Pulmozyme® dornase alfa INHALATION SOLUTION

Discussing Pulmozyme With Your Doctor

Use this Discussion Guide to help prepare for your doctor's appointment and get the answers you'll need for your everyday treatment with Pulmozyme.

1. Which dose of Pulmozyme is right for me?
2. Why is Pulmozyme an important part of my cystic fibrosis treatment regimen?
3. What nebulizers can I use to take Pulmozyme?
4. How can I fit my Pulmozyme treatment into my daily routine?
5. What are the possible side effects of Pulmozyme?
6. Should I continue using Pulmozyme even when I can't feel it?

(ADDITIONAL QUESTIONS)

7. _____
8. _____
9. _____
10. _____
11. _____
12. _____

Please see the Indication and Usage and Important Safety Information on the next page and see the accompanying full Pulmozyme Prescribing Information for additional Important Safety Information.

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M-US-00005906 (v1.0) 6/20

Pulmozyme® dornase alfa INHALATION SOLUTION

Discussing Pulmozyme With Your Doctor

Indication and Usage

Pulmozyme (dornase alfa) is indicated for daily administration along with standard therapies for the management of cystic fibrosis (CF) patients to improve pulmonary function.

In CF patients with an FVC ≥ 40% of predicted, daily administration of Pulmozyme has also been shown to reduce the risk of respiratory tract infections requiring injectable antibiotics.

Important Safety Information

Pulmozyme should not be used in patients who are allergic to any of its ingredients.

Patients may experience the following when using Pulmozyme: change in or loss of their voice, discomfort in the throat, rash, chest pain, red watery eyes, runny nose, lowering of lung function, fever, indigestion, and shortness of breath. There have been no reports of severe allergic reactions caused by the administration of Pulmozyme. Mild to moderate hives and mild skin rash have been observed and have been short-lived.

Pediatric Use

The safety and effectiveness of Pulmozyme have been established in patients 5 years of age and older. While clinical trial data are limited in patients younger than 5 years of age, the use of Pulmozyme should be considered for pediatric CF patients who may experience potential benefit in lung function or who may be at risk of respiratory tract infection.

The safety of Pulmozyme given by daily inhalation for 2 weeks has been studied using 98 CF patients with 65 of them aged 3 months to <5 years (younger group) and 33 aged 5 years to <10 years (older group). The PARI BABY™ reusable nebulizer (which uses a face mask instead of a mouthpiece) was used in patients who were unable to show that they could breathe in or out using their mouth throughout the entire treatment period. Overall, the kind of side effects observed in children was similar to those seen in larger trials in older patients.

You are encouraged to report side effects to Genentech and the FDA. You may report side effects to the FDA at **1-800-FDA-1088** or **www.fda.gov/medwatch**. You may also report side effects to Genentech at **1-888-835-2555**.

Please see the accompanying full Pulmozyme Prescribing Information for additional Important Safety Information. If you have questions, please discuss them with your CF Care Team.

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M-US-00005906 (v1.0) 6/20

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PULMOZYME safely and effectively. See full prescribing information for PULMOZYME.

PULMOZYME® (dornase alfa) inhalation solution, for inhalation use
Initial U.S. Approval: 1993

---------- INDICATIONS AND USAGE----------
PULMOZYME is a recombinant DNase enzyme indicated in conjunction with standard therapies for the management of cystic fibrosis (CF) patients to improve pulmonary function. (1)

----------DOSAGE AND ADMINISTRATION ----------
- The recommended dosage is one 2.5 mg single-use ampule inhaled once daily using a recommended nebulizer. (2.1)
- Some patients may benefit from twice daily administration. (2.1)

---------- DOSAGE FORMS AND STRENGTHS----------
Inhalation Solution: 2.5 mg/2.5 mL clear, colorless solution in single-use ampules. (3)

---------- CONTRAINDICATIONS ----------
PULMOZYME is contraindicated in patients with known hypersensitivity to dornase alfa, Chinese Hamster Ovary cell products, or any component of the product. (4)

----------WARNINGS AND PRECAUTIONS----------
None.

---------- ADVERSE REACTIONS----------
The most common adverse reactions (occurring in ≥3% of patients treated with PULMOZYME over placebo) seen in clinical trials in CF patients were: voice alteration, pharyngitis, rash, laryngitis, chest pain, conjunctivitis, rhinitis, decrease in FVC of ≥10%, fever, and dyspnea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 01/2018

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

PULMOZYME® (dornase alfa) is indicated for daily administration in conjunction with standard therapies for the management of cystic fibrosis (CF) patients to improve pulmonary function.

In CF patients with an FVC ≥ 40% of predicted, daily administration of PULMOZYME has also been shown to reduce the risk of respiratory tract infections requiring parenteral antibiotics.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage for use in most cystic fibrosis patients is one 2.5 mg single-use ampule inhaled once daily using a recommended jet nebulizer/compressor system or eRapid™ Nebulizer System.

Some patients may benefit from twice daily administration *[see Clinical Studies (14)]*.

2.2 Directions for Use

Administer PULMOZYME via the eRapid Nebulizer System or via a jet nebulizer connected to an air compressor with an adequate air flow and equipped with a mouthpiece or suitable face mask (see Table 1). No data are currently available to support the administration of PULMOZYME with other nebulizer systems.

Do not dilute or mix PULMOZYME with other drugs in the nebulizer. Mixing of PULMOZYME with other drugs could lead to adverse physicochemical and/or functional changes in PULMOZYME or the admixed compound.

Table 1. Recommended Jet Nebulizers/Compressors and Nebulizer Systems

Jet Nebulizer	**Compressor**
Hudson T Up-draft II® with	Pulmo-Aide®
Marquest Acorn II® with	Pulmo-Aide®
PARI LC® Plus with	PARI PRONEB®
**PARI BABY™ with	PARI PRONEB®
Durable Sidestream® with	MOBILAIRE™
Durable Sidestream® with	Porta-Neb®
Nebulizer System	
eRapid™ Nebulizer System*	

*Consisting of the eRapid™ Nebulizer Handset with eBase™ Controller.

**Patients who are unable to inhale or exhale orally throughout the entire nebulization period may use the PARI BABY™ nebulizer.

The patient should follow the manufacturer's instructions on the use and maintenance of the equipment, including cleaning and disinfection procedures.

