Cough; Creo-Terpin; Creomulsion; Delsym; DexAlone; Diabe-Tuss DM; ElixSure Childrens Cough; Hold DM; Little Colds Cough Formula; PediaCare Childrens Long-Acting Cough; PediaCare Infants Long-Acting Cough; Robitussin Pediatric; Scot-Tussin DM Cough Chasers; Silphen DM; Simply Cough; Sucrets DM; Theraflu Cough; Triaminic Long Acting Cough; Trocal; Vicks 44 Cough Relief; ***Venez.:*** Bromodel†; Detofan†; Hidrofan†; Libolar; Metordex†; Mexobron†; Promedin; Tilodrin.

Multi-ingredient: numerous preparations are listed in Part 3.

Dimemorfan Phosphate *(rINNM)*

AT-17; Dimémorfane, Phosphate de; Dimemorfani Phosphas; Fosfato de dimemorfano. (+)-3,9a-Dimethylmorphinan phosphate.

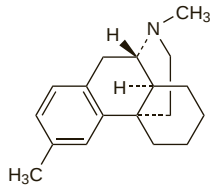
Димеморфана Фосфат

$C_{18}H_{25}N,H_3PO_4$ = 353.4.

CAS — 36309-01-0 (dimemorfan); 36304-84-4 (dimemorfan phosphate).

ATC — R05DA11.

ATC Vet — QR05DA11.



(dimemorfan)

Pharmacopoeias. In *Jpn.*

Profile

Dimemorfan phosphate is a centrally acting cough suppressant used for non-productive cough (p.1547). It is given orally in doses of 10 to 20 mg three or four times daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Tusben; ***Spain:*** Dastosin.

Dimethoxanate Hydrochloride *(BANM, rINNM)*

Diméthoxanate, Chlorhydrate de; Dimethoxanati Hydrochloridum; Hidrocloruro de dimetoxanato. 2-(2-Dimethylaminoethoxy)ethyl phenothiazine-10-carboxylate hydrochloride.

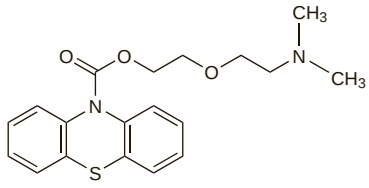
Диметоксаната Гидрохлорид

$C_{19}H_{22}N_2O_3S,HCl$ = 394.9.

CAS — 477-93-0 (dimethoxanate); 518-63-8 (dimethoxanate hydrochloride).

ATC — R05DB28.

ATC Vet — QR05DB28.



(dimethoxanate)

Profile

Dimethoxanate hydrochloride is a centrally acting cough suppressant used for non-productive cough (p.1547). It is given orally in usual doses of 37.5 mg three or four times daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Cotrane.

Dornase Alfa *(BAN, USAN, rINN)*

Deoxyribonuclease; Desoxyribonuclease; DNase I; Dornasa alfa; Dornasum Alfa; Dornaz Alfa; rhDNase. Deoxyribonuclease I (human recombinant).

Дорназа Альфа

$C_{1321}H_{1995}N_{339}O_{396}S_9$ = 29249.6.

CAS — 143831-71-4; 132053-08-8.

ATC — B06AA10; R05CB13.

ATC Vet — QB06AA10; QR05CB13.

Description. Dornase alfa is a recombinant enzyme having the same amino acid sequence and glycosylation pattern as human deoxyribonuclease I.

Adverse Effects

Common adverse effects with dornase alfa aerosol include pharyngitis, hoarseness of the voice, and chest pain. Occasionally laryngitis, conjunctivitis, and skin rashes and urticaria have been reported. There may be a transient decline in pulmonary function on beginning therapy with dornase alfa.

Uses and Administration

Dornase alfa acts as a mucolytic by hydrolysing DNA that has accumulated in sputum from decaying neutrophils. It is used as a nebulised solution in patients with cystic fibrosis; in the UK its indication is limited to patients with a forced vital capacity (FVC) greater than 40% of predicted value and to patients over 5 years of age, but in the USA it may also be given for advanced disease (FVC less than 40%) and to younger children. The usual dose is 2500 units (2.5 mg) of dornase alfa given once daily via a jet nebuliser. This dose may be given twice daily to patients over 21 years of age.

Bovine deoxyribonuclease has been used similarly. It has also been used topically, often with fibrinolysin, as a debriding agent for inflammatory and infected lesions. Bovine deoxyribonuclease has also been given by injection.

