hypercholesterolemia. Subcutaneous administration has been tested in trials but is not currently an approved route of administration.	**IgG4 isotype mAb** **Chemical formula:** N/A **MW**: 146 kDa
Half-life: Plasma half-life is 11-17 days Elimination half-life is variable based on serum concentration. At the recommended dosing schedule, levels remain detectable up to approximately 20 weeks.	**BBB**: N/A As a mAb, it is likely not penetrant at therapeutically relevant levels.	
Clinical trials: Evinacumab has been tested in Phase 1 trials in hyperlipidemia (n=83; n=56), Phase 2 trials in hypercholesterolemia (n=272), severe hypertriglyceridemia (n=51), and HoFH (n=9) and a Phase 3 trial in HoFH (n=65).	**Observational studies**: Some real-world studies suggest similar safety and efficacy profiles relative to RCTs.	

What is it?

Evinacumab (REGN1500) is a fully human IgG4 monoclonal antibody (mAb) that binds to angiopoietin-like 3 (ANGPTL3), which plays a role in plasma lipid metabolism through the inhibition of lipoprotein lipase (LPL) and endothelial lipase [1]. Individuals with loss-of-function mutations in ANGPTL3 have relatively low levels of triglycerides and low-density lipoprotein-cholesterol (LDL-C), suggesting that inhibition of ANGPTL3 is likely to induce lipid lowering and promote cardioprotection [2]. ANGPTL3 is produced in the liver, and secreted into the bloodstream. Evinacumab does not impact the production

of ANGPTL3 in the liver, but rather, binds to it in the blood and then inhibits its downstream activity [1]. It has been tested in clinical trials in the context of hypercholesterolemia, and hypertriglyceridemia.

In 2021, evinacumab was approved by the FDA for use as an adjunct to other lipid-lowering therapies in patients aged 12 and older with homozygous familial hypercholesterolemia (HoFH) (FDA). In 2023, the label was expanded to include children with HoFH aged 5 to 11 years old (Press release). In the US, evinacumab is marketed by Regeneron Pharmaceuticals under the tradename Evkeeza®. In 2021, the EMA approved evinacumab for patients aged 5 and older with HoFH, and in 2024, expanded the marketing authorization to include patients with HoFH aged six months and older (EMA). Outside of the US, evinacumab is marketed under the tradename Evkeeza® by Ultragenyx Pharmaceuticals.

Neuroprotective Benefit: Evinacumab has not been tested for neuroprotection.

Types of evidence:

- 0 meta-analyses or systematic reviews
- 0 clinical trials
- 0 observational studies
- 0 laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

There is no evidence to date on evinacumab's capacity to reduce the risk for dementia. Elevated LDL-C has been designated a modifiable risk factor for dementia [3], thus through its mechanism of lowering levels of LDL-C, it would potentially play a role in dementia risk reduction.

Human research to suggest benefits to patients with dementia:

Evinacumab has not been tested in dementia patients.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

Evinacumab does not get into the brain and is not expected to have any direct neuroprotective effects. It may offer indirect effects through the lowering of atherogenic lipids.

APOE4 interactions: Not established

Aging and related health concerns: Evinacumab reduces levels of atherogenic lipid classes, such as LDL-C, in a distinct manner from other lipid-lowering agents. It remains to be determined whether this will translate to a reduction in cardiovascular risk.

Types of evidence:

- 2 meta-analyses of RCTs
- 1 Phase 3 trial in HoFH (+ long-term extension study)
- 2 Phase 2 trials for hypercholesterolemia
- 1 Phase 2 trial in severe hypertriglyceridemia
- 2 Phase 1 trials in hyperlipidemia
- 0 observational studies
- Numerous laboratory studies

Loss-of-function mutations in ANGPTL3 have been associated with lower levels of triglycerides and LDL-C as well as a decreased risk for cardiovascular disease [2]. By targeting and inhibiting ANGPTL3, evinacumab was developed to try to mimic the lipid lowering and cardioprotective effects of those mutations. Evinacumab is only one of several clinically tested ANGPTL3-lowering therapies, but it is the only one that has received FDA approval to date (for more information on the biology of ANGPTL3 and the other therapies, see the ANGPTL3-Targeted Therapies report). The LDL-C lowering appears to stem from the reduction in levels of VLDL-C, the precursor to LDL-C [1]. Evinacumab is considered to be particularly beneficial in patients with hypercholesterolemia that is refractory to current lipid-lowering therapies, because its LDL-C lowering capacity is not dependent on the presence of the LDL receptor (LDLR).