When PULMOZYME is administered with the eRapid Nebulizer System, advise patients to replace the handset after 90 uses, regardless of whether the EasyCare cleaning aid is used. Since delivery data are not available for PULMOZYME administered with the eRapid handset beyond 90 administrations, delivery of the appropriate therapeutic dose of PULMOZYME cannot be assured beyond 90 administrations. The eRapid Nebulizer System should only be used by adults and children who can use a mouthpiece, and not by younger children who need a mask to take PULMOZYME.

2.3 Storage and Handling

Store PULMOZYME ampules in their protective foil pouch under refrigeration and protected from light. Refrigerate ampules during transport and do not expose to room temperatures for a total time of 24 hours.

Each PULMOZYME ampule should be squeezed prior to use in order to check for leaks. Discard ampules if the solution is cloudy or discolored. Once opened, the entire contents of the ampule must be used or discarded.

3 DOSAGE FORMS AND STRENGTHS

Inhalation Solution: 2.5 mg/2.5 mL clear, colorless solution in single-use ampules.

4 CONTRAINDICATIONS

PULMOZYME is contraindicated in patients with known hypersensitivity to dornase alfa, Chinese Hamster Ovary cell products, or any component of the product.

5 WARNINGS AND PRECAUTIONS

None.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to PULMOZYME in 902 patients, with exposures ranging from 2 weeks of daily administration up to once or twice daily administration for six months. PULMOZYME was studied in both placebo-controlled and uncontrolled trials (n=804 and n=98). The population of patients in placebo-controlled trials was with FVC $\geq$ 40% of predicted (n=643) or with more advanced pulmonary disease, FVC < 40% of predicted (n=161). The population in the uncontrolled trial included 98 pediatric patients with CF ranging from 3 months to 10 years of age. More than half of the patients received PULMOZYME 2.5 mg by inhalation once a day (n=581), while the rest of patients (n=321) received PULMOZYME 2.5 mg by inhalation twice a day.

Placebo-Controlled Trials

Trial 1: Trial 1 was a randomized, placebo-controlled clinical trial in patients with FVC ≥ 40% of predicted. In this trial, over 600 patients received PULMOZYME once or twice daily for six months. The most common adverse reaction (risk difference ≥5%) was voice alteration. The proportion of most adverse events was similar for patients on PULMOZYME and on placebo, probably reflecting the sequelae of the underlying lung disease. In most cases reactions that were increased were mild, transient in nature, and did not require alterations in dosing. Few patients experienced adverse reactions resulting in permanent discontinuation from PULMOZYME, and the proportion of discontinuations were similar for placebo (2%) and PULMOZYME (3%). Adverse reactions occurring in a higher proportion (greater than 3%) of PULMOZYME treated patients than in placebo-treated patients are listed in Table 2.

Trial 2: Trial 2 was a randomized, placebo-controlled trial in patients with more advanced pulmonary disease (FVC < 40% of predicted) who were treated for 12 weeks. In this trial, the safety profile of PULMOZYME was similar to that reported in patients with less advanced pulmonary disease (FVC ≥ 40% of predicted). Adverse reactions that were reported in this trial with a higher proportion (greater than 3%) in the PULMOZYME treated patients are listed in Table 2.

Table 2. Adverse Reactions Increased 3% or More in PULMOZYME Treated Patients Over Placebo in CF Clinical Trials

Adverse Reactions (of any severity or seriousness)	**Trial 1** CF Patients with FVC ≥ 40% of predicted treated for 24 weeks			**Trial 2** CF Patients with FVC <40% of predicted treated for 12 weeks	
	Placebo n=325	Pulmozyme QD n=322	Pulmozyme BID n=321	Placebo n=159	Pulmozyme QD n=161
Voice alteration	7%	12%	16%	6%	18%
Pharyngitis	33%	36%	40%	28%	32%
Rash	7%	10%	12%	1%	3%
Laryngitis	1%	3%	4%	1%	3%
Chest Pain	16%	18%	21%	23%	25%
Conjunctivitis	2%	4%	5%	0%	1%
Rhinitis	Differences were less than 3%			24%	30%
FVC decrease of ≥10% of predicted°				17%	22%
Fever				28%	32%
Dyspepsia				0%	3%
Dyspnea (when reported as serious)	Differences were less than 3%			12%†	17%†

° Single measurement only, does not reflect overall FVC changes.

† Total reports of dyspnea (regardless of severity or seriousness) had a difference of less than 3% in Trial 2.

Mortality rates observed in controlled trials were similar for the placebo and PULMOZYME treated patients. Causes of death were consistent with progression of cystic fibrosis and included apnea, cardiac arrest, cardiopulmonary arrest, cor pulmonale, heart failure, massive hemoptysis, pneumonia, pneumothorax, and respiratory failure.

Uncontrolled Trial

Trial 3: The safety of PULMOZYME, 2.5 mg by inhalation, was studied with 2 weeks of daily administration in 98 pediatric patients with cystic fibrosis 3 months to 10 years of age (65 aged 3 months to < 5 years, 33 aged 5 to ≤ 10 years). The PARI BABY™ reusable nebulizer (which uses a facemask instead of a mouthpiece) was utilized in patients unable to demonstrate the ability to inhale or exhale orally throughout the entire treatment period (54/65, 83% of the younger and 2/33, 6% of the older patients). Overall, the nature of adverse reactions was similar to that seen in the placebo-controlled trials. The number of patients reporting cough was higher in the younger age group as compared to the older age group (29/65, 45% compared to 10/33, 30%) as was the number reporting moderate to severe cough (24/65, 37% as compared to 6/33, 18%). The number of patients reporting rhinitis was higher in the

younger age group as compared to the older age group (23/65, 35% compared to 9/33, 27%) as was the number reporting rash (4/65, 6% as compared to 0/33).

Allergic Reactions

There have been no reports of anaphylaxis attributed to the administration of PULMOZYME. Urticaria, mild to moderate, and mild skin rash have been observed and have been transient. Within all of the studies, a small percentage (average of 2-4%) of patients treated with PULMOZYME developed serum antibodies to PULMOZYME. None of these patients developed anaphylaxis, and the clinical significance of serum antibodies to PULMOZYME is unknown.

6.2 Postmarketing Experience

Postmarketing spontaneous reports and prospectively collected safety data from observational studies confirm the safety profile to be as described in clinical trials [*see Adverse Reactions (6.1)*].

7 DRUG INTERACTIONS

Available data indicate there are no clinically important drug-drug interactions with PULMOZYME.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk summary

There are no adequate and well-controlled studies with PULMOZYME in pregnant women. However, animal reproduction studies have been conducted with dornase alfa. In these studies, no evidence of fetal harm was observed in rats and rabbits at doses of dornase alfa up to approximately 600 times the maximum recommended human dose (MRHD).

