

Entry and Stopping Criteria for Treatment with Dornase Alfa

Distribution of dornase alfa is from pharmacies at hospital out-patient departments and retail pharmacies as nominated by patient and selected retail pharmacies in the Northern region, Western Bay of Plenty and the greater Wellington/Kapiti Coast region that have an exclusive contract (HP1) to dispense Pulmozyme.

The following conditions, which need to be met for subsidy, were established by paediatricians and physicians with expertise in the treatment of cystic fibrosis (including a nominee from the Thoracic Society of Australia and New Zealand (New Zealand Branch)); and the New Zealand Cystic Fibrosis Association and the Respiratory Committee of the NZ Paediatric Society in conjunction with the Pharmaceutical and Therapeutics Advisory Committee (PTAC).

1. Assessment at cystic fibrosis clinics

Patients must be assessed at regional cystic fibrosis clinics or centres which are under the control of specialist respiratory physicians/paediatricians with experience and expertise in the management of cystic fibrosis and the prescribing of dornase alfa under the Pharmaceutical Schedule is limited to such physicians.

2. Measurement of lung function

The measurement of lung function is to be conducted by experienced, qualified respiratory technicians. Allowance needs to be made for age/height related changes in children's lung function measurement. Spirometry should be the best of three measurements with repeat Spirometry under the same circumstances.

Adherence to American Thoracic Society (ATS) criteria for lung function testing is required, as referred to in:

- (a) American Journal of Respiratory and Critical Care Medicine 1995; 152:1107-36; and
- (b) The New England Journal of Medicine 1994; 331: 25-30.

3. Inclusion of patients in a national data-base

All patients having treatment with dornase alfa should be included in the national cystic fibrosis database. Prescribing physicians/paediatricians are required to supply updated patient information on a six monthly basis.

4. Patients Eligible for Initiation of dornase alfa therapy

Cystic fibrosis patients who are eligible for an initial trial of four weeks of dornase alfa are those:

- (a) willing to undertake a trial of dornase alfa;
- (b) five years or older;

- (c) with FEV1 less than 65% predicted (for age, gender and height);
- (d) who are clinically stable as documented by 3 consistent (or stable) baseline measurements of FEV1 and FVC within the six weeks prior to application;
- (e) who have evidence of chronic suppurative disease (cough and sputum most days of the week, or greater than three respiratory tract infections of more than two weeks' duration in any twelve months);
- (f) who are provided with written acknowledgement of the nature of the trial of therapy and that continued treatment may not be recommended or made available;
- (g) be willing to continue with other standard treatments including secretion removal techniques, pancreatic enzyme supplements, vitamin supplements, etc.

This phase of initial therapy is limited to four weeks' treatment with dornase alfa at a dose of 2.5 mg daily.

Immediately prior to instigation of dornase alfa therapy, a further baseline measurement of FEV1 & FVC (best of three measurements) should be undertaken. Only if continuing stability is demonstrated should the trial be commenced. If previous bronchial hyper-reactivity has been demonstrated it is recommended that respiratory function tests should always be done 10 to 15 minutes after treatment with a bronchodilator. Other lung volume measurements recorded in the previous 12 months should also be included in the application.

5. Application for Initial one month Trial of DN'ase

Physicians/Paediatricians who have patients who seem to fulfil the eligibility criteria should apply to the Cystic Fibrosis Advisory Panel (the **Panel**) via the co-ordinator by mail at:

Cystic Fibrosis Advisory Panel
c/- PHARMAC
P O Box 10-254
Wellington

or by email to cffpanel@pharmac.govt.nz. Application forms and other data related to trials are available from the coordinator. The Panel consists of at least three physicians/paediatricians experienced in the management of cystic fibrosis and appointed by PHARMAC. Applications should be in writing to the Panel (completion of the questionnaire plus additional clinical details).

If a Panel member's patient is being considered, that Panel member may not partake in the decision making process. To be successful, an application must be approved by at least two Panel members.

6. Continuation of therapy

At or towards the end of the initial four weeks' trial, patients must be reassessed and further lung function measurements be undertaken (test under conditions as above). To be eligible for continued treatment, the following criteria must be met: -

- (a) patients willing to continue with treatment (implying a lack of significant adverse effects and improved quality of life); and
- (b) at least a 10% improvement in baseline FEV₁.

Approval for continued treatment will be by the Panel (greater than or equal to two members approval required).

7. Retesting

Patients whose FEV₁ has not increased by 10% or more after four weeks of treatment at the recommended dose may apply for a further trial of dornase alfa after a three month period. Up to three trials may be undertaken within a twelve month period.

Abandoned Trials

If an infective exacerbation supervenes in an initial trial, which is severe enough to require intensive management (IV antibiotics and hospitalisation) and is associated with a deterioration of 10% or more in lung function, the trial should be abandoned and the Panel notified. To be eligible for a re-trial the following criteria must be met:

- (a) a period of clinical stability following recovery from the infective exacerbation; and
- (b) lung function test demonstrating an FEV₁ consistent with pre-treatment values is submitted to the Panel.

If FEV₁ post-exacerbation is not consistent with baseline values obtained pre-treatment, two further FEV₁ measurements taken within a six week period demonstrating clinical stability should be supplied to the Panel prior to a re-trial being approved. Up to three trials may be undertaken within a twelve month period.

8. Six month trials

It is important that other aspects of treatment, such as physiotherapy, be continued. Following an initial six months therapy, a further assessment should be undertaken.

To be eligible for continued treatment the following criteria must be met:

- (a) Patient willingness to continue with treatment. This requires a formal assessment by the physician that in their opinion, and in the opinion of the patient (or the patient's family, in the case of paediatric patients) that DN^aase is continuing to produce worthwhile benefits. Such an