Hypercholesterolemia: BENEFIT

Evinacumab exerts a mixed, but generally favorable effect on the circulating lipid profile, as it lowers atherogenic lipid particles, such as LDL-C, apoB, and triglyceride-rich lipoproteins, but also lowers levels of potentially protective HDL-C. A meta-analysis of five RCTs testing evinacumab including 568

participants found that, relative to placebo, evinacumab use was associated with a reduction in LDL-C of -33.123% (95% confidence interval [CI] -48.639% to -17.606%), a reduction in triglycerides of -50.959% (95% CI -56.555% to -45.362%), as well as a reduction in HDL-C of -12.773% (95% CI, -16.359% to -9.186%) [4]. A network meta-analysis comparing the LDL-C lowering capacity of evinacumab alongside three approved PCSK9 inhibitors (alirocumab, evolocumab, and inclisiran) found that while there were no significant differences in LDL-C lowering capacity, it scored behind the PCSK9 mAbs in the SUCRA ranking for best intervention on this metric [5]. It should be noted, however, that the analysis only included two RCTs testing evinacumab (n=225), compared with 11 RCTs for alirocumab (n=4,131) and six RCTs for evolocumab (n=2,789).

Evinacumab was approved as an adjunctive therapy for patients with homozygous familial hypercholesterolemia (HoFH) with elevated LDL-C that is not adequately managed by traditional lipid lowering therapies, such as statins and PCSK9 inhibitors, based on the results of the Phase 3 ELIPSE trial. Due to the presence of mutations that negatively impact LDLR expression and function, this patient population has limited responses to these traditional LDL-C lowering therapies whose efficacy involves the enhancement of LDLR. Cell culture studies including lymphocytes from patients with spectrum of LDLR activity confirmed that evinacumab does not alter or depend on LDLR activity, such that LDL-C lowering achieved with evinacumab is not related to the baseline function of LDLR [6].

An open-label proof-of-concept Phase 2 trial in this population (NCT02265952) included nine adults with HoFH with chronically elevated LDL-C (376.0±240.9 mg/dL) despite aggressive traditional lipid-lowering therapy [7]. By week four, LDL-C levels decreased by an average of -49±23% (range -25% to -90%), apoB levels decreased by an average of -46±18%, and triglyceride levels decreased by an average of -47±17%. HDL-C levels also decreased by an average of -36±16%.

The randomized, double-blind, placebo-controlled Phase 3 ELIPSE trial (NCT03399786) included 65 patients (age 12 and older) with HoFH [8]. Due to the presence of two null variants, LDLR function was completely absent in 21 of the participants (32%). Participants were randomized to either placebo (n=22) or evinacumab (n=43) at a dose of 15 mg/kg administered by intravenous injection every 4 weeks (q4w) for 24 weeks. Evinacumab treatment led to a significant reduction in LDL-C relative to placebo, with a between-group least squares mean difference of -49.0% (95% CI -65.0% to -33.15%), and absolute reduction of -132.1 mg/dL (95% CI -175.3 to -88.9). The degree of LDL-C lowering was not impacted by the presence of null or loss of function LDLR mutations, or the type of background lipid-lowering medication (i.e. statins, ezetimibe, PCSK9 inhibitors, etc.). A reduction in LDL-C of at least 30% was

achieved by 84% of participants treated with evinacumab, relative to only 18% treated with placebo (Odds ratio [OR]: 25.2, 95% CI 5.7 to 110.5). Significant reductions in apoB (-36.9%, 95% CI -48.6% to -25.2%), total cholesterol (-48.4%, 95% CI -58.7 to -38.1), and triglycerides (-50.4%, 95 % CI -65.6 to -35.2) were also observed with evinacumab relative to placebo. Levels of HDL-C were reduced by -29.6% in those treated with evinacumab, while levels increased by 0.8% in those treated with placebo.