The background risk of major birth defects and miscarriage for the cystic fibrosis population is unknown. However, the background risk in the U.S. general population of major birth defects is 2-4% and of miscarriage is 15-20% of clinically recognized pregnancies.

Data

Animal Data

Reproductive studies have been performed in rats and rabbits at intravenous doses of dornase alfa up to 10 mg/kg/day (approximately 600 times the MRHD in adults). In a combined embryo-fetal development and pre- and post-natal development study, no evidence of maternal toxicity, embryotoxicity, or teratogenicity was observed when dornase alfa was administered to dams throughout organogenesis (Gestation days 6 to 17). Dornase alfa did not elicit adverse effects on fetal or neonatal growth when administered to dams throughout most of gestation and delivery (Gestation days 6 to 25) and nursing (Post-partum days 6 to 21).

A pharmacokinetic study in Cynomolgus monkeys found no detectable levels of dornase alfa in fetal blood or amniotic fluid on gestation day 150 (end of gestation) from mothers that were administered an intravenous bolus dose (0.1 mg/kg) followed by an intravenous infusion dose (0.080 mg/kg) over a 6-hour period during pregnancy.

8.2 Lactation

Risk Summary

It is not known whether PULMOZYME is present in human milk. In a pharmacokinetic study in Cynomolgus monkeys, levels of dornase alfa detected in milk were less than 0.1% of the maternal serum concentration at 24 hours after dosing [intravenous bolus dose (0.1 mg/kg) of dornase alfa followed by an intravenous infusion (0.080 mg/kg/hr) over a 6-hour period] on post-partum day 14. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for PULMOZYME and any potential adverse effects on the breastfed child from PULMOZYME or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of PULMOZYME have been established in pediatric patients 5 years of age and older [*see Adverse Reactions (6) and Clinical Studies (14)]*. The safety of PULMOZYME, 2.5 mg by inhalation, was studied with 2 weeks of daily administration in 65 patients with cystic fibrosis aged 3 months to < 5 years *[see Adverse Reactions (6.1)]*. While clinical trial data are limited in pediatric patients younger than 5 years of age, the use of PULMOZYME should be considered for pediatric CF patients who may experience potential benefit in pulmonary function or who may be at risk of respiratory tract infection.

8.5 Geriatric Use

Cystic fibrosis is primarily a disease of children and young adults. Clinical studies of PULMOZYME did not include sufficient numbers of subjects aged 65 or older to determine whether they respond differently from younger subjects.

10 OVERDOSAGE

Single-dose inhalation studies in rats and monkeys at doses up to 180-times higher than doses routinely used in clinical studies are well tolerated. Single dose oral administration of PULMOZYME in doses up to 200 mg/kg are also well tolerated by rats.

Cystic fibrosis patients have received up to 20 mg BID for up to 6 days and 10 mg BID intermittently (2 weeks on/2 weeks off drug) for 168 days. These doses were well tolerated.

11 DESCRIPTION

Dornase alfa is a recombinant human deoxyribonuclease I (rhDNase), an enzyme which selectively cleaves DNA. The protein is produced by genetically engineered Chinese Hamster Ovary (CHO) cells containing DNA encoding for the native human protein, deoxyribonuclease I (DNase). The product is purified by column chromatography and tangential flow filtration. The purified glycoprotein contains 260 amino acids with an approximate molecular weight of 37,000 daltons. The primary amino acid sequence is identical to that of the native human enzyme.

PULMOZYME (dornase alfa) inhalation solution is administered by inhalation of an aerosol mist produced by a compressed air driven nebulizer or an approved nebulizer system [*see Clinical Studies (14) and Dosage and Administration (2)*]. PULMOZYME is a sterile, clear, colorless, highly purified solution in single-use ampules. Each ampule delivers 2.5 mL of the solution to the nebulizer bowl. Each mL of

aqueous solution contains 1 mg dornase alfa, calcium chloride dihydrate (0.15 mg) and sodium chloride (8.77 mg). The solution contains no preservative. The nominal pH of the solution is 6.3.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

PULMOZYME is recombinant human deoxyribonuclease I (rhDNase), an enzyme which selectively cleaves DNA. In preclinical *in vitro* studies, PULMOZYME hydrolyzes the DNA in sputum of CF patients and reduces sputum viscoelasticity. In CF patients, retention of viscous purulent secretions in the airways contributes both to reduced pulmonary function and to exacerbations of infection. Purulent pulmonary secretions contain very high concentrations of extracellular DNA released by degenerating leukocytes that accumulate in response to infection.

12.3 Pharmacokinetics

When 2.5 mg PULMOZYME was administered by inhalation to eighteen CF patients, mean sputum concentrations of 3 µg/mL DNase were measurable within 15 minutes. Mean sputum concentrations declined to an average of 0.6 µg/mL two hours following inhalation. Inhalation of up to 10 mg TID of PULMOZYME by 4 CF patients for six consecutive days did not result in a significant elevation of serum concentrations of DNase above normal endogenous levels. After administration of up to 2.5 mg of PULMOZYME twice daily for six months to 321 CF patients, no accumulation of serum DNase was noted. Dornase alfa is expected to be metabolized by proteases present in biological fluids. A human intravenous dose study suggested an elimination half-life of 3-4 hours for dornase alfa.

PULMOZYME, 2.5 mg by inhalation, was administered daily to 98 patients aged 3 months to ≤ 10 years, and bronchoalveolar lavage (BAL) fluid was obtained within 90 minutes of the first dose. BAL DNase concentrations were detectable in all patients but showed a broad range, from 0.007 to 1.8 µg/mL. Over an average of 14 days of exposure, serum DNase concentrations (mean ± s.d.) increased by 1.1 ± 1.6 ng/mL for the 3 months to < 5 year age group and by 0.8 ± 1.2 ng/mL for the 5 to ≤ 10 year age group. The relationship between BAL or serum DNase concentration and adverse experiences and clinical outcomes is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

PULMOZYME produced no treatment-related increases in the incidence of tumors in a lifetime study in Sprague Dawley rats that were administered inhaled doses up to 0.246 mg/kg/day (approximately 30 times the MRHD in adults). There was no increase in the development of benign or malignant neoplasms and no occurrence of unusual tumor types in rats after lifetime exposure.

PULMOZYME tested negative in the following genotoxicity assays: the *in vitro* Ames assay, *in vitro* mouse lymphoma assay, and *in vivo* mouse bone marrow micronucleus assay. No evidence of impairment of fertility was observed in male and female rats that received intravenous doses up to 10 mg/kg/day (approximately 600 times the MRHD in adults).

