Evolocumab

Enzymes (1) Biointeractions (1)

IDENTIFICATION

Name

Evolocumab

Accession Number

DB09303

Type

Biotech

Groups

Approved

Biologic Classification

Protein Based Therapies
Monoclonal antibody (mAb)

Description

Evolocumab is a monoclonal antibody designed for the treatment of hyperlipidemia by Amgen. It is a subcutaneous injection approved by the FDA for individuals on maximum statin therapy who still require additional LDL-cholesterol lowering. It is approved for both homozygous and heterozygous familial cholesterolemia as an adjunct to other first-line therapies. Evolocumab is a human IgG2 monoclonal antibody that inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9). PCSK9 is a protein that targets LDL receptors for degradation, therefore reducing the liver's ability to remove LDL-cholesterol (LDL-C), or "bad" cholesterol, from the blood. Evolocumab is designed to bind to PCSK9 and inhibit PCSK9 from binding to LDL receptors on the liver surface, resulting in more LDL receptors on the surface of the liver to remove LDL-C from the blood. Evolocumab is the second PCSK9 inhibitor on the market, first being alirocumab.

Protein structure

Protein chemical formula

$C_{6242}H_{9648}N_{1668}O_{1996}S_{56}$

Protein average weight

141800.0 Da

Sequences

Not Available

Synonyms

Not Available

External IDs

AMG-145

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END	
Repatha	Solution	120 mg	Subcutaneous	Amgen	2017-04-04	Not applicable	
Repatha	Solution	140 mg	Subcutaneous	Amgen	2015-09-28	Not applicable	
Repatha	Injection, solution	140 mg	Subcutaneous	Amgen Europe B.V.	2015-07-17	Not applicable	
Repatha	Injection, solution	140 mg	Subcutaneous	Amgen Europe B.V.	2015-07-17	Not applicable	
Repatha	Injection, solution	140 mg/mL	Subcutaneous	Amgen	2015-08-31	Not applicable	
Repatha	Injection, solution	140 mg	Subcutaneous	Amgen Europe B.V.	2015-07-17	Not applicable	

Repatha	Kit		Subcutaneous	Amgen	2016-08-01	Not applicable	
Repatha	Injection, solution	140 mg/mL	Subcutaneous	Amgen	2015-08-31	Not applicable	
Repatha	Injection, solution	140 mg	Subcutaneous	Amgen Europe B.V.	2015-07-17	Not applicable	

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Categories

Amino Acids, Peptides, and Proteins

Antibodies

Blood Proteins

Cardiovascular System

Globulins

Immunoglobulins

Immunoproteins

Lipid Modifying Agents

Lipid Modifying Agents, Plain

PCSK9 Inhibitor

Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) Inhibitors

Proteins

Serum Globulins

UNII

LKC0U3A8NJ

CAS number

1256937-27-5

PHARMACOLOGY

Indication

additional LDL-cholesterol lowering.

Structured Indications

Atherosclerotic Cardiovascular Diseases

Heterozygous Familial Hypercholesterolemia

Homozygous Familial Hypercholesterolemia

Pharmacodynamics

Not Available

Mechanism of action

Evolocumab is a human IgG monoclonal antibody which targets PCSK9 (proprotein convertase subtilisin/kexin type 9). PCSK9 is a serine protease produced by the liver which binds LDL receptors and creates a complex to be targeted for lysosomal degradation. LDL receptors typically bind LDL-cholesterol ("bad" cholesterol) for cellular reuptake, therefore the formation of these complexes with PCSK9 inhibits LDL receptor recycling to the cell surface, resulting in decreased cellular reuptake of LDL-C and increased levels of free LDL-C in the plasma. Individuals with familial hypercholesterolemia often may have "gain of function" mutations in the PCSK9 molecules in their body, resulting in increased LDL-C plasma levels and a consequent cardiovascular risk. Evolocumab is able to bind both the normal PCSK9 and the "gain of function" mutant, D374Y. The exact mechanism of the binding has not been published, however the precursor molecule, mAb1, is indicative of the interaction. The mAb1 molecule binds on the catalytic site of PCSK9 next to the binding site for the LDL receptor and creates hydrogen bonds and hydrophobic interactions, resulting in the steric inhibition of binding between PCSK9 and the LDL receptor. Because the formation of complexes between LDL receptor and PCSK9 are prevented, the internalized LDL receptors are less likely to be degrated by lysosomes and may recycle to the surface of the cell to serve their function of removing LDL from the blood.

Absorption

Total bioavailability from subcutaneous injection was 82% in cynomolgus monkeys.

Volume of distribution

Not Available

Protein binding

Not Available

Metabolism

Route of elimination

Not Available

Half life

Not Available

Clearance

Evolocumab showed non-linear, dose-dependent clearance in healthy volunteers; clearance decreased with increasing dose.