LDL-C is a measure of the amount of cholesterol carried by LDL particles. Evidence suggests that aside from the amount of cholesterol, the level of LDL particles (LDL-P) is also an indicator of cardiovascular risk, thus effective therapies should aim to lower both LDL-C and LDL-P [9]. NMR spectroscopy was used to assess lipoprotein particle sizes and concentrations during the 24-week double-blind period [9]. NMR analysis indicated a median reduction in LDL-P of -49.6% with evinacumab, relative to a reduction of -5.1% with placebo. Median levels of small and medium VLDL particles were also reduced with evinacumab by -41.0% (vs. -1.9% for placebo) and -87.1% (vs. -25.0% for placebo), respectively.

Sixty-four of the participants continued in the study for the 24-week open-label extension period and were treated with evinacumab (I5 mg/kg i.v. q4w) [9]. By the end of the 48 weeks, LDL-C was reduced by an average of -46.3% (134.3 ± 117.3 mg/dL), with a reduction from baseline of -42.7% and -55.8%, in those originally randomized to evinacumab and placebo, respectively.
An open-label trial (NCT03409744) included 116 participants with HoFH from the Phase 2 proof-of-concept (NCT02265952) and Phase 3 ELIPSE (NCT03399786) trials who were treated with evinacumab (15 mg/kg i.v. q4w) for a median of 104.3 weeks (range 28.3 to 196.3) [10]. Reductions in LDL-C, apoB, non-HDL-C, total cholesterol, fasting triglycerides, and Lp(a) were stable until at least week 120. A similar degree of lowering was achieved in those transitioning to evinacumab from placebo and those continuing with evinacumab treatment. The study included 102 adults and 14 adolescents. The adolescent participants achieved a slightly greater degree of LDL-C lowering relative to adult participants (-55.4% vs -41.7%). A PK/PD modeling study identified a similar trend in that the proportion of patients likely to achieve LDL-C lowering of ≥50% with evinacumab decreased with age, with 84.6% of pediatric patients (aged 5-12) likely to attain this target, but only 53.4% of adult patients (≥18 years) were likely to achieve this goal [11].
Some of the cohorts in the open-label extension of the ELIPSE trial have continued to be followed for several years. Five participants from the Italian cohort have been followed for over five years and experienced a median decrease in LDL-C of -84.5%, from 323 mg/dL (range 203 to 587) at study entry to 51.0 mg/dL (range 46 to 106) seven years later [12]. Similar trends were observed for total cholesterol (-74%), non-HDL-C (-80%), HDL-C (-32%), and triglycerides (-61%) over this time period.

Based on the outcomes of other lipid-lowering therapies, significant reductions in LDL-C are expected to decrease the risk for adverse cardiovascular events. While the ELIPSE trial did not assess the impact on cardiovascular outcomes, data from the French cohort of the open-label extension study suggest that evinacumab may have a protective effect [13]. Over a median a period of 3.5 years, none of the 12 evinacumab-treated participants experienced an adverse cardiovascular event (event-free survival 100%). Meanwhile, five out of 21 participants in reference cohort in this population (REFERCHOL cohort) experienced 13 cardiovascular events over a median four-year period (event-free survival 76%). Further studies are needed to confirm whether evinacumab meaningfully reduces adverse cardiovascular events.

Since frequent intravenous infusions can impose a high burden for patients, alternative routes of administration, such as subcutaneous injection, may improve access. A double-blind, randomized, placebo-controlled Phase 2 trial (NCT03175367) including 202 patients with homozygous or heterozygous familial hypercholesterolemia and 64 patients with non-familial refractory hypercholesterolemia (LDL-C ≥70 mg/dL with atherosclerosis or LDL-C ≥100 mg/dL without atherosclerosis) tested evinacumab via intravenous and subcutaneous routes of administration on top of traditional lipid-lowering therapies [14]. Most participants were taking a PCSK9 inhibitor, around half were taking a high-intensity statin, and around a third were taking ezetimibe. Evinacumab was tested at intravenous doses of 15 mg/kg qw4 or 5 mg/kg q4w for 24 weeks, and subcutaneous doses of 450 mg weekly, 300 mg weekly, or 300 mg q2w for 16 weeks. The change in LDL-C from baseline over 16 weeks was largely similar for the i.v. 15 mg/kg q4w (-49.9%), s.c. 450 mg qw (-47.2%), and s.c. 300 mg qw (-44.0%) doses. Reductions from baseline in HDL-C (-31.4%, -27.9%, and -30.3%, respectively), apoB (-42.3%, -38.8%, and -32.5%, respectively), and triglycerides (-51.3%, -53.4%, and -47.7%, respectively) were also similar across these dosing regimens. A smaller degree of LDL-C lowering (and other lipid lowering) was observed for the i.v. 5 mg/kg q4w (-23.5%) and s.c. 300 mg q2w (-38.5%) doses.

