PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

PULMOZYME® Inhalation solution

COMPOSITION

Each single-use ampoule contains 2 500 U (corresponding to 2,5 mg) of dornase alfa per 2,5 mℓ, corresponding to 1,0 mg/mℓ dornase alfa.

Inactive excipients: Sodium chloride, Calcium chloride dihydrate and Water for injection.

PHARMACOLOGICAL CLASSIFICATION

A 30.4 Biologicals Other

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Recombinant human DNase is a genetically engineered version of a naturally occurring human enzyme which cleaves extracellular DNA.

In vitro, dornase alfa hydrolyses DNA in infected sputum and greatly reduces the viscoelasticity of cystic fibrosis sputum.

Pharmacokinetic properties

***Absorption**:* Inhalation studies conducted in rats and non-human primates show a low percentage of dornase alfa systemic absorption, < 15 % for rats and < 2 % for monkeys. Consistent with the results of these animal studies, dornase alfa, administered to patients as an inhaled aerosol shows low systemic exposure.

Absorption of dornase alfa from the gastro-intestinal tract following oral administration to rats is negligible.

DNase is normally present in human serum. Inhalation of up to 40 mg dornase alfa for up to six days did not result in significant elevation of serum DNase concentrations above normal endogenous levels after 24 hours. No increase in serum DNase concentration greater than 10 ng/mℓ was observed. Following administration of 2,5 mg of dornase alfa twice daily for twenty-four weeks, mean serum concentrations of DNase at trough were no different from mean pre-treatment baseline value of 3,5 ± 0,1 ng/mℓ; suggesting low systemic absorption or accumulation.

Distribution*:* Studies in rats and monkeys have shown that, following intravenous administration, dornase alfa was cleared rapidly from the serum. The initial volume of distribution was similar to serum volume in these studies.

Inhalation of 2,5 mg dornase alfa results in mean sputum concentration of dornase alfa of approximately 3 µg/mℓ within 15 minutes in CF patients. Concentrations of dornase alfa in sputum rapidly decline following inhalation.

Elimination: Studies in rats indicate that, following aerosol administration, the disappearance half-life of dornase alfa from the lungs is 11 hours.

INDICATIONS

Management of cystic fibrosis (CF) patients, with a forced vital capacity (FVC) of greater than 40 % of predicted value, and over 5 years of age.

CONTRA-INDICATIONS

PULMOZYME should not be administered to patients with known hypersensitivity to the product or its constituents.

Pregnancy and lactation.

Safety and efficacy in children younger than 5 years has not been established.

INTERACTIONS

Standard cystic fibrosis therapies, such as antibiotics, bronchodilators, pancreatic enzymes, vitamins, inhaled and systemic corticosteroids and analgesics can be used safely in conjunction with PULMOZYME. However, PULMOZYME should not be mixed in the nebuliser with these therapies.

PREGNANCY AND LACTATION

Pregnancy: The safety of dornase alfa has not been established in pregnant women.

Lactation: When PULMOZYME is administered to humans according to the dosage recommendation, there is minimal systemic absorption. Nevertheless, dornase alfa should not be administered to a breast-feeding woman.

DOSAGE AND DIRECTIONS FOR USE

PULMOZYME is recommended to be administered daily at a dose of 2,5 mg, once a day to CF patients ≥ 5 years of age.

Inhale the contents of one ampoule (2,5 mℓ of solution) undiluted using a recommended jet nebuliser/compressor system. See Instructions for use/handling.

Some patients over the age of 21 may benefit from twice daily administration. Most patients gain optimal benefit from continued daily use of PULMOZYME. Studies demonstrating the reduction in the rate of exacerbations of respiratory tract infections have involved chronic, daily administration of dornase alfa. Therefore, patients should be instructed to take their medications every day, without a break. For patients on PULMOZYME therapy who experience exacerbation of respiratory tract infection, administration of PULMOZYME can be safely continued.

The patient should continue his/her standard medical care including their standard regimen of chest physiotherapy. Safety and efficacy have not been demonstrated in patients with forced vital capacity less than 40 % of predicted. There is no clinical experience in the use of PULMOZYME in patients under the age of 5 years.

Instructions for use/Handling: The contents of one 2,5 mg (2 500 U) single-use ampoule of PULMOZYME sterile solution for inhalation should be inhaled once a day using a recommended jet nebuliser. PULMOZYME should not be mixed with other drugs of solutions in the nebuliser. See Incompatabilities.

The complete contents of a single ampoule should be placed in the bowl of a jet nebuliser/compressor system, such as the Hudson T Up-draft II/Pulmo-Aide, Airlife Misty/Pulmo-Aide, customised Respirgard/Pulmo-Aide, or AcornII/Pulmo-Aide.

