4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and special precautions for use

None.

4.5 Interaction with other medicinal products and other forms of interaction

Pulmozyme can be effectively and safely used in conjunction with standard cystic fibrosis therapies such as antibiotics, bronchodilators, pancreatic enzymes, vitamins, inhaled and systemic corticosteroids, and analgesics.

4.6 Pregnancy and lactation

Pregnancy

The safety of dornase alfa has not been established in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, or embryofetal development (see section 5.3). Caution should be exercised when prescribing dornase alfa to pregnant women.

Lactation

When dornase alfa is administered to humans according to the dosage recommendation, there is minimal systemic absorption; therefore no measurable concentrations of dornase alfa would be expected in human milk. Nevertheless, caution should be exercised when dornase alfa is administered to a breast-feeding woman (see section 5.3).

4.7 Effects on ability to drive and use machines

Pulmozyme has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The adverse event data reflect the clinical trial and post-marketing experience of using Pulmozyme at the recommended dose regimen.

Adverse reactions attributed to Pulmozyme are rare (< 1/1000). In most cases, the adverse reactions are mild and transient in nature and do not require alterations in Pulmozyme dosing.

Eye disorders:
Conjunctivitis.

Respiratory, thoracic and mediastinal disorders:
Dysphonia, dyspnea, pharyngitis, laryngitis, rhinitis (all non-infectious).

Gastrointestinal disorders:
Dyspepsia.

Skin and subcutaneous tissue disorders:
Rash, urticaria.
General disorders:
Chest pain (pleuritic/non-cardiac), pyrexia.

Investigations:
Pulmonary function tests decreased.

Patients who experience adverse events common to cystic fibrosis can, in general, safely continue administration of Pulmozyme as evidenced by the high percentage of patients completing clinical trials with Pulmozyme.

In clinical trials, few patients experienced adverse events resulting in permanent discontinuation from dornase alfa, and the discontinuation rate was observed to be similar between placebo (2%) and dornase alfa (3%).

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

Less than 5% of patients treated with dornase alfa have developed antibodies to dornase alpha and none of these patients have developed IgE antibodies to dornase alfa. Improvement in pulmonary function tests has still occurred even after the development of antibodies to dornase alfa.

4.9 Overdose

The effect of Pulmozyme overdosage has not been established. In clinical studies, 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 section 5.2).