

# Galcanezumab

Targets (2)

## IDENTIFICATION

### Name

Galcanezumab

### Accession Number

DB14042

### Type

Biotech

### Groups

Investigational

### Biologic Classification

Protein Based Therapies  
Monoclonal antibody (mAb)

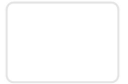
### Description

LY2951742/galcanezumab is a fully humanized monoclonal antibody against human calcitonin gene-related peptide (CGRP) that is developed by ELi Lilly and Company <sup>[1]</sup>. This therapy is given as a single subcutaneous injection twice a month and ongoing clinical trials for the agent are for episodic and chronic migraine as well as cluster headaches <sup>[5]</sup>.

### Protein chemical formula

Not Available

### Protein average weight



```
IQKFADRVTITADKSTSTAYMELSSLRSED TAVYYCARLSDYVSGFGYWGQGT TVTSSA  
STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSG  
LYSLSSVTVPSSSLGKTYTCNV DHKPSNTKVKDRVESKYGPPCPPCPAPEAAGGPSVF  
LFPPKPKDTLMISRTPEVTCVVDV SQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYR  
VVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKN  
QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVL DSDGSFFLYSRLTVDKSRWQEGN  
VFSCSVMHEALHNHYTQKSLSLGLG
```

>galcanezumab|Light

```
DIQMTQSPSSLSASVGDRVTITCRASKDISKYL NWYQQKPGKAPKLLIYYTSGYHSGVPS  
RFSGSGSGTDFTLTISLQPEDFATYYCQQGDALPPT FGGGKVEIKRTVAAPSVFIFPP  
SDEQLKSGTASVCLLNRFYPREAKVQWKVDNAL QSGNSQESVTEQDSKDSTYLSSTLT  
LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
```

[Download FASTA Format](#)

## Synonyms

Not Available

## External IDs

LY2951742

## Categories

Not Available

## UNII

[55KHL3P693](#)

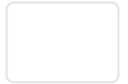
## CAS number

1578199-75-3

## PHARMACOLOGY

### Indication

Galcanezumab is a humanized monoclonal antibody that may be effective in migraine prophylaxis by binding endogenous human calcitonin gene-related peptide (CGRP) <sup>[3]</sup>.



[1]. Additionally, post hoc efficacy analyses showed that 32% in the galcanezumab group versus 18% in the placebo group were complete responders [1]. Finally, the most commonly reported adverse events associated with galcanezumab use are headache, nasopharyngitis, hematuria, dermatitis, diarrhea, toothache, and increased alanine aminotransferase (ALT) [3].

## Mechanism of action

Galcanezumab is a fully humanized monoclonal antibody designed and manufactured specifically against calcitonin gene-related peptide (CGRP) [1]. It binds avidly to human CGRP, with a binding affinity (Kd) of 31 pM (4.5 ng/mL).

Studies since 1985 have demonstrated that CGRP levels increase during acute migraine attacks in migraine-suffering patients but normalize after efficacious sumatriptan therapy [6]. Moreover, research has also shown that intravenous administration of CGRP can induce migraine-like attacks in migraine-suffering patients [6]. For all these reasons, the binding of CGRP to interfere with its activity was specifically designed to be the form and mechanism of action for galcanezumab to take advantage of in reversing the migraine-inducing activity of natural CGRP. The binding of galcanezumab to natural endogenous CGRP subsequently interferes with its activities, such as its binding to CGRP receptors, for example.

Studies have also shown that humanized monoclonal antibodies against CGRP have proven successful in reducing the frequency of migraine headaches in early clinical trials as a preventative therapeutic [3].

### A Calcitonin gene-related peptide 1

antibody

Human

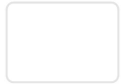
### A Calcitonin gene-related peptide 2

antibody

Human

## Absorption

Following single dose subcutaneous administration, there appeared to be an extended period of absorption, with a median time to peak concentration (Tmax) between Days 7 and 14 [3]. Cmax and the area under the concentration-time curve from dosing to infinity (AUC (0-∞)) are generally considered to be dose proportional over a dose range [3].



### Protein binding

Readily accessible data regarding the protein binding of galcanezumab is not available.

### Metabolism

Monoclonal antibody agents like galcanezumab are not expected to generate toxic metabolites as they generally undergo proteolysis to their constituent amino acids [7].

### Route of elimination

Monoclonal antibody agents like galcanezumab are generally not eliminated via hepatic, renal, or biliary routes [7].

### Half life

The mean serum half-life of galcanezumab is similar at all dose levels at about 25-30 days [3].

### Clearance

It is noted that the clearance of galcanezumab is by proteolysis [3].

### Toxicity

The most common adverse effects associated with galcanezumab during clinical trials include headache, nasopharyngitis, hematuria, and contact dermatitis [3]. However, with the exception of hematuria which was not present in placebo treatment arms, the frequencies of these events were similar to placebo [3]. Additional frequently reported adverse effects in subjects receiving galcanezumab were diarrhea, toothache, and increased alanine aminotransferase (ALT) [3].