14 CLINICAL STUDIES

Trial in CF Patients with FVC ≥40% of Predicted

PULMOZYME has been evaluated in a randomized, placebo-controlled trial of clinically stable cystic fibrosis patients, 5 years of age and older, with baseline forced vital capacity (FVC) greater than or equal to 40% of predicted and receiving standard therapies for cystic fibrosis. Patients were treated with placebo (325 patients), 2.5 mg of PULMOZYME once a day (322 patients), or 2.5 mg of PULMOZYME twice a day (321 patients) for six months administered via a Hudson T Up-draft II® nebulizer with a Pulmo-Aide® compressor.

Both doses of PULMOZYME resulted in significant reductions in the number of patients experiencing respiratory tract infections requiring use of parenteral antibiotics compared with the placebo group. Administration of PULMOZYME reduced the relative risk of developing a respiratory tract infection by 27% and 29% for the 2.5 mg daily dose and the 2.5 mg twice daily dose, respectively (see Table 3). The data suggest that the effects of PULMOZYME on respiratory tract infections in older patients (> 21 years) may be smaller than in younger patients, and that twice daily dosing may be required in the older patients. Patients with baseline FVC > 85% may also benefit from twice a day dosing (see Table 3). The reduced risk of respiratory infection observed in PULMOZYME treated patients did not directly correlate with improvement in FEV_1 during the initial two weeks of therapy.

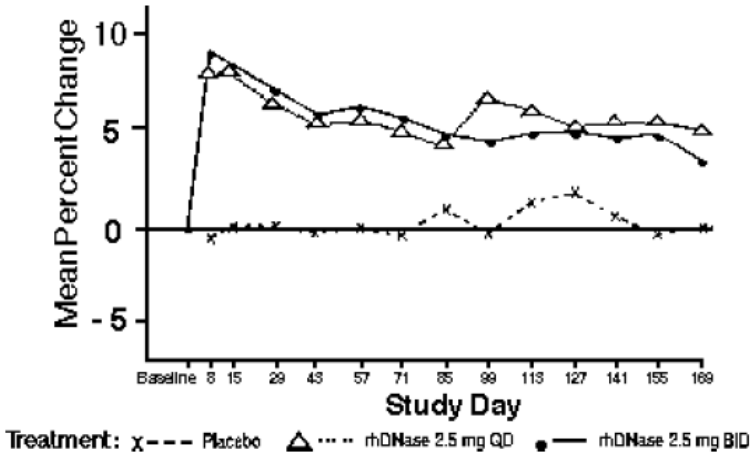
Within 8 days of the start of treatment with PULMOZYME, mean FEV_1 increased 7.9% in those treated once a day and 9.0% in those treated twice a day compared to the baseline values. The overall mean FEV_1 during long-term therapy increased 5.8% from baseline at the 2.5 mg daily dose level and 5.6% from baseline at the 2.5 mg twice daily dose level. Placebo recipients did not show significant mean changes in pulmonary function testing (see Figure 1).

For patients 5 years of age or older with baseline FVC greater than or equal to 40%, administration of PULMOZYME decreased the incidence of occurrence of first respiratory tract infection requiring parenteral antibiotics, and improved mean FEV_1, regardless of age or baseline FVC.

Table 3. Incidence of First Respiratory Tract Infection Requiring Parenteral Antibiotics in Patients with FVC ≥40% of Predicted

	Placebo N=325	2.5 mg QD N=322	2.5 mg BID N=321
Percent of Patients Infected	43%	34%	33%
Relative Risk (vs placebo)		0.73	0.71
p-value (vs placebo)		0.015	0.007
Subgroup by Age and Baseline FVC	Placebo % (N)	2.5 mg QD % (N)	2.5 mg BID % (N)
Age			
5-20 years	42% (201)	25% (199)	28% (184)
21 years and older	44% (124)	48% (123)	39% (137)
Baseline FVC			
40-85% Predicted	54% (194)	41% (201)	44% (203)
>85% Predicted	27% (131)	21% (121)	14% (118)

Figure 1. Mean Percent Change from Baseline FEV_1 in Patients with FVC ≥40% of Predicted



Trial in CF Patients with FVC <40% of Predicted

PULMOZYME has also been evaluated in a second randomized, placebo-controlled trial in clinically stable patients with baseline FVC < 40% of predicted. Patients were enrolled and treated with placebo (162 patients) or PULMOZYME 2.5 mg QD (158 patients) for twelve weeks. In patients who received PULMOZYME, there was an increase in mean change (as percent of baseline) compared to placebo in FEV_1 (9.4% vs. 2.1%, $p < 0.001$) and in FVC (12.4% vs. 7.3%, $p < 0.01$). PULMOZYME did not significantly reduce the risk of developing a respiratory tract infection requiring parenteral antibiotics

(54% of PULMOZYME patients vs. 55% of placebo patients had experienced a respiratory tract infection by 12 weeks, relative risk = .93, p = 0.62).

The effect of PULMOZYME on exercise tolerance has not been established in adult and pediatric patients.

Other Studies

Clinical trials have indicated that PULMOZYME therapy can be continued or initiated during an acute respiratory exacerbation.

Short-term dose ranging studies demonstrated that doses in excess of 2.5 mg BID did not provide further improvement in FEV_1. Patients who have received drug on a cyclical regimen (i.e., administration of PULMOZYME 10 mg BID for 14 days, followed by a 14 day wash out period) showed rapid improvement in FEV_1 with the initiation of each cycle and a return to baseline with each PULMOZYME withdrawal.

16 HOW SUPPLIED/STORAGE AND HANDLING

PULMOZYME (dornase alfa) inhalation solution is a sterile, clear, colorless solution supplied in:

- 30 unit cartons containing 5 foil pouches of 6 single-use ampules. Each 2.5 mL ampule contains 2.5 mg of dornase alfa (1 mg/mL): NDC 50242-100-40.

Storage and Handling

Store PULMOZYME under refrigeration (2°C to 8°C/36°F to 46°F) in their protective foil to protect from light. Do not use beyond the expiration date stamped on the ampule. Store unused ampules in their protective foil pouch under refrigeration. Refrigerate PULMOZYME during transport and do not expose to room temperatures for a total time of 24 hours.

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved Patient Labeling (Instructions for Use).

Storage and Handling Information

Instruct patients on the proper techniques to store and handle PULMOZYME. PULMOZYME must be stored in the refrigerator at 2 to 8°C (36 to 46°F) and protected from light. It should be kept refrigerated during transport and should not be exposed to room temperatures for a total time of 24 hours.

