Dornase alfa

Targets (1)

IDENTIFICATION

Name

Dornase alfa

Accession Number

DB00003 (BTD00001, BIOD00001)

Type

Biotech

Groups

Approved

Biologic Classification

Protein Based Therapies
Recombinant Enzymes

Description

Dornase alfa is a biosynthetic form of human deoxyribunuclease I (DNase I) enzyme. It is produced in genetically modified Chinese hamster ovary (CHO) cells using recombinant DNA technology. The 260-amino acid sequence of dornase alfa is identical to the endogenous human enzyme. Dornase alfa cleaves extracellular DNA to 5´-phosphodinucleotide and 5´-phosphooligonucleotide end products without affecting intracellular DNA. In individuals with cystic fibrosis, extracellular DNA, which is an extremely viscous anion, is released by degenerating leukocytes that accumulate during inflammatory responses to infections. Enzymatic breakdown of this extracellular DNA appears to reduce sputum viscosity and viscoelasticity.

Protein structure

Protein chemical formula

$C_{1321}H_{1999}N_{339}O_{396}S_9$

Protein average weight

29253.9 Da

Sequences

```
>Dornase alfa sequence
LKIAAFNIQTFGETKMSNATLVSYIVQILSRYDIALVQEVRDSHLTAVGKLLDNLNQDAP
DTYHYVVSEPLGRNSYKERYLFVYRPDQVSAVDSYYYDDGCEPCGNDTFNREPAIVRFFS
RFTEVREFAIVPLHAAPGDAVAEIDALYDVYLDVQEKWGLEDVMLMGDFNAGCSYVRPSQ
WSSIRLWTSPTFQWLIPDSADTTATPTHCAYDRIVVAGMLLRGAVVPDSALPFNFQAAYG
LSDQLAQAISDHYPVEVMLK
```

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Synonyms

Deoxyribonuclease (human clone 18-1 protein moiety)

Dornase alfa, recombinant

Dornase alpha

Recombinant deoxyribonuclease (DNAse)

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Pulmozyme	Solution	1 mg/1mL	Respiratory (inhalation)	Genentech, Inc.	1993-12-30	Not applicable		
Pulmozyme 1mg/ml	Solution	1 mg	Respiratory (inhalation)	Hoffmann La Roche	1994-12-31	Not applicable		

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International/Other Brands

Amino Acids, Peptides, and Proteins

Cough and Cold Preparations

Decreased Respiratory Secretion Viscosity

Deoxyribonuclease I

Deoxyribonucleases

Endodeoxyribonucleases

Endonucleases

Enzymes

Enzymes and Coenzymes

Esterases

Expectorants

Hydrolases

Proteins

Recombinant Human Deoxyribonuclease 1

Recombinant Proteins

UNII

953A26OA1Y

CAS number

143831-71-4

PHARMACOLOGY

Indication

Used as adjunct therapy in the treatment of cystic fibrosis.

Associated Conditions

Cystic Fibrosis (CF)

contain very high concentrations of extracellular DNA released by degenerating leukocytes that accumulate in response to these infections. Dornase alfa hydrolyzes the DNA in sputum of CF patients and reduces sputum viscosity and viscoelasticity. The enzyme does not appear to affect sputum in the absence of an inflammatory response to infection, nor does it affect the sputum of healthy individuals.

Mechanism of action

Dornase alfa is a biosynthetic form of human DNase I. The enzyme is involved in endonucleolytic cleavage of extracellular DNA to 5´-phosphodinucleotide and 5´-phosphooligonucleotide end products. It has no effect on intracellular DNA. Optimal activity is dependent on the presence of divalent cations such as calcium and magnesium. Extracellular DNA is a viscous anionic polymer and its breakdown appears to improve the viscosity and viscoelasticity of purulent sputum of individuals with CF, thus reducing airflow obstruction. Dornase alfa does not seem to have any effect on non-purulent sputum.

A DNA

Not Available

Human

Absorption

Studies in rats and monkeys after inhalation of dornase alfa shows very little systemic absorption (less than 15% for rats and less than 2% for monkeys). The results were also witnessed in patients. Dornase alfa is also associated with very low accumulation with no serum concentration greater than 10ng/mL observed no matter the dose administered. Bioavailability: mean sputum concentrations of dornase alfa can be measured after 15 minutes. Onset is achieved within 3 to 7 days. Peak concentrations are achieved after 9 days.

Volume of distribution

In studies in rats and monkeys, the initial volume of distribution is similar to the serum volume. Concentrations in sputum decline rapidly after inhalation.

Protein binding

Not Available

Metabolism

Route of elimination

Not Available

Half life

Not Available

Clearance

Studies in rats indicate that, following aerosol administration, the disappearance half-life of dornase alfa from the lungs is 11 hours. In humans, sputum DNase levels declined below half of those detected immediately post-administration within 2 hours but effects on sputum rheology persisted beyond 12 hours.

Toxicity

Adverse reactions occur at a frequency of < 1/1000 and are usually mild and transient in nature. Reported adverse effects include chest pain (pleuritic/non-cardiac), fever, dyspepsia, voice alteration (hoarseness), pharyngitis, dyspnea, laryngitis, rhinitis, decreased lung function, rash, urticaria, and conjunctivitis. There is no evidence of carcinogenic or mutagenic properties. The safety of dornase alfa has not been studied in pregnant women, nursing women and children under the age of 5 years old.

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

No interactions found.

Food Interactions

General References

1. Cramer GW, Bosso JA: The role of dornase alfa in the treatment of cystic fibrosis. Ann Pharmacother. 1996 Jun;30(6):656-61. [PubMed:8792953]
2. Jones AP, Wallis C: Dornase alfa for cystic fibrosis. Cochrane Database Syst Rev. 2010 Mar 17;(3):CD001127. doi: 10.1002/14651858.CD001127.pub2. [PubMed:20238314]
3. Riethmueller J, Kumpf M, Borth-Bruhns T, Brehm W, Wiskirchen J, Sieverding L, Ankele C, Hofbeck M, Baden W: Clinical and in vitro effect of dornase alfa in mechanically ventilated pediatric non-cystic fibrosis patients with atelectases. Cell Physiol Biochem. 2009;23(1-3):205-10. doi: 10.1159/000204109. Epub 2009 Feb 18. [PubMed:19255515]

External Links

UniProt

P24855

Genbank

M55983

PubChem Substance

46507792

ChEMBL

CHEMBL1201431

Therapeutic Targets Database

DAP000981

PharmGKB

PA10318

RxList

RxList Drug Page

Drugs.com

Drugs.com Drug Page

Wikipedia

Dornase_alfa

ATC Codes

- R — RESPIRATORY SYSTEM

AHFS Codes

44:00.00 — Enzymes

FDA label

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MSDS

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CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
0	Unknown Status	Supportive Care	Head and Neck Carcinoma	1
1	Active Not Recruiting	Treatment	Peritoneal dialysis therapy / Peritoneal Dialysis, Continuous Ambulatory	1
1	Recruiting	Treatment	Healthy Volunteers	1
1	Withdrawn	Supportive Care	Coughing / Sjögren's Syndrome	1
1, 2	Recruiting	Treatment	Eye Dryness	1
1, 2	Recruiting	Treatment	Eye Dryness / Graft versus host disease in eye	1
2	Completed	Treatment	Asthma Bronchial	1
2	Completed	Treatment	Cystic Fibrosis (CF)	1
2	Completed	Treatment	Cystic Fibrosis (CF) / Sinusitis	1
2	Completed	Treatment	Lower Respiratory Tract Infection (LRTI) / Lung Transplant Infection	1

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Genentech, Inc

Packagers

Cardinal Health

Catalent Pharma Solutions

F Hoffmann-La Roche Ltd.

Genentech Inc.

Meda AB

Medpointe Pharmaceuticals

Dosage forms

Search

FORM	ROUTE	STRENGTH
Solution	Respiratory (inhalation)	1 mg/1mL
Solution	Respiratory (inhalation)	1 mg

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Prices

Search

UNIT DESCRIPTION	COST	UNIT
Pulmozyme 1 mg/ml Solution 2.5ml Plastic Container	77.06USD	plastic
Pulmozyme 1 mg/ml ampul	37.05USD	ml
Lufyllin 400 mg tablet	4.81USD	tablet
Lufyllin-400 tablet	4.62USD	tablet
Lufyllin-GG 200-200 mg tablet	3.99USD	tablet
Lufyllin-gg tablet	3.84USD	tablet
Lufyllin 200 mg tablet	3.21USD	tablet

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Patents

Search

PATENT NUMBER	PEDIATRIC EXTENSION	APPROVED	EXPIRES (ESTIMATED)	
CA2184581	No	2005-02-22	2015-02-28	
CA2137237	No	2004-10-26	2013-05-28	

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PROPERTIES

State

Liquid

Experimental Properties

PROPERTY	VALUE	SOURCE
melting point (°C)	67 °C	Chan, H.K. et al., Pharm Res. 13:756-761 (1996)
hydrophobicity	-0.083	Not Available
isoelectric point	4.58	Not Available

TAXONOMY

Description

Not Available

Kingdom

Organic Compounds

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

TARGETS

1. DNA

Kind
Nucleotide

Organism
Human

Pharmacological action
Yes

General Function: Used for biological information storage. **Specific Function:**

1. Cramer GW, Bosso JA: The role of dornase alfa in the treatment of cystic fibrosis. Ann Pharmacother. 1996 Jun;30(6):656-61. [PubMed:8792953]

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