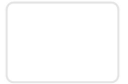
### Affected organisms

Humans and other mammals

### Pathways

Not Available

### Pharmacogenomic Effects/ADRs



## Drug Interactions ⓘ

Not Available

## Food Interactions

Not Available

## REFERENCES

### General References

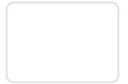
1. Pellesi L, Guerzoni S, Pini LA: Spotlight on Anti-CGRP Monoclonal Antibodies in Migraine: The Clinical Evidence to Date. *Clin Pharmacol Drug Dev.* 2017 Nov;6(6):534-547. doi: 10.1002/cpdd.345. Epub 2017 Apr 14. [[PubMed:28409893](#)]
2. Benemei S, Cortese F, Labastida-Ramirez A, Marchese F, Pellesi L, Romoli M, Vollesen AL, Lampl C, Ashina M: Triptans and CGRP blockade - impact on the cranial vasculature. *J Headache Pain.* 2017 Oct 10;18(1):103. doi: 10.1186/s10194-017-0811-5. [[PubMed:29019093](#)]
3. Monteith D, Collins EC, Vandermeulen C, Van Hecken A, Raddad E, Scherer JC, Grayzel D, Schuetz TJ, de Hoon J: Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of the CGRP Binding Monoclonal Antibody LY2951742 (Galcanezumab) in Healthy Volunteers. *Front Pharmacol.* 2017 Oct 17;8:740. doi: 10.3389/fphar.2017.00740. eCollection 2017. [[PubMed:29089894](#)]
4. Dodick DW, Goadsby PJ, Silberstein SD, Lipton RB, Olesen J, Ashina M, Wilks K, Kudrow D, Kroll R, Kohrman B, Bargar R, Hirman J, Smith J: Safety and efficacy of ALD403, an antibody to calcitonin gene-related peptide, for the prevention of frequent episodic migraine: a randomised, double-blind, placebo-controlled, exploratory phase 2 trial. *Lancet Neurol.* 2014 Nov;13(11):1100-1107. doi: 10.1016/S1474-4422(14)70209-1. Epub 2014 Oct 5. [[PubMed:25297013](#)]
5. Vollbracht S, Rapoport AM: New treatments for headache. *Neurol Sci.* 2014 May;35 Suppl 1:89-97. doi: 10.1007/s10072-014-1747-z. [[PubMed:24867844](#)]
6. 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](#)]
7. Presentation on CGRP, MONOCLONAL ANTIBODIES AND SMALL MOLECULES (-GEPANTS) [[File](#)]

### External Links

Wikipedia

[Galcanezumab](#)

## CLINICAL TRIALS



PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1	Completed	Not Available	<a href="#">Migraines</a>	1
1	Completed	Basic Science	<a href="#">Healthy Volunteers</a>	1
1	Completed	Basic Science	<a href="#">Migraine Disorders</a>	1
1	Completed	Other	<a href="#">Healthy Volunteers</a>	1
2	Active Not Recruiting	Treatment	<a href="#">Migraines</a>	1
2	Completed	Treatment	<a href="#">Migrainous Headache</a>	2
2	Terminated	Treatment	<a href="#">Knee Osteoarthritis (Knee OA)</a>	1
3	Active Not Recruiting	Treatment	<a href="#">Chronic Cluster Headache</a>	1
3	Active Not Recruiting	Treatment	<a href="#">Chronic Migraine</a>	1
3	Active Not Recruiting	Treatment	<a href="#">Migraines</a>	3

Showing 1 to 10 of 15 entries

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## PHARMACOECONOMICS

### Manufacturers

Not Available

### Packagers

Not Available

### Dosage forms

Not Available

### Prices

Not Available

### Patents

**State**

Solid

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**Experimental Properties**

Not Available

**TAXONOMY****Description**

Not Available

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**Kingdom**

Organic Compounds

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**Super Class**

Organic Acids

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**Class**

Carboxylic Acids and Derivatives

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**Sub Class**

Amino Acids, Peptides, and Analogues

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**Direct Parent**

Peptides

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**Alternative Parents**

Not Available

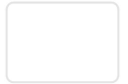
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**Substituents**

Not Available

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**Molecular Framework**



## TARGETS

**1. Calcitonin gene-related peptide 1****Kind**

Protein

**Organism**

Human

**Pharmacological action** Yes**Actions** Antibody**General Function**

Receptor binding

**Specific Function**

CGRP induces vasodilation. It dilates a variety of vessels including the coronary, cerebral and systemic vasculature. Its abundance in the CNS also points toward a neurotransmitter or neuromodulato...

**Gene Name**

CALCA

**Uniprot ID**[P06881](#)**Uniprot Name**

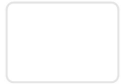
Calcitonin gene-related peptide 1

**Molecular Weight**

13897.755 Da

## References





## 2. Calcitonin gene-related peptide 2

### Kind

Protein

### Organism

Human

### Pharmacological action

Yes

### Actions

Antibody

### General Function

Neuropeptide hormone activity

### Specific Function

CGRP induces vasodilation. It dilates a variety of vessels including the coronary, cerebral and systemic vasculature. Its abundance in the CNS also points toward a neurotransmitter or neuromodulato...

### Gene Name

CALCB

### Uniprot ID

[P10092](#)

### Uniprot Name

Calcitonin gene-related peptide 2

### Molecular Weight

13705.56 Da

### References

1. Monteith D, Collins EC, Vandermeulen C, Van Hecken A, Raddad E, Scherer JC, Grayzel D, Schuetz TJ, de Hoon J: Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of



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