Advise patients to squeeze each ampule prior to use in order to check for leaks. The solution should be discarded if it is cloudy or discolored. Once opened, the entire contents of the ampule must be used or discarded.

Instruct patients in the proper use and maintenance of the jet nebulizer/compressor system or eRapid Nebulizer System used in PULMOZYME delivery.

Instruct patients not to dilute or mix PULMOZYME with other drugs in the nebulizer. Mixing of PULMOZYME with other drugs could lead to adverse physicochemical and/or functional changes in PULMOZYME or the admixed compound.

Use with the eRapid Nebulizer System

Instruct patients and caregivers to read and follow the directions in both the PULMOZYME Instructions for Use and in the Manufacturer's eRapid Nebulizer System Instruction Booklet.

Instruct patients and caregivers to clean the handset, including the medication reservoir, medicine cap, aerosol head, and mouthpiece, after each use. Instruct patients and caregivers to disinfect the handset, including the medication reservoir, medicine cap, aerosol head, and mouthpiece, after each day of use.

Instruct patients to replace the handset after 90 uses, regardless of whether the EasyCare cleaning aid is used. Since delivery data are not available for PULMOZYME administered with the eRapid handset beyond 90 administrations, delivery of the appropriate therapeutic dose of PULMOZYME cannot be assured beyond 90 administrations.

Pulmozyme® (dornase alfa)
Inhalation Solution

Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990
US License No. 1048

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PULMOZYME safely and effectively. See full prescribing information for PULMOZYME.

PULMOZYME® (dornase alfa) inhalation solution, for inhalation use
Initial U.S. Approval: 1993

---------- INDICATIONS AND USAGE----------
PULMOZYME is a recombinant DNase enzyme indicated in conjunction with standard therapies for the management of cystic fibrosis (CF) patients to improve pulmonary function. (1)

----------DOSAGE AND ADMINISTRATION ----------
- The recommended dosage is one 2.5 mg single-use ampule inhaled once daily using a recommended nebulizer. (2.1)
- Some patients may benefit from twice daily administration. (2.1)

---------- DOSAGE FORMS AND STRENGTHS----------
Inhalation Solution: 2.5 mg/2.5 mL clear, colorless solution in single-use ampules. (3)

---------- CONTRAINDICATIONS ----------
PULMOZYME is contraindicated in patients with known hypersensitivity to dornase alfa, Chinese Hamster Ovary cell products, or any component of the product. (4)

----------WARNINGS AND PRECAUTIONS----------
None.

---------- ADVERSE REACTIONS----------
The most common adverse reactions (occurring in ≥3% of patients treated with PULMOZYME over placebo) seen in clinical trials in CF patients were: voice alteration, pharyngitis, rash, laryngitis, chest pain, conjunctivitis, rhinitis, decrease in FVC of ≥10%, fever, and dyspnea. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 01/2018

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

PULMOZYME® (dornase alfa) is indicated for daily administration in conjunction with standard therapies for the management of cystic fibrosis (CF) patients to improve pulmonary function.

In CF patients with an FVC ≥ 40% of predicted, daily administration of PULMOZYME has also been shown to reduce the risk of respiratory tract infections requiring parenteral antibiotics.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage

The recommended dosage for use in most cystic fibrosis patients is one 2.5 mg single-use ampule inhaled once daily using a recommended jet nebulizer/compressor system or eRapid™ Nebulizer System.

Some patients may benefit from twice daily administration *[see Clinical Studies (14)]*.

2.2 Directions for Use

Administer PULMOZYME via the eRapid Nebulizer System or via a jet nebulizer connected to an air compressor with an adequate air flow and equipped with a mouthpiece or suitable face mask (see Table 1). No data are currently available to support the administration of PULMOZYME with other nebulizer systems.

Do not dilute or mix PULMOZYME with other drugs in the nebulizer. Mixing of PULMOZYME with other drugs could lead to adverse physicochemical and/or functional changes in PULMOZYME or the admixed compound.

Table 1. Recommended Jet Nebulizers/Compressors and Nebulizer Systems

Jet Nebulizer	**Compressor**
Hudson T Up-draft II® with	Pulmo-Aide®
Marquest Acorn II® with	Pulmo-Aide®
PARI LC® Plus with	PARI PRONEB®
**PARI BABY™ with	PARI PRONEB®
Durable Sidestream® with	MOBILAIRE™
Durable Sidestream® with	Porta-Neb®
Nebulizer System	
eRapid™ Nebulizer System*	

*Consisting of the eRapid™ Nebulizer Handset with eBase™ Controller.

**Patients who are unable to inhale or exhale orally throughout the entire nebulization period may use the PARI BABY™ nebulizer.

The patient should follow the manufacturer's instructions on the use and maintenance of the equipment, including cleaning and disinfection procedures.

When PULMOZYME is administered with the eRapid Nebulizer System, advise patients to replace the handset after 90 uses, regardless of whether the EasyCare cleaning aid is used. Since delivery data are not available for PULMOZYME administered with the eRapid handset beyond 90 administrations, delivery of the appropriate therapeutic dose of PULMOZYME cannot be assured beyond 90 administrations. The eRapid Nebulizer System should only be used by adults and children who can use a mouthpiece, and not by younger children who need a mask to take PULMOZYME.

2.3 Storage and Handling

Store PULMOZYME ampules in their protective foil pouch under refrigeration and protected from light. Refrigerate ampules during transport and do not expose to room temperatures for a total time of 24 hours.

Each PULMOZYME ampule should be squeezed prior to use in order to check for leaks. Discard ampules if the solution is cloudy or discolored. Once opened, the entire contents of the ampule must be used or discarded.

3 DOSAGE FORMS AND STRENGTHS

Inhalation Solution: 2.5 mg/2.5 mL clear, colorless solution in single-use ampules.

4 CONTRAINDICATIONS

PULMOZYME is contraindicated in patients with known hypersensitivity to dornase alfa, Chinese Hamster Ovary cell products, or any component of the product.

5 WARNINGS AND PRECAUTIONS

None.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to PULMOZYME in 902 patients, with exposures ranging from 2 weeks of daily administration up to once or twice daily administration for six months. PULMOZYME was studied in both placebo-controlled and uncontrolled trials (n=804 and n=98). The population of patients in placebo-controlled trials was with FVC $\geq$ 40% of predicted (n=643) or with more advanced pulmonary disease, FVC < 40% of predicted (n=161). The population in the uncontrolled trial included 98 pediatric patients with CF ranging from 3 months to 10 years of age. More than half of the patients received PULMOZYME 2.5 mg by inhalation once a day (n=581), while the rest of patients (n=321) received PULMOZYME 2.5 mg by inhalation twice a day.