Hypertriglyceridemia: POTENTIAL BENEFIT

The ability of evinacumab to effectively lower triglycerides was found to be variable across populations with hypertriglyceridemia in Phase 1 and Phase 2 studies. Evinacumab significantly reduced triglycerides as well as VLDL, apoB, and apoC3 levels in patients with mixed dyslipidemia (LDL-C ≥100 mg/dL and modestly elevated triglycerides >150 and ≤450 mg/dL), and those with moderate hypertriglyceridemia (≥450 and <1,500 mg/dL), but was less effective in the context of severe hypertriglyceridemia (>1,000 mg/dL) associated with mutations in the LPL pathway.

In a Phase 1 single ascending dose (SAD) trial (NCT01749878) in patients with mixed dyslipidemia (n=83) single subcutaneous doses of evinacumab dose-dependently lowered triglycerides, with placebo-adjusted reductions up to -55% for the highest tested dose of 250 mg [15]. A similar degree of triglyceride lowering was achieved with the three tested doses administered intravenously, 5, 10, and 20 mg/kg, with placebo-adjusted reductions of -80.3%, -88.0% and -83.9%, respectively. While the higher i.v. doses did not increase the degree of triglyceride lowering, they did extend the duration of the effect. Triglyceride levels were reduced to a similar degree in a multiple ascending dose (MAD) trial (NCT02107872) in the same population (n=56), with median placebo-adjusted reductions of -88.2% in the 20 mg/kg q4w i.v. group, -51.9% in the 300 qw s.c. group, and -50.3% 450 qw s.c. group [15]. Significant reductions were also observed in the 20 mg/kg q4w i.v. and 300 mg qw s.c. groups for VLDL-C (-91.2% and -53.9%, respectively), apoB (-30.7% and -23.7%, respectively), and LDL-C (-25.1%, and -22.0%, respectively). Single intravenous doses of 10 mg/kg evinacumab significantly reduced triglycerides by a median of -81.8% (vs -20.6%) and VLDL-C by -82.2% (vs -0.8%) in a cohort of patients with moderate hypertriglyceridemia (n=7) compared to placebo [16]. These participants also experienced an increase in LDL-C up to 54.4% with evinacumab (vs 5.5% for placebo). However, the response to evinacumab (250 mg s.c. or 20 mg/kg i.v.) was highly variable in a cohort of patients with LPL pathway variants and severe hypertriglyceridemia (n=9), with triglyceride reductions ranging from -0.9% to -93.2%. LDL-C levels increased by 74.4% (vs -12.5% for placebo) and 79.6% (vs -53.4% for placebo) for the evinacumab 20 mg/kg i.v. and 250 mg s.c. dosing groups, respectively [16]. The increase in LDL-C levels is thought to arise due to the enhanced conversion of VLDL-C to LDL-C particles.

A similar trend was observed in a randomized, placebo-controlled Phase 2 trial in patients with severe hypertriglyceridemia (n=51) (NCT03452228) treated with evinacumab (15 mg/kg i.v. q4w) for 12 weeks [17]. The study included three cohorts with hypertriglyceridemia and chylomicronemia syndrome (buildup of chylomicrons due to impaired breakdown of lipid particles) associated with different genetic backgrounds: familial with bi-allelic loss-of-function LPL pathway mutations (n=17); multifactorial with heterozygous loss-of-function LPL pathway mutations (n=15); and multifactorial without LPL pathway mutations (n=19). The study overall did not meet its primary endpoint of the mean percent triglyceride lowering, but the values were not normally distributed. A post hoc analysis of the median percent change in triglycerides revealed stark differences in the triglyceride lowering across the cohorts depending on the level of LPL functionality. Significant median percent reductions in triglycerides were observed with evinacumab in those with LPL function (-81.7%) and partial LPL function (-64.8%), but not in patients lacking LPL function, indicating that the triglyceride lowering effect of evinacumab is dependent on LPL [18]. There was a trend toward an increase in LDL-C levels, however, there were also

trends toward reductions in non-HDL-C, apoB, and remnant cholesterol, suggesting an overall improvement to the lipid profile.
These studies suggest that certain subpopulations with elevated triglycerides may benefit from evinacumab, but it has not yet been approved for use as a triglyceride lowering therapy.