Toxicity

Not Available

Affected organisms

Not Available

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

Search

DRUG	INTERACTION	DRUG GROUP
Anthrax immune globulin human	The therapeutic efficacy of Anthrax immune globulin human can be decreased when used in combination with Evolocumab.	Approved
Bacillus calmette-guerin substrain connaught live antigen	The therapeutic efficacy of Bacillus calmette-guerin substrain connaught live antigen can be decreased when used in combination with Evolocumab.	Approved, Investigational

Bacillus calmette-guerin substrain tice live antigen	The therapeutic efficacy of Bacillus calmette-guerin substrain tice live antigen can be decreased when used in combination with Evolocumab.	Approved
BCG vaccine	The therapeutic efficacy of BCG vaccine can be decreased when used in combination with Evolocumab.	Investigational
Clostridium tetani toxoid antigen (formaldehyde inactivated)	The therapeutic efficacy of Clostridium tetani toxoid antigen (formaldehyde inactivated) can be decreased when used in combination with Evolocumab.	Approved
Corynebacterium diphtheriae toxoid antigen (formaldehyde inactivated)	The therapeutic efficacy of Corynebacterium diphtheriae toxoid antigen (formaldehyde inactivated) can be decreased when used in combination with Evolocumab.	Approved
G17DT	The therapeutic efficacy of G17DT can be decreased when used in combination with Evolocumab.	Investigational
GI-5005	The therapeutic efficacy of GI-5005 can be decreased when used in combination with Evolocumab.	Investigational
Hepatitis A Vaccine	The therapeutic efficacy of Hepatitis A Vaccine can be decreased when used in combination with Evolocumab.	Approved
Hepatitis B Vaccine (Recombinant)	The therapeutic efficacy of Hepatitis B Vaccine (Recombinant) can be decreased when used in combination with Evolocumab.	Approved, Withdrawn

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Food Interactions

Not Available

REFERENCES

General References

1. Authors unspecified: Evolocumab (Repatha)--a second PCSK9 inhibitor to lower LDL-Cholesterol. Med Lett Drugs Ther. 2015 Oct 12;57(1479):140-1. [PubMed:26445204]
2. Page MM, Watts GF: Evolocumab in the treatment of dyslipidemia: pre-clinical and clinical pharmacology. Expert Opin Drug Metab Toxicol. 2015;11(9):1505-15. doi: 10.1517/17425255.2015.1073712. [PubMed:26293511]

External Links

KEGG Drug

D10557

PubChem Substance

ChEMBL

CHEMBL2364655

Drugs.com

Drugs.com Drug Page

Wikipedia

Evolocumab

ATC Codes

C10AX13 — Evolocumab

- C10AX — Other lipid modifying agents
- C10A — LIPID MODIFYING AGENTS, PLAIN
- C10 — LIPID MODIFYING AGENTS
- C — CARDIOVASCULAR SYSTEM

AHFS Codes

24:06.24 — Proprotein Convertase Subtilisin Kexin Type 9 (PCSK9) Inhibitors

FDA label

Download (1.18 MB)

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
0	Recruiting	Prevention	Dyslipidemia Associated With Type II Diabetes Mellitus / Percutaneous Coronary Intervention / Type 2 Diabetes Mellitus	1
1	Completed	Treatment	Hyperlipidemias	1
1	Completed	Treatment	Hyperlipidemias / Mixed hypercholesterolemia	1
2	Active Not Recruiting	Treatment	Atherosclerotic Cardiovascular Diseases / Hypercholesterolemia, Familial / Symptomatic Atherosclerosis / Type2 Diabetes	1

	Recruiting			
2	Completed	Treatment	High Blood Cholesterol Level	1
2	Completed	Treatment	Hypercholesterolemia and High Risk for Cardiovascular Events	1
2	Completed	Treatment	Hypercholesterolemia, Familial	1
2	Completed	Treatment	Hyperlipidemias	3
2	Not Yet Recruiting	Treatment	Acute Coronary Syndromes (ACS)	1

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PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Search

FORM	ROUTE	STRENGTH
Injection, solution	Subcutaneous	140 mg
Injection, solution	Subcutaneous	140 mg/mL
Kit	Subcutaneous	
Solution	Subcutaneous	120 mg
Solution	Subcutaneous	140 mg

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Prices

Not Available

PROPERTIES

State

Liquid

Experimental Properties

Not Available

TAXONOMY

Description

Not Available

Kingdom

Organic Compounds

Super Class

Organic Acids

Class

Carboxylic Acids and Derivatives

Sub Class

Amino Acids, Peptides, and Analogues

Direct Parent

Peptides

Alternative Parents

Not Available

Substituents

Not Available

Molecular Framework

External Descriptors

Not Available

ENZYMES

1. Proprotein convertase subtilisin/kexin type 9

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Inhibitor

General Function

Very-low-density lipoprotein particle receptor binding

Specific Function

Crucial player in the regulation of plasma cholesterol homeostasis. Binds to low-density lipid receptor family members: low density lipoprotein receptor (LDLR), very low density lipoprotein recepto...

Gene Name

PCSK9

Uniprot ID

Q8NBP7

Uniprot Name

Proprotein convertase subtilisin/kexin type 9

Molecular Weight

74285.545 Da

References

10.1517/17425255.2015.1073712. [PubMed:26293511]

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