Placebo-Controlled Trials

Trial 1: Trial 1 was a randomized, placebo-controlled clinical trial in patients with FVC ≥ 40% of predicted. In this trial, over 600 patients received PULMOZYME once or twice daily for six months. The most common adverse reaction (risk difference ≥5%) was voice alteration. The proportion of most adverse events was similar for patients on PULMOZYME and on placebo, probably reflecting the sequelae of the underlying lung disease. In most cases reactions that were increased were mild, transient in nature, and did not require alterations in dosing. Few patients experienced adverse reactions resulting in permanent discontinuation from PULMOZYME, and the proportion of discontinuations were similar for placebo (2%) and PULMOZYME (3%). Adverse reactions occurring in a higher proportion (greater than 3%) of PULMOZYME treated patients than in placebo-treated patients are listed in Table 2.

Trial 2: Trial 2 was a randomized, placebo-controlled trial in patients with more advanced pulmonary disease (FVC < 40% of predicted) who were treated for 12 weeks. In this trial, the safety profile of PULMOZYME was similar to that reported in patients with less advanced pulmonary disease (FVC ≥ 40% of predicted). Adverse reactions that were reported in this trial with a higher proportion (greater than 3%) in the PULMOZYME treated patients are listed in Table 2.

Table 2. Adverse Reactions Increased 3% or More in PULMOZYME Treated Patients Over Placebo in CF Clinical Trials

Adverse Reactions (of any severity or seriousness)	**Trial 1** CF Patients with FVC ≥ 40% of predicted treated for 24 weeks			**Trial 2** CF Patients with FVC <40% of predicted treated for 12 weeks	
	Placebo n=325	Pulmozyme QD n=322	Pulmozyme BID n=321	Placebo n=159	Pulmozyme QD n=161
Voice alteration	7%	12%	16%	6%	18%
Pharyngitis	33%	36%	40%	28%	32%
Rash	7%	10%	12%	1%	3%
Laryngitis	1%	3%	4%	1%	3%
Chest Pain	16%	18%	21%	23%	25%
Conjunctivitis	2%	4%	5%	0%	1%
Rhinitis	Differences were less than 3%			24%	30%
FVC decrease of ≥10% of predicted°				17%	22%
Fever				28%	32%
Dyspepsia				0%	3%
Dyspnea (when reported as serious)	Differences were less than 3%			12%†	17%†

° Single measurement only, does not reflect overall FVC changes.

† Total reports of dyspnea (regardless of severity or seriousness) had a difference of less than 3% in Trial 2.

Mortality rates observed in controlled trials were similar for the placebo and PULMOZYME treated patients. Causes of death were consistent with progression of cystic fibrosis and included apnea, cardiac arrest, cardiopulmonary arrest, cor pulmonale, heart failure, massive hemoptysis, pneumonia, pneumothorax, and respiratory failure.

Uncontrolled Trial

Trial 3: The safety of PULMOZYME, 2.5 mg by inhalation, was studied with 2 weeks of daily administration in 98 pediatric patients with cystic fibrosis 3 months to 10 years of age (65 aged 3 months to < 5 years, 33 aged 5 to ≤ 10 years). The PARI BABY™ reusable nebulizer (which uses a facemask instead of a mouthpiece) was utilized in patients unable to demonstrate the ability to inhale or exhale orally throughout the entire treatment period (54/65, 83% of the younger and 2/33, 6% of the older patients). Overall, the nature of adverse reactions was similar to that seen in the placebo-controlled trials. The number of patients reporting cough was higher in the younger age group as compared to the older age group (29/65, 45% compared to 10/33, 30%) as was the number reporting moderate to severe cough (24/65, 37% as compared to 6/33, 18%). The number of patients reporting rhinitis was higher in the

younger age group as compared to the older age group (23/65, 35% compared to 9/33, 27%) as was the number reporting rash (4/65, 6% as compared to 0/33).

Allergic Reactions

There have been no reports of anaphylaxis attributed to the administration of PULMOZYME. Urticaria, mild to moderate, and mild skin rash have been observed and have been transient. Within all of the studies, a small percentage (average of 2-4%) of patients treated with PULMOZYME developed serum antibodies to PULMOZYME. None of these patients developed anaphylaxis, and the clinical significance of serum antibodies to PULMOZYME is unknown.

6.2 Postmarketing Experience

Postmarketing spontaneous reports and prospectively collected safety data from observational studies confirm the safety profile to be as described in clinical trials [*see Adverse Reactions (6.1)*].

7 DRUG INTERACTIONS

Available data indicate there are no clinically important drug-drug interactions with PULMOZYME.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk summary

There are no adequate and well-controlled studies with PULMOZYME in pregnant women. However, animal reproduction studies have been conducted with dornase alfa. In these studies, no evidence of fetal harm was observed in rats and rabbits at doses of dornase alfa up to approximately 600 times the maximum recommended human dose (MRHD).

The background risk of major birth defects and miscarriage for the cystic fibrosis population is unknown. However, the background risk in the U.S. general population of major birth defects is 2-4% and of miscarriage is 15-20% of clinically recognized pregnancies.

Data

Animal Data

Reproductive studies have been performed in rats and rabbits at intravenous doses of dornase alfa up to 10 mg/kg/day (approximately 600 times the MRHD in adults). In a combined embryo-fetal development and pre- and post-natal development study, no evidence of maternal toxicity, embryotoxicity, or teratogenicity was observed when dornase alfa was administered to dams throughout organogenesis (Gestation days 6 to 17). Dornase alfa did not elicit adverse effects on fetal or neonatal growth when administered to dams throughout most of gestation and delivery (Gestation days 6 to 25) and nursing (Post-partum days 6 to 21).

A pharmacokinetic study in Cynomolgus monkeys found no detectable levels of dornase alfa in fetal blood or amniotic fluid on gestation day 150 (end of gestation) from mothers that were administered an intravenous bolus dose (0.1 mg/kg) followed by an intravenous infusion dose (0.080 mg/kg) over a 6-hour period during pregnancy.

8.2 Lactation

Risk Summary

It is not known whether PULMOZYME is present in human milk. In a pharmacokinetic study in Cynomolgus monkeys, levels of dornase alfa detected in milk were less than 0.1% of the maternal serum concentration at 24 hours after dosing [intravenous bolus dose (0.1 mg/kg) of dornase alfa followed by an intravenous infusion (0.080 mg/kg/hr) over a 6-hour period] on post-partum day 14. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for PULMOZYME and any potential adverse effects on the breastfed child from PULMOZYME or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of PULMOZYME have been established in pediatric patients 5 years of age and older [*see Adverse Reactions (6) and Clinical Studies (14)]*. The safety of PULMOZYME, 2.5 mg by inhalation, was studied with 2 weeks of daily administration in 65 patients with cystic fibrosis aged 3 months to < 5 years *[see Adverse Reactions (6.1)]*. While clinical trial data are limited in pediatric patients younger than 5 years of age, the use of PULMOZYME should be considered for pediatric CF patients who may experience potential benefit in pulmonary function or who may be at risk of respiratory tract infection.

8.5 Geriatric Use

Cystic fibrosis is primarily a disease of children and young adults. Clinical studies of PULMOZYME did not include sufficient numbers of subjects aged 65 or older to determine whether they respond differently from younger subjects.

10 OVERDOSAGE

Single-dose inhalation studies in rats and monkeys at doses up to 180-times higher than doses routinely used in clinical studies are well tolerated. Single dose oral administration of PULMOZYME in doses up to 200 mg/kg are also well tolerated by rats.

Cystic fibrosis patients have received up to 20 mg BID for up to 6 days and 10 mg BID intermittently (2 weeks on/2 weeks off drug) for 168 days. These doses were well tolerated.

11 DESCRIPTION

Dornase alfa is a recombinant human deoxyribonuclease I (rhDNase), an enzyme which selectively cleaves DNA. The protein is produced by genetically engineered Chinese Hamster Ovary (CHO) cells containing DNA encoding for the native human protein, deoxyribonuclease I (DNase). The product is purified by column chromatography and tangential flow filtration. The purified glycoprotein contains 260 amino acids with an approximate molecular weight of 37,000 daltons. The primary amino acid sequence is identical to that of the native human enzyme.

PULMOZYME (dornase alfa) inhalation solution is administered by inhalation of an aerosol mist produced by a compressed air driven nebulizer or an approved nebulizer system [*see Clinical Studies (14) and Dosage and Administration (2)*]. PULMOZYME is a sterile, clear, colorless, highly purified solution in single-use ampules. Each ampule delivers 2.5 mL of the solution to the nebulizer bowl. Each mL of

aqueous solution contains 1 mg dornase alfa, calcium chloride dihydrate (0.15 mg) and sodium chloride (8.77 mg). The solution contains no preservative. The nominal pH of the solution is 6.3.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

PULMOZYME is recombinant human deoxyribonuclease I (rhDNase), an enzyme which selectively cleaves DNA. In preclinical *in vitro* studies, PULMOZYME hydrolyzes the DNA in sputum of CF patients and reduces sputum viscoelasticity. In CF patients, retention of viscous purulent secretions in the airways contributes both to reduced pulmonary function and to exacerbations of infection. Purulent pulmonary secretions contain very high concentrations of extracellular DNA released by degenerating leukocytes that accumulate in response to infection.

12.3 Pharmacokinetics

When 2.5 mg PULMOZYME was administered by inhalation to eighteen CF patients, mean sputum concentrations of 3 µg/mL DNase were measurable within 15 minutes. Mean sputum concentrations declined to an average of 0.6 µg/mL two hours following inhalation. Inhalation of up to 10 mg TID of PULMOZYME by 4 CF patients for six consecutive days did not result in a significant elevation of serum concentrations of DNase above normal endogenous levels. After administration of up to 2.5 mg of PULMOZYME twice daily for six months to 321 CF patients, no accumulation of serum DNase was noted. Dornase alfa is expected to be metabolized by proteases present in biological fluids. A human intravenous dose study suggested an elimination half-life of 3-4 hours for dornase alfa.

PULMOZYME, 2.5 mg by inhalation, was administered daily to 98 patients aged 3 months to ≤ 10 years, and bronchoalveolar lavage (BAL) fluid was obtained within 90 minutes of the first dose. BAL DNase concentrations were detectable in all patients but showed a broad range, from 0.007 to 1.8 µg/mL. Over an average of 14 days of exposure, serum DNase concentrations (mean ± s.d.) increased by 1.1 ± 1.6 ng/mL for the 3 months to < 5 year age group and by 0.8 ± 1.2 ng/mL for the 5 to ≤ 10 year age group. The relationship between BAL or serum DNase concentration and adverse experiences and clinical outcomes is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

PULMOZYME produced no treatment-related increases in the incidence of tumors in a lifetime study in Sprague Dawley rats that were administered inhaled doses up to 0.246 mg/kg/day (approximately 30 times the MRHD in adults). There was no increase in the development of benign or malignant neoplasms and no occurrence of unusual tumor types in rats after lifetime exposure.

PULMOZYME tested negative in the following genotoxicity assays: the *in vitro* Ames assay, *in vitro* mouse lymphoma assay, and *in vivo* mouse bone marrow micronucleus assay. No evidence of impairment of fertility was observed in male and female rats that received intravenous doses up to 10 mg/kg/day (approximately 600 times the MRHD in adults).

14 CLINICAL STUDIES

Trial in CF Patients with FVC ≥40% of Predicted

PULMOZYME has been evaluated in a randomized, placebo-controlled trial of clinically stable cystic fibrosis patients, 5 years of age and older, with baseline forced vital capacity (FVC) greater than or equal to 40% of predicted and receiving standard therapies for cystic fibrosis. Patients were treated with placebo (325 patients), 2.5 mg of PULMOZYME once a day (322 patients), or 2.5 mg of PULMOZYME twice a day (321 patients) for six months administered via a Hudson T Up-draft II® nebulizer with a Pulmo-Aide® compressor.

Both doses of PULMOZYME resulted in significant reductions in the number of patients experiencing respiratory tract infections requiring use of parenteral antibiotics compared with the placebo group. Administration of PULMOZYME reduced the relative risk of developing a respiratory tract infection by 27% and 29% for the 2.5 mg daily dose and the 2.5 mg twice daily dose, respectively (see Table 3). The data suggest that the effects of PULMOZYME on respiratory tract infections in older patients (> 21 years) may be smaller than in younger patients, and that twice daily dosing may be required in the older patients. Patients with baseline FVC > 85% may also benefit from twice a day dosing (see Table 3). The reduced risk of respiratory infection observed in PULMOZYME treated patients did not directly correlate with improvement in FEV_1 during the initial two weeks of therapy.

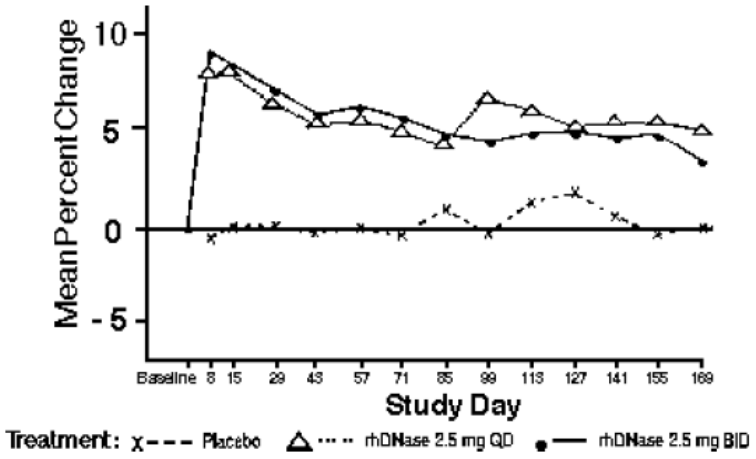
Within 8 days of the start of treatment with PULMOZYME, mean FEV_1 increased 7.9% in those treated once a day and 9.0% in those treated twice a day compared to the baseline values. The overall mean FEV_1 during long-term therapy increased 5.8% from baseline at the 2.5 mg daily dose level and 5.6% from baseline at the 2.5 mg twice daily dose level. Placebo recipients did not show significant mean changes in pulmonary function testing (see Figure 1).

For patients 5 years of age or older with baseline FVC greater than or equal to 40%, administration of PULMOZYME decreased the incidence of occurrence of first respiratory tract infection requiring parenteral antibiotics, and improved mean FEV_1, regardless of age or baseline FVC.

Table 3. Incidence of First Respiratory Tract Infection Requiring Parenteral Antibiotics in Patients with FVC ≥40% of Predicted

	Placebo N=325	2.5 mg QD N=322	2.5 mg BID N=321
Percent of Patients Infected	43%	34%	33%
Relative Risk (vs placebo)		0.73	0.71
p-value (vs placebo)		0.015	0.007
Subgroup by Age and Baseline FVC	Placebo % (N)	2.5 mg QD % (N)	2.5 mg BID % (N)
Age			
5-20 years	42% (201)	25% (199)	28% (184)
21 years and older	44% (124)	48% (123)	39% (137)
Baseline FVC			
40-85% Predicted	54% (194)	41% (201)	44% (203)
>85% Predicted	27% (131)	21% (121)	14% (118)

Figure 1. Mean Percent Change from Baseline FEV_1 in Patients with FVC ≥40% of Predicted



Trial in CF Patients with FVC <40% of Predicted

PULMOZYME has also been evaluated in a second randomized, placebo-controlled trial in clinically stable patients with baseline FVC < 40% of predicted. Patients were enrolled and treated with placebo (162 patients) or PULMOZYME 2.5 mg QD (158 patients) for twelve weeks. In patients who received PULMOZYME, there was an increase in mean change (as percent of baseline) compared to placebo in FEV_1 (9.4% vs. 2.1%, $p < 0.001$) and in FVC (12.4% vs. 7.3%, $p < 0.01$). PULMOZYME did not significantly reduce the risk of developing a respiratory tract infection requiring parenteral antibiotics

(54% of PULMOZYME patients vs. 55% of placebo patients had experienced a respiratory tract infection by 12 weeks, relative risk = .93, p = 0.62).

The effect of PULMOZYME on exercise tolerance has not been established in adult and pediatric patients.

Other Studies

Clinical trials have indicated that PULMOZYME therapy can be continued or initiated during an acute respiratory exacerbation.

Short-term dose ranging studies demonstrated that doses in excess of 2.5 mg BID did not provide further improvement in FEV_1. Patients who have received drug on a cyclical regimen (i.e., administration of PULMOZYME 10 mg BID for 14 days, followed by a 14 day wash out period) showed rapid improvement in FEV_1 with the initiation of each cycle and a return to baseline with each PULMOZYME withdrawal.

16 HOW SUPPLIED/STORAGE AND HANDLING

PULMOZYME (dornase alfa) inhalation solution is a sterile, clear, colorless solution supplied in:

- 30 unit cartons containing 5 foil pouches of 6 single-use ampules. Each 2.5 mL ampule contains 2.5 mg of dornase alfa (1 mg/mL): NDC 50242-100-40.

Storage and Handling

Store PULMOZYME under refrigeration (2°C to 8°C/36°F to 46°F) in their protective foil to protect from light. Do not use beyond the expiration date stamped on the ampule. Store unused ampules in their protective foil pouch under refrigeration. Refrigerate PULMOZYME during transport and do not expose to room temperatures for a total time of 24 hours.

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved Patient Labeling (Instructions for Use).

Storage and Handling Information

Instruct patients on the proper techniques to store and handle PULMOZYME. PULMOZYME must be stored in the refrigerator at 2 to 8°C (36 to 46°F) and protected from light. It should be kept refrigerated during transport and should not be exposed to room temperatures for a total time of 24 hours.

Advise patients to squeeze each ampule prior to use in order to check for leaks. The solution should be discarded if it is cloudy or discolored. Once opened, the entire contents of the ampule must be used or discarded.

Instruct patients in the proper use and maintenance of the jet nebulizer/compressor system or eRapid Nebulizer System used in PULMOZYME delivery.

Instruct patients not to dilute or mix PULMOZYME with other drugs in the nebulizer. Mixing of PULMOZYME with other drugs could lead to adverse physicochemical and/or functional changes in PULMOZYME or the admixed compound.

Use with the eRapid Nebulizer System

Instruct patients and caregivers to read and follow the directions in both the PULMOZYME Instructions for Use and in the Manufacturer's eRapid Nebulizer System Instruction Booklet.

Instruct patients and caregivers to clean the handset, including the medication reservoir, medicine cap, aerosol head, and mouthpiece, after each use. Instruct patients and caregivers to disinfect the handset, including the medication reservoir, medicine cap, aerosol head, and mouthpiece, after each day of use.

Instruct patients to replace the handset after 90 uses, regardless of whether the EasyCare cleaning aid is used. Since delivery data are not available for PULMOZYME administered with the eRapid handset beyond 90 administrations, delivery of the appropriate therapeutic dose of PULMOZYME cannot be assured beyond 90 administrations.

Pulmozyme® (dornase alfa)
Inhalation Solution

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