PULMOZYME may also be used in conjunction with a reusable jet nebuliser/compressor system, such as the Pari LL/Inhalerboy or Master, Aiolos/2 Ailos, Side Stream/CR50 or MobilAire or Porta-Neb.

Patients who are unable to inhale or exhale orally throughout the entire nebulisation period may use the Pari Baby nebuliser with a tight fitting face mask.

Ultrasonic nebulisers may be unsuitable for delivery of PULMOZYME because they may inactivate PULMOZYME or have unacceptable aerosol delivery characteristics. The manufacturer's instructions on the use and maintenance of the nebuliser and compressor should be followed. Containment of the aerosol is not necessary. PULMOZYME ampoules are for single administration only.

Incompatibilities: PULMOZYME is an unbuffered aqueous solution and should not be diluted or mixed with other drugs in the nebuliser bowl. Mixing of this solution could lead to adverse structural and/or functional changes in PULMOZYME or the admixed compound.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS

Side effects reported in clinical trials have been listed below according to system organ class and frequency of occurrence according to the following convention:

Rare (≥ 1/10 000 < 1/1 000)

In most cases, the adverse reactions are mild and transient in nature and do not require alterations in PULMOZYME dosing.

Eye disorders*:*

Rare: Conjunctivitis.

Respiratory, thoracic and mediastinal disorders:

Rare: Dysphonia, dyspnoea, pharyngitis, laryngitis, rhinitis (all non-infectious), cough.

Gastrointestinal disorders:

Rare: Dyspepsia.

Skin and subcutaneous tissue disorders:

Rare: Rash, urticaria.

General disorders and administration site conditions:

Rare: Chest pain (pleuritic/non-cardiac), pyrexia.

Investigations:

Rare: Pulmonary function tests decreased.

Upon initiation of dornase alfa therapy, pulmonary function may decline and expectoration of sputum may increase.

Less than 5 % of patients treated with dornase alfa have developed antibodies to dornase alfa. Improvement in pulmonary function tests has still occurred even after the development of antibodies to dornase alfa.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

The effect of PULMOZYME overdosage has not been established. Results of clinical studies and preclinical inhalation studies in rats and monkeys have shown there is minimal systemic absorption of dornase alfa.

Cystic fibrosis patients have inhaled up to 20 mg PULMOZYME twice daily (16 times the recommended daily dose) for up to 6 days and 10 mg twice daily (8 times the recommended dose) intermittently (2 weeks on/2 weeks off drug) for 168 days. Six adult non-cystic fibrosis patients received a single intravenous dose of 125 µg/kg of dornase alfa, followed 7 days later by 125 µg/kg subcutaneously for two consecutive 5-day periods, without either neutralising antibodies to DNase or any change in serum antibodies against double-stranded DNA being detected. All of these doses were well tolerated.

Systemic toxicity of PULMOZYME has not been observed and is not expected due to the poor absorption and short serum half-life of dornase alfa. Systemic treatment of overdose is therefore unlikely to be necessary. See Pharmacokinetic properties.

IDENTIFICATION

PULMOZYME inhalation solution is clear and colourless.

PRESENTATION

PULMOZYME is supplied in single use low density polyethylene plastic ampoules. Each ampoule contains 2,5 mg dornase alfa per 2,5 mℓ ampoule. The ampoules are enclosed in a laminated foil pouch containing 6 ampoules per pouch. Each carton contains 30 PULMOZYME ampoules.

STORAGE INSTRUCTIONS

PULMOZYME should be stored in a refrigerator at 2 - 8 °C. The ampoules should be stored in the foil pouch in the outer carton and protected from light (direct sunlight).

Avoid exposure to excessive heat. A single brief exposure to elevated temperatures (≤ 24 hours at up to 30 °C) does not affect product stability. PULMOZYME should not be used after the expiry date.

The ampoules are for single administration only.

Keep out of reach of children.

REGISTRATION NUMBER

28/30.4/0675

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE REGISTRATION CERTIFICATE

Roche Products (Pty) Ltd

90 Bekker Road, Hertford Office Park,

Building E, Vorna Valley, Midrand,

Johannesburg, 1686

South Africa

Roche Ethical Assistance Line toll-free: 0800 21 21 25

DATE OF PUBLICATION OF THIS PACKAGE INSERT

Registration: 23 December 1994

Last Revision: 16 February 2022

Approved Manufacturer:

Woodstock Sterile Solutions, Inc.

2210 Lake Shore Drive

Woodstock, IL 60098

USA