Residual risk: POTENTIAL BENEFIT
Triglyceride-rich lipoproteins (TRLs) and their cholesterol-enriched remnants are thought to play a role in residual cardiovascular risk, or the risk for atherosclerotic cardiovascular disease that remains after effective LDL-C lowering [19]. Elevated levels of triglycerides in the liver promote the production of VLDL. Triglycerides are removed from VLDL and chylomicrons via LPL as well as the enzymes hepatic triglyceride lipase and endothelial lipase. In the liver, these VLDL remnants can be eliminated or converted to LDLs. The reduction in triglycerides and VLDLs observed with evinacumab likely reflect the enhancement of LPL and endothelial lipase activity stemming from the inhibition of ANGPTL3.
A post hoc analysis of three RCTs found that levels of TRLs decreased by over 50% with the highest tested doses of evinacumab (15 mg/kg q4w i.v. or 300 mg qw s.c. or 450 mg qw s.c.), while levels of TRLs generally increased in the corresponding placebo groups [20]. This suggests that evinacumab and other ANGPTL3 lowering therapies may play a role in reducing triglyceride-mediated residual cardiovascular risk.

Preclinical and early clinical studies (from Nick's 2020 ANGPTL3-Targeted Therapies report)
Evinacumab treatment in a mouse model of atherosclerosis (APOE*3Leiden.CETP) reduced total cholesterol, triglycerides, and apoB. It also reduced atherosclerotic lesion size (-39%) and necrotic content in severe type IV and V lesions (-45%) [2]. Triglycerides, non-HDL-C, and HDL-C were also reduced in dyslipidemic cynomolgus monkeys after evinacumab treatment [21].
In a phase 1 single-ascending dose safety study in 83 patients, evinacumab (given either intravenously up to 20mg/kg or subcutaneously up to 250 mg) reduced levels of triglycerides by up to 76%, LDL-C by up to 23.2%, and HDL-C by up to 18.4%[4].

Safety: Evinacumab is generally well-tolerated. Reported cases of liver enzyme elevations in trials were relatively low. Commonly reported adverse events include fatigue, dizziness, and nasal-respiratory infections. It may also induce fetal abnormalities.

Types of evidence:

- 2 meta-analyses of RCTs
- 1 Phase 3 trial in HoFH (+ long-term extension study)
- 2 Phase 2 trials for hypercholesterolemia
- 1 Phase 2 trial in severe hypertriglyceridemia
- 2 Phase 1 trials in mixed dyslipidemia
- 1 Post hoc analysis of 3 RCTs
- 1 observational study of real-world use in HoFH
- Numerous laboratory studies

Evinacumab has been found to be well-tolerated and demonstrated good safety in clinical trials and published reports of real-world use [4; 22]. Meta-analyses and post-hoc analyses of RCTs indicate that the adverse event rates were largely balanced between evinacumab and placebo arms in patient populations with dyslipidemias [4; 20].

In the Phase 3 ELIPSE trial in patients with homozygous familial hypercholesterolemia (HoFH) (n=65), adverse event rates were higher in the placebo-treated group, and there were no adverse cardiovascular events in either treatment group over the 24-week double-blind treatment period [8]. An influenza-like illness was more common in the evinacumab-treated group (11% vs 0%), while none of the participants developed anti-drug antibodies to evinacumab over the course of the study. Notably, rates of liver enzyme elevations (ALT and AST) were not elevated with evinacumab. In the 24-week open-label extension period (n=64), only four participants experienced mild to moderate treatment-emergent adverse events that were considered drug related, which included a hypersensitivity reaction, infusion-related reactions, fatigue, itching, and muscle spasms [9]. There were no drug-related serious adverse events and no clinically relevant changes in liver enzymes or functional parameters. In an open-label extension study with follow-up out to 2.5 years including HoFH patients (n=116) from multiple RCTs, there were two cases of treatment-emergent anti-evinacumab antibodies, and two cases of liver function abnormalities considered related to evinacumab [10].

