Erenumab

Targets (1)

This drug entry is a **stub** and has not been fully annotated. It is scheduled to be annotated soon.

IDENTIFICATION

Name

Erenumab

Accession Number

DB14039

Type

Biotech

Groups

Approved

Biologic Classification

Protein Based Therapies
Monoclonal antibody (mAb)

Description

Erenumab (AMG-334) (INN; trade name Aimovig) is a human monoclonal antibody against the calcitonin gene-related peptide receptor (CGRPR) designed for the prevention of migraine.

Protein chemical formula

Protein average weight

Not Available

Sequences

```
> Erenumab (Heavy chain)
QVQLVESGGGVVQPGRSLRLSCAASGFTFSSFGMHWVRQAPGKGLEWVAVISFDGSIKYS
VDSVKGRFTISRDNSKNTLFLQMNSLRAEDTAVYYCARDRLNYYDSSGYYHYKYYGMAVW
GQGTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGV
HTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCP
APPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKP
REEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTL
PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLT
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
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> Erenumab (Light chain)
QSVLTQPPSVSAAPGQKVTISCSGSSSNIGNNYVSWYQQLPGTAPKLLIYDNNKRPSGIP
DRFSGSKSGTSTTLGITGLQTGDEADYYCGTWDSRLSAVVFGGGTKLTVLGQPKANPTVT
LFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGSPVKAGVETTKPSKQSNNKYAASS
YLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
```

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Synonyms

Not Available

External IDs

AMG 334 / AMG-334

Categories

Not Available

UNII

Not Available

CAS number

1582205-90-0

Indication

Erenumab is indicated for the preventative treatment of migraine in adults [FDA Label].

Structured Indications

Not Available

Pharmacodynamics

As a human monoclonal antibody designed to specifically bind with and antagonize the calcitonin gene-related peptide (CGRP) receptor, there is the possibility that erenumab could interfere with natural activities of CGRP that may not be immediately or directly associated with migraines. For example, at peripheral synapses, CGRP released from trigeminal terminals results in vasodilation by way of CGRP receptor on smooth muscle cells of meningeal and cerebral blood vessels, making CGRP a potent general arterial vasodilator [1]. Antagonism of CGRP receptors responsible for such vasodilation could theoretically result in vasoconstriction and raises in blood pressure.

In a randomised, double-blind, placebo-controlled study in healthy volunteers, concomitant administration of erenumab (140 mg intravenous, single dose) with sumatriptan (12 mg subcutaneous, given as two 6 mg doses separated by one hour) had no effect on resting blood pressure compared with sumatriptan alone, however [FDA Label]. Please note that erenumab is indicated for subcutaneous use only, though [FDA Label].

Mechanism of action

Erenumab is a human monoclonal antibody that has been designed to bind specifically to the calcitonin gene-related peptide (CGRP) receptor and antagonize the CGRP receptor function [FDA Label].

Studies since 1985 have demonstrated that CGRP levels increase during acute migraine attacks in migraine-suffering patients but normalize after efficacious sumatriptan therapy [1]. Moreover, research has also shown that intravenous administration of CGRP can induce

migraine-like attacks in migraine-suffering patients [1]. For all these reasons, the binding and antagonism of CGRP receptors was designed to be mechanism of action for erenumab to take advantage of in reversing the migraine-inducing activity of natural CGRP.

CGRP and its receptor are expressed in both the peripheral and the central nervous system [2]. In addition to playing a role in cranial nociception, CGRP is also a potent general arterial

vessels [A].

U Calcitonin gene-related peptide type 1 receptor

Not Available

Human

Absorption

Following a single subcutaneous dose of 70 mg or 140 mg erenumab administered to healthy adults, the median peak serum concentrations were attained in about 6 days, and the estimated absolute bioavailability was approximately 82% [FDA Label].

Volume of distribution

After a single 140 mg intravenous dose, the mean (SD) volume of distribution during the terminal phase (Vz) was estimated to be approximately 3.86 (0.77) L [FDA Label].

Protein binding

Readily accessible data regarding the protein binding of erenumab is not available, although it is reported that erenumab is capable of 50% to 99% total inhibition of calcitonin gene-related peptide receptors with dosages of 255 ng/mL and 1134 ng/mL, respectively [2].

Metabolism

Erenumab CGRP antibodies demonstrate a low risk for drug-drug interactions and hepatotoxicity since they are predominantly metabolized by degradation into peptides and single amino acids [1].

Route of elimination

Two elimination phases are observed for erenumab. At low concentrations, the elimination is mainly through saturable binding to target (CGRP receptor), while at higher concentrations the elimination of erenumab is primarily through a non-specific, non-saturable proteolytic pathway [FDA Label]. These phases correspond to studies that demonstrated two parallel elimination pathways: (a) a slow non-specific elimination pathway through the hepatic reticuloendothelial system, and (b) a rapid saturable elimination pathway mediated by degradation or internalization of the erenumab-receptor complex [2].

Half life

Less than 2-fold accumulation was observed in trough serum concentrations (Cmin) for episodic and chronic migraine patients following subcutaneous administration of 70 mg once-monthly and 140 mg once-monthly doses [FDA Label]. Serum trough concentrations approached steady state by 3 months of dosing [FDA Label]. The effective half-life of erenumab was observed to be 28 days [FDA Label].

Clearance

Certain studies show that the population estimate of linear clearance is independent of erenumab concentrations and stays approximately constant at 0.214 L/day (95% CI: 0.191–0.243) [2]. In contrast, the nonlinear clearance is dependent on the target receptor density and the amount of erenumab bound to the receptors [2]. Nevertheless, the maximal nonlinear clearance was observed to be about 1.84L/day [2].

Toxicity

Not Available

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

Not Available

Food Interactions

Not Available

REFERENCES

1. Deen M, Correnti E, Kamm K, Kelderman T, Papetti L, Rubio-Beltran E, Vigneri S, Edvinsson L, Maassen Van Den Brink A: Blocking CGRP in migraine patients - a review of pros and cons. J Headache Pain. 2017 Sep 25;18(1):96. doi: 10.1186/s10194-017-0807-1. [PubMed:28948500]
2. Vu T, Ma P, Chen JS, de Hoon J, Van Hecken A, Yan L, Wu LS, Hamilton L, Vargas G: Pharmacokinetic-Pharmacodynamic Relationship of Erenumab (AMG 334) and Capsaicin-Induced Dermal Blood Flow in Healthy and Migraine Subjects. Pharm Res. 2017 Sep;34(9):1784-1795. doi: 10.1007/s11095-017-2183-6. Epub 2017 Jun 7. [PubMed:28593473]

External Links

KEGG Drug

D10928

Wikipedia

Erenumab

FDA label

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CLINICAL TRIALS

Clinical Trials

Not Available

PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Not Available

Patents

Not Available

PROPERTIES

State

Solid

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

Substituents

Not Available

Molecular Framework

Not Available

External Descriptors

Not Available

TARGETS

1. Calcitonin gene-related peptide type 1 receptor

Kind

Protein

Organism

Human

Pharmacological action

Unknown

General Function

Receptor for calcitonin-gene-related peptide (CGRP) together with RAMP1 and receptor for adrenomedullin together with RAMP3 (By similarity). Receptor for adrenomedullin together with RAMP2. The activity of this receptor is mediated by G proteins which activate adenylyl cyclase.

Specific Function

Adrenomedullin receptor activity

Gene Name

CALCRL

Uniprot ID

Q16602

Calcitonin gene-related peptide type 1 receptor

Molecular Weight

52928.98 Da

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