Cenegermin

Targets (1) Biointeractions (1)

IDENTIFICATION

Name	Cenegermin
Accession Number	DB13926
Type	Biotech
Groups	Approved, Investigational
Biologic Classification	Protein Based Therapies Other protein based therapies

Description

Cenegermin is a human beta-nerve growth factor (beta-ngf)-(1-118)- peptide (non-covalent dimer) produced in escherichia coli. It received European Union Approval in July, 2017 for the treatment of moderate to severe neurotrophic keratitis. Cenegermin received approval from the US FDA a year later in August of 2018 [1].

Neurotrophic keratitis is a degenerative disease resulting from a loss of corneal sensation [1]. The loss of corneal sensation impairs corneal health causing progressive damage to the top layer of the cornea, including corneal thinning, ulceration, and perforation in severe cases [1]. The prevalence of neurotrophic keratitis has been estimated to be less than five in 10,000 individuals [1].

While the prevalence of neurotrophic keratitis is low, the impact of this serious condition and its associated sequelae on an individual patient can be debilitating. Many currently available therapeutic options for treating the condition involve surgical interventions - surgeries that are typically only palliative [1]. The approval of cenegermin consequently provides a novel topical treatment that has the potential capacity to offer total corneal healing for many patients who may use the agent [1].

In particular, cenegermin was granted Priority Review designation, under which the FDA's goal is to take action on an application within six months of application filing where the agency determines that the drug, if approved, would provide a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious condition [1]. Cenegermin also received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases [1].

Protein chemical formula	Not Available
Protein average weight	Not Available
Sequences	Not Available
Synonyms	cenegermin-bkbj rhNGF

Prescription Products

Show 10 entries Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END

Showing 1 to 1 of 1 entries

International/Other Brands	Oxervate (Dompe farmaceutici s.p.a.)
Categories	Not Available
UNII	B6E7K36KT8
CAS number	1772578-74-1

PHARMACOLOGY

Indication	Cenegermin is indicated for the treatment of moderate (persistent epithelial defect) or severe (corneal ulcer) neurotrophic keratitis in adults [Label].
Associated Conditions	Neurotrophic Keratitis
Pharmacodynamics	Little to no pharmacodynamic studies have yet been conducted in humans [Label].
Mechanism of action	Cenegermin is a recombinant form of human nerve growth factor [Label]. Neurotrophic keratitis is a degenerative disease resulting from a loss of corneal sensation [1]. The loss of corneal sensation impairs corneal health causing progressive damage to the top layer of the cornea, including corneal thinning, ulceration, and perforation in severe cases [1]. Nerve growth factor is subsequently an endogenous protein involved in the differentiation and maintenance of neurons, which acts through specific high-affinity (i.e., TrkA) and low-affinity (i.e. p75NTR) nerve growth factor receptors [Label]. Nerve growth factor receptors are expressed in the anterior segment of the eye (cornea, conjunctiva, iris, ciliary body, and lens), by the lacrimal gland, and by posterior segment intraocular tissues [Label]. The treatment with cenegermin, administered as eye drops, is intended to allow restoration of corneal integrity [Label].

TARGET	ACTIONS	ORGANISM
U High affinity nerve growth factor receptor	stimulator	Humans

Absorption	Cenegermin is mostly removed from the eye with the tear production and through the naso-lacrimal duct; the minor portion that is absorbed occurs mostly in the conjunctiva and peri-orbital tissue and to a minor extent through the cornea following ocular administration [2]. Pharmacokinetic profiling of patients included in studies found no accumulation effect of cenegermin [2]. In general, the systemic absorption of cenegermin is negligible [2].
Volume of distribution	After eye drop administration, cenegermin is distributed particularly in the anterior portion of the eye, although a study with radiolabelled cenegermin in rats has shown that it also reaches the retina and other posterior parts of the eye at doses significantly higher than those administered by eye drops in humans to treat neurotrophic keratitis [2]. At the ocular doses, cenegermin is not distributed throughout body tissues as there is no systemic absorption above the natural baseline levels [2].
Protein binding	In general, the systemic absorption of cenegermin is negligible [2].
Metabolism	Ocularly administered cenegermin is mainly eliminated by tear secretion and the remainder mostly biotransformed by local tissue proteases [2].
Route of elimination	Cenegermin administered by eye drops is mostly eliminated with the tear secretion [2].

Elimination	
Half life	Half life data specific to human administration is not readily accessible or available [Label].
Clearance	ALthough the systemic absorption of cenegermin is negligible in general [2], clearance data specific to human administration is not readily accessible or available [Label].
Toxicity	There are no data from the use of cenegermin in pregnant women [Label]. Systemic exposure to cenegermin is negligible or does not occur [2]. As a precautionary measure, it is preferable to avoid the use of OXERVATE during pregnancy [2]. It is not known whether cenegermin is excreted in human milk [Label]. A risk to the suckling child cannot be excluded [2]. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from this therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman [2]. The safety and effectiveness of cenegermin have been established in the pediatric population [Label]. Use of cenegermin in this population is supported by evidence from adequate and well controlled trials of cenegermin in adults with additional safety data in pediatric patients from 2 years of age and older [Label]. Of the total number of subjects in clinical studies of cenegermin, 43.5 % were 65 years old and over [Label]. No overall differences in safety or effectiveness were observed between elderly and younger adult patients [Label]. There are no data on the effects of cenegermin on human fertility [Label].
Affected organisms	Humans and other mammals
Pathways	Not Available
Pharmacogenomic Effects/ADRs	Not Available

INTERACTIONS

Drug Interactions	Not Available
Food Interactions	Not Available

REFERENCES

General References

1. Dompe Farmaceutici SpA Cenegermin FDA Approval Press Release [Link]
2. Cenegermin EMA Label [File]
3. Cenegermin EMA Assessment Report [File]

External Links	Wikipedia	Cenegermin
FDA label	Download (575 KB)	

CLINICAL TRIALS

Clinical Trials

Show 10 entries Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1	Completed	Treatment	Glaucoma	1
1, 2	Completed	Treatment	Corneal Inflammation / Neurotrophic Keratitis / Ulcerative keratitis	1

2	Completed	Treatment	Dry Eye Syndrome (DES)	1
2	Completed	Treatment	Eye Dryness	1
2	Completed	Treatment	Neurotrophic Keratitis	1
2	Completed	Treatment	Ocular Discomfort	1

Showing 1 to 7 of 7 entries

PHARMACOECONOMICS

Manufacturers Not Available

Packagers Not Available

Dosage forms

Show 10 entries Search

FORM	ROUTE	STRENGTH
Solution / drops	Ophthalmic	20 ug/1mL

Showing 1 to 1 of 1 entries

Prices 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 Not Available

Substituents Not Available

Molecular Framework Not Available

External Descriptors Not Available

1. High affinity nerve growth factor receptor

Details

Kind	Protein
Organism	Humans
Pharmacological action	Unknown
Actions	Stimulator
General Function	Transmembrane receptor protein tyrosine kinase activity
Specific Function	Receptor tyrosine kinase involved in the development and the maturation of the central and peripheral nervous systems through regulation of proliferation, differentiation and survival of sympatheti...
Gene Name	NTRK1
Uniprot ID	P04629
Uniprot Name	High affinity nerve growth factor receptor
Molecular Weight	87496.465 Da

Drug created on December 01, 2017 11:18 / Updated on December 22, 2018 12:43

This project is supported by the **Canadian Institutes of Health Research** (award #111062), **Alberta Innovates - Health Solutions**, and by **The Metabolomics Innovation Centre (TMIC)**, a nationally-funded research and core facility that supports a wide range of cutting-edge metabolomic studies. TMIC is funded by **Genome Alberta**, **Genome British Columbia**, and **Genome Canada**, a not-for-profit organization that is leading Canada's national genomics strategy with funding from the federal government. Maintenance, support, and commercial licensing is provided by **OMx Personal Health Analytics, Inc.** Designed by **Educe Design & Innovation Inc.**