Guselkumab

Targets (1) Biointeractions (1)

IDENTIFICATION

Name

Guselkumab

Accession Number

DB11834

Type

Biotech

Groups

Approved, Investigational

Biologic Classification

Protein Based Therapies
Monoclonal antibody (mAb)

Description

Guselkumab is a human immunoglobulin G1 lambda (IgG1λ) monoclonal antibody that selectively blocks interleukin-23. IL-23 is an inflammatory cytokine that activates the CD4+ T-helper (Th17) cell pathway to mediate the inflammatory cascade that induces psoriatic plaque formation [2]. In clinical trials, guselkumab demonstrated improved skin clearance and symptomatic improvements in dermatological manifestations of psoriasis.

Developed by Janssen, the subcutenous injection form of guselkumab was approved in July 2017 under the market name Tremfya for the treatment of adult patients with moderate-to-severe plaque psoriasis.

Protein chemical formula

$C_{6402}H_{9864}N_{1676}O_{1994}S_{42}$

Sequences

```
>Heavy chain
EVQLVQSGAEVKKPGESLKISCKGSGYSFSNYWIGWVRQMPGKGLEWMGIIDPSNSYTRY
SPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARWYYKPFDVWGQGTLVTVSSAST
KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY
SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV
FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG
NVFSCSVMHEALHNHYTQKSLSLSPGK
```

```
>Light chain
QSVLTQPPSVSGAPGQRVTISCTGSSSNIGSGYDVHWYQQLPGTAPKLLIYGNSKRPSGV
PDRFSGSKSGTSASLAITGLQSEDEADYYCASWTDGLSLVVFGGGTKLTVLGQPKAAPSV
TLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAAS
SYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
```

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Synonyms

Not Available

External IDs

CNTO1959

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Tremfya	Injection	100 mg/mL	Subcutaneous	Janssen Biotech, Inc.	2017-07-13	Not applicable		
Tremfya	Solution	100 mg	Subcutaneous	Janssen Pharmaceuticals	2017-11-27	Not applicable		

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Categories

Amino Acids, Peptides, and Proteins

Globulins

Immunoglobulins

Immunoproteins

Interleukin-23 Antagonist

Misc. Skin and Mucous Membrane Agents

Proteins

Serum Globulins

UNII

089658A12D

CAS number

1350289-85-8

PHARMACOLOGY

Indication

Indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Associated Conditions

Severe Plaque psoriasis

Moderate Plaque psoriasis

Pharmacodynamics

Guselkumab is shown to reduce serum levels of IL-17A, IL-17F and IL-22 [Label].

Mechanism of action

Guselkumab targets the p19 alpha subunit of IL-23. While IL-23 promotes the normal inflammatory and immune responses, the p19 and p40 subunits of IL-23 are found to be over-expressed in the condition of psoriasis and other autoimmune inflammatory skin diseases [2, 4]. Guselkumab selectively binds to the p19 subunit of IL-23 in dendritic cells and keratinocytes and blocks its interaction with IL-23 receptor, which further prevents the release of other pro-inflammatory cytokines and chemokines via stimulation of immune cells such as Th17 cells [Label]. Thus,

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A	Interleukin-23 subunit alpha
	blocker
	Human

Absorption

Following a 100mg subcutaneous administration, the peak plasma concentration (Cmax) of guselkumab is 8.09 ± 3.68 mcg/mL which is reached after approximately 5.5 days [Label].

Volume of distribution

The apparent volume of distribution is 13.5 L [Label].

Protein binding

Not Available

Metabolism

Like other human IgG monoclonal antibodies, guselkumab is expected to be degraded into small peptides and amino acids via catabolic pathways [Label].

Route of elimination

Like other human IgG monoclonal antibodies, guselkumab is expected to be both renally and fecally excreted as smaller peptide units.

Half life

Mean half-life of guselkumab is approximately 15 to 18 days in subjects with plaque psoriasis [Label].

Clearance

Apparent clearance in subjects with plaque psoriasis is 0.516 L/day [Label].

Toxicity

Animal studies to assess the effect of guselkumab on carcinogenesis, mutagenesis and impairment on fertility have not been conducted. When subcutaneously injected into guinea pigs, the doses of guselkumab up to 100mg/kg twice-weekly demonstrated no effects on fertility parameters [Label].

Affected organisms

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 Guselkumab.	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 Guselkumab.	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 Guselkumab.	Approved
BCG vaccine	The therapeutic efficacy of BCG vaccine can be decreased when used in combination with Guselkumab.	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 Guselkumab.	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 Guselkumab.	Approved
G17DT	The therapeutic efficacy of G17DT can be decreased when used in combination with Guselkumab.	Investigational
GI-5005	The therapeutic efficacy of GI-5005 can be decreased when used in combination with Guselkumab.	Investigational
Hepatitis A Vaccine	The therapeutic efficacy of Hepatitis A Vaccine can be decreased when used in combination with Guselkumab.	Approved

Hepatitis B Vaccine (Recombinant)	The therapeutic efficacy of Hepatitis B Vaccine (Recombinant) can be decreased when used in combination with Guselkumab.	Approved, Withdrawn

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Food Interactions

Not Available

REFERENCES

General References

1. Sofen H, Smith S, Matheson RT, Leonardi CL, Calderon C, Brodmerkel C, Li K, Campbell K, Marciniak SJ Jr, Wasfi Y, Wang Y, Szapary P, Krueger JG: Guselkumab (an IL-23-specific mAb) demonstrates clinical and molecular response in patients with moderate-to-severe psoriasis. J Allergy Clin Immunol. 2014 Apr;133(4):1032-40. doi: 10.1016/j.jaci.2014.01.025. [PubMed:24679469]
2. Levin AA, Gottlieb AB: Specific targeting of interleukin-23p19 as effective treatment for psoriasis. J Am Acad Dermatol. 2014 Mar;70(3):555-61. doi: 10.1016/j.jaad.2013.10.043. Epub 2013 Dec 24. [PubMed:24373779]
3. Gaspari AA, Tyring S: New and emerging biologic therapies for moderate-to-severe plaque psoriasis: mechanistic rationales and recent clinical data for IL-17 and IL-23 inhibitors. Dermatol Ther. 2015 Jul-Aug;28(4):179-93. doi: 10.1111/dth.12251. [PubMed:26201310]
4. Fitch E, Harper E, Skorcheva I, Kurtz SE, Blauvelt A: Pathophysiology of psoriasis: recent advances on IL-23 and Th17 cytokines. Curr Rheumatol Rep. 2007 Dec;9(6):461-7. [PubMed:18177599]

External Links

PubChem Substance

347911245

Wikipedia

Guselkumab

AHFS Codes

84:92.00 — Misc. Skin and Mucous Membrane Agents

FDA label

Download (672 KB)

CLINICAL TRIALS

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1	Completed	Not Available	Healthy Volunteers	1
1	Completed	Treatment	Healthy Volunteers	1
1	Completed	Treatment	Psoriasis	2
1	Not Yet Recruiting	Other	Healthy Volunteers	1
2	Active Not Recruiting	Treatment	Psoriatic Arthritis	1
2	Completed	Treatment	Palmoplantaris Pustulosis	1
2	Completed	Treatment	Psoriasis	1
2, 3	Recruiting	Treatment	Crohn's Disease (CD)	1
3	Active Not Recruiting	Treatment	Palmoplantar Pustulosis	1
3	Active Not Recruiting	Treatment	Psoriasis	5

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PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Search

FORM	ROUTE	STRENGTH
Injection	Subcutaneous	100 mg/mL
Solution	Subcutaneous	100 mg

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Prices

Not Available

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

TARGETS

1. Interleukin-23 subunit alpha

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Blocker

General Function

Not Available

Specific Function

Associates with IL12B to form the IL-23 interleukin, a heterodimeric cytokine which functions in innate and adaptive immunity. IL-23 may constitute with IL-17 an acute response to infection in peri...

Gene Name

IL23A

Uniprot ID

Q9NPF7

Uniprot Name

Interleukin-23 subunit alpha

Molecular Weight

20729.56 Da

References

10.1007/s13555-015-0092-3. Epub 2015 Dec 29. [PubMed:26714681]

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