Administration in children. Although in some countries dornase alfa is not recommended for use in children under 5 years of age, a study[1] to assess the delivery of dornase alfa to the lungs of children with cystic fibrosis aged between 3 months and 5 years, showed that the amounts present in the lower airways were comparable to those in older children. It also appeared to be safe in these younger patients during the 2-week study period.

1. Wagener JS, *et al.* Aerosol delivery and safety of recombinant human deoxyribonuclease in young children with cystic fibrosis: a bronchoscopic study. *J Pediatr* 1998; **133:** 486–91.

Asthma. There are reports of the use of dornase alfa to liquefy mucus plugs and relieve an attack of acute severe asthma (p.1108) in children.[1-3] However, a randomised controlled study[4] found that adding a single dose of nebulised dornase alfa to standard emergency treatment has no benefits in children with moderate to severe acute asthma.

1. Greally P. Human recombinant DNase for mucus plugging in status asthmaticus. *Lancet* 1995; **346:** 1423–4.
2. Patel A, *et al.* Intratracheal recombinant human deoxyribonuclease in acute life-threatening asthma refractory to conventional treatment. *Br J Anaesth* 2000; **84:** 505–7.
3. Durward A, *et al.* Resolution of mucus plugging and atelectasis after intratracheal rhDNase therapy in a mechanically ventilated child with refractory status asthmaticus. *Crit Care Med* 2000; **28:** 560–2.
4. Boogaard R, *et al.* Recombinant human deoxyribonuclease for the treatment of acute asthma in children. *Thorax* 2008; **63:** 141–6.

Chronic obstructive pulmonary disease. A large phase III study in patients hospitalised for acute exacerbations of chronic bronchitis (p.1112) was halted prematurely because of a non-significant trend to increased mortality in patients given dornase alfa.[1]

1. Hudson TJ. Dornase in treatment of chronic bronchitis. *Ann Pharmacother* 1996; **30:** 674–5.

Cystic fibrosis. There is good evidence that inhalation therapy with dornase alfa can produce modest but useful improvement in lung function in some patients with cystic fibrosis (p.166). Most studies have concentrated on patients with mild or moderate disease (forced vital capacity at least 40% of the predicted value) in whom FEV_1 and forced vital capacity have shown improvements generally of the order of 5 to 10%,[1-3] and in whom more prolonged therapy (24 weeks) has been shown to reduce the risk of exacerbations of respiratory infections, and hence the need for intravenous antibacterial therapy.[3] There is also evidence that benefit may occur in patients with more severe disease.[4] A systematic review[5] of studies concluded that there is evidence to show that dornase alfa therapy over a 1-month period is associated with improved lung function. Furthermore, a randomised, multicentre, placebo-controlled study[6] in children showed that dornase alfa maintained lung function and reduced the risk of exacerbations over a period of 96 weeks. However, only a minority of patients, perhaps about one-third,[7] benefit from the drug, and at present there is no way of identifying those who will respond other than by a therapeutic trial.[8,9]

Given the high cost of therapy, which is not entirely recouped by savings in acute care, there has been some controversy about the appropriate use of dornase alfa:[10-13] it seems to be generally felt that it should be reserved for specialist use in cystic fibrosis clinics, but that patients should not be denied a trial where appropriate. Most responders with mild to moderate impairment of lung function will show improvements within 2 weeks, although in more severely affected patients a 6-week trial is advocated.[8] A review of the use of dornase alfa in cystic fibrosis concluded that dosing on alternate days would be as effective as daily dosing, and would reduce costs and treatment time.[14]

1. Ramsey BW, *et al.* Efficacy and safety of short-term administration of aerosolized recombinant human deoxyribonuclease in patients with cystic fibrosis. *Am Rev Respir Dis* 1993; **148:** 145–51.
2. Ranasinha C, *et al.* Efficacy and safety of short-term administration of aerosolised recombinant human DNase I in adults with stable stage cystic fibrosis. *Lancet* 1993; **342:** 199–202.
3. Fuchs H, *et al.* Effect of aerosolized recombinant human DNase on exacerbations of respiratory symptoms and on pulmonary function in patients with cystic fibrosis. *N Engl J Med* 1994; **331:** 637–42.
4. McCoy K, *et al.* Effects of 12-week administration of dornase alfa in patients with advanced cystic fibrosis lung disease. *Chest* 1996; **110:** 889–95.
5. Jones AP, *et al.* Dornase alpha for cystic fibrosis. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2003 (accessed 15/07/08).
6. Quan JM, *et al.* A two-year randomized, placebo-controlled trial of dornase alfa in young patients with cystic fibrosis with mild lung function abnormalities. *J Pediatr* 2001; **139:** 813–20.
7. Davis PB. Evolution of therapy for cystic fibrosis. *N Engl J Med* 1994; **331:** 672–3.
8. Conway SP, Littlewood JM. rhDNase in cystic fibrosis. *Br J Hosp Med* 1997; **57:** 371–2.
9. Ledson MJ, *et al.* Targeting of dornase alpha therapy in adult cystic fibrosis. *J R Soc Med* 1998; **91:** 360–4.
10. Anonymous. Dornase alfa for cystic fibrosis. *Drug Ther Bull* 1995; **33:** 15–16.
11. Spencer D, Weller P. Dornase-alfa for cystic fibrosis. *Lancet* 1995; **345:** 1307.
12. Bush A, *et al.* Dornase alfa for cystic fibrosis. *BMJ* 1995; **310:** 1533.
13. Robert G, *et al.* Dornase alfa for cystic fibrosis. *BMJ* 1995; **311:** 813.
14. Suri R. The use of human deoxyribonuclease (rhDNase) in the management of cystic fibrosis. *BioDrugs* 2005; **19:** 135–44.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Pulmozyme; ***Austral.:*** Pulmozyme; ***Austria:*** Pulmozyme; ***Belg.:*** Pulmozyme; ***Braz.:*** Pulmozyme; ***Canad.:*** Pulmozyme; ***Chile:*** Viscozyme; ***Cz.:*** Pulmozyme; ***Denm.:*** Pulmozyme; ***Fin.:*** Pulmozyme; ***Fr.:*** Pulmozyme; ***Ger.:*** Pulmozyme; ***Gr.:*** Pulmozyme; ***Hung.:*** Pulmozyme; ***Irl.:*** Pulmozyme; ***Israel:*** Pulmozyme; ***Ital.:*** Pulmozyme; ***Mex.:*** DNSM; Pulmozyme; ***Neth.:*** Pulmozyme; ***Norw.:*** Pulmozyme; ***NZ:*** Pulmozyme; ***Pol.:*** Pulmozyme; ***Port.:*** Pulmozyme; ***Rus.:*** Pulmozyme (Пульмозим); ***S.Afr.:*** Pulmozyme; ***Spain:*** Pulmozyme; ***Swed.:*** Pulmozyme; ***Switz.:*** Pulmozyme; ***Turk.:*** Pulmozyme; ***UK:*** Pulmozyme; ***USA:*** Pulmozyme.

Multi-ingredient: ***Arg.:*** Clorfibrase; ***Austria:*** Fibrolan; ***Braz.:*** Cauterex; Dermofibrin C†; Fibrabene; Fibrase; Fibrinase c/Cloranfenicol; Gino-Cauterex; Gino-Fibrase; Procutan†; ***Chile:*** Elase; ***Cz.:*** Fibrolan; ***Fr.:*** Elase; ***Ger.:*** Fibrolan†; ***Hung.:*** Fibrolan; ***Ital.:*** Elase†; ***Malaysia:*** Elase; ***Mex.:*** Fibrase; Fibrase SA; Ridasa; ***Pol.:*** Fibrolan; ***Switz.:*** Fibrolan.

Dropropizine *(BAN, rINN)*

Dropropitsiini; Dropropizin; Dropropizina; Dropropizinum; UCB-1967. 3-(4-Phenylpiperazin-1-yl)propane-1,2-diol.

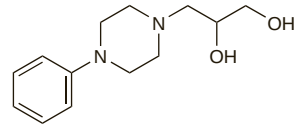
Дропропизин

$C_{13}H_{20}N_2O_2$ = 236.3.

CAS — 17692-31-8.

ATC — R05DB19.

ATC Vet — QR05DB19.



Levodropropizine *(BAN, rINN)*

DF-526; Levdropropizine; Levodropropitsiini; Levodropropizin; Levodropropizina; Levodropropizinas; Lévodropropizine; Levodropropizinum. The (–)-(*S*)-isomer of dropropizine.

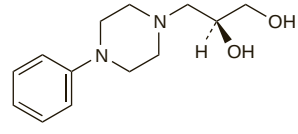
Леводропропизин

$C_{13}H_{20}N_2O_2$ = 236.3.

CAS — 99291-25-5.

ATC — R05DB27.

ATC Vet — QR05DB27.



Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Levodropropizine). A white or almost white powder. Slightly soluble in water and in alcohol; freely soluble in dilute acetic acid and in methyl alcohol. A 2.5% solution in water has a pH of 9.2 to 10.2. Protect from light.

Profile

Dropropizine is a cough suppressant reported to have a peripheral action in non-productive cough (p.1547). It is given orally usually in a dose of 30 mg three or four times daily. Levodropropiz-