A similar safety profile has been observed in cohorts of the open-label study with longer follow-up periods. In a French cohort with a median follow-up of 3.5 years, there were a few mild adverse events which resolved on their own, including swelling, tingling, headache, and fatigue [13]. In an Italian cohort

with at least five years of follow-up, there were no reported treatment-emergent adverse events or meaningful changes in laboratory measures [12]. There have been no cases of adverse cardiovascular events to date in either cohort. It should be noted that patients with HoFH tend to be treated with multiple lipid-lowering therapies, such as statins, ezetimibe, LDL apheresis, lomitapide, and PCSK9 inhibitors, thus these studies indicate that evinacumab can be safely used in combination with a variety of other lipid-lowering medications.

A relatively similar safety profile has been observed in other clinically tested patient populations, such as mixed dyslipidemia and moderate hypertriglyceridemia [9; 15]. In a Phase 1 SAD trial in participants with mixed dyslipidemia (n=83), there was a higher percentage of participants experiencing liver enzyme elevations with evinacumab relative to placebo (ALT 11.3% vs 0%) (AST 6.5% vs 0%) [15]. While the adverse event profile was also similar in participants with severe hypertriglyceridemia, a subset of this population experienced a shift in their lipid profile resulting in an increase in LDL-C [16; 17]. Adverse events occurring more frequently with evinacumab in this population included abdominal pain, headache, constipation, abdominal discomfort, liver enzyme (ALT and AST) elevations, back pain, contusion, dizziness, herpes zoster and sinusitis [17].
Since evinacumb's lipid lowering mechanism involves the inhibition of LPL, it does not effectively lower lipids in individuals with mutations in the LPL pathway [17; 18].

Evinacumab is approved for use with i.v. administration, but several trials have included arms testing it with subcutaneous administration. The safety profile was largely comparable between the i.v. and s.c. routes of administration [14; 15]. In a Phase 2 trial in patients with hypercholesterolemia, including 160 participants receiving s.c. treatment and 106 participants receiving i.v. treatment, there were no clinically significant differences in adverse events between the two groups [14]. Relative to placebo, adverse events that occurred more frequently with subcutaneous evinacumab were urinary tract infection (11% vs. 8%), injection-site erythema (6% vs. 3%), arthralgia (5% vs. 3%), and myalgia (5% vs. 0%). Adverse events more common with intravenous evinacumab, relative to placebo were abdominal pain (6% vs. 0%), back pain (7% vs. 6%), dizziness (7% vs. 0%), fatigue (7% vs. 6%), pain in an arm or leg (7% vs. 6%), nausea (7% vs. 0%), and nasopharyngitis (12% vs. 6%).

The FDA prescribing label for evinacumab indicates that the most common adverse reactions (≥5%) reported in clinical studies (≥5%) were nasopharyngitis, influenza-like illness, dizziness, rhinorrhea, nausea, and fatigue.
The label for evinacumab contains warnings for hypersensitivity reactions as well as for embryo-fetal

abnormalities. As a result, it is recommended that individuals taking this medication use contraception during treatment and for at least five months after completing the last dose.

Drug interactions: According to Drugs.com, there are three known drug interactions with evinacumab. Efgartigimod alfa, rozanolixizumab, and nipocalimab, which are monoclonal antibodies targeting the neonatal Fc receptor, and used in the treatment of myasthenia gravis, can reduce blood levels and efficacy of evinacumab.

Sources and dosing:

Evinacumab is approved in the US for use in patients, aged 5 years and older, with homozygous familial hypercholesterolemia (HoFH), as an adjunct to other LDL-C lowering therapies. It is marketed by Regeneron under the tradename Evkeeza®. Outside of the US, it is marketed by Ultragenyx Pharmaceutical Inc. In early 2025, the European Commission extended the approval for Evkeeza® to children with HoFH aged six months and older (Press release).
The recommended dose in this population is 15 mg/kg administered via intravenous infusion over 60 minutes every 4 weeks.

Research underway:

According to Clinicaltrials.gov, there are currently no active trials testing evinacumab.

Search terms:
Pubmed, Google: Evinacumab

- Cardiovascular, cholesterol, clinical trial, meta-analysis, safety

Websites visited for Evinacumab:

- Clinicaltrials.gov
- Drugs.com
- WebMD.com
- DrugBank.ca
- Cafepharma

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