



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 deoxyribonuclease 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

C₁₃₂₁H₁₉₉₉N₃₃₉O₃₉₆S₉

Protein average weight

29253.9 Da

Sequences

```
>Dornase alfa sequence
LKIAAFNIQTFGETKMSNATLVSYIVQILSRVDIALVQEV RDSHLTAVGKLLDNLNQDAP
DTYHYVWSEPLGRNSYKERYLFVYRPDQVSAVDSYYYDDGCEPCGNDTFNREPAIVRFFS
RFTEVREFAIIVPLHAAPGDAVAEIDALYDVYLDVQEKWGLEDMVMGDFNAGCSYVRPSQ
WSSIRLWTSPTFQWLIPDSADTTATPTHCA YDRIVVAGMLLRGAVVPDSALPFNFQAAYG
LSDQLAQAI SDHYPVEVMLK
```

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Synonyms

Deoxyribonuclease (human clone 18-1 protein moiety)

Dornase alfa, recombinant

Dornase alpha

Recombinant deoxyribonuclease (DNase)

Prescription Products

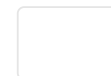
Search

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.

 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 [i](#)

Not Available

INTERACTIONS

Drug Interactions [i](#)

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[Download](#) (131 KB)**MSDS**[Download](#) (10.4 KB)

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

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Meda AB

Medpointe Pharmaceuticals

Dosage forms

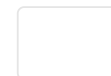
FORM	↕ ROUTE	↕ STRENGTH	↕
Solution	Respiratory (inhalation)	1 mg/1mL	
Solution	Respiratory (inhalation)	1 mg	

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Prices

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

PATENT NUMBER	PEDIATRIC EXTENSION	APPROVED	EXPIRES (ESTIMATED)	
CA2184581	<input type="radio"/> No	2005-02-22	2015-02-28	
CA2137237	<input type="radio"/> 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](#)]

Drug created on June 13, 2005 07:24 / Updated on October 30, 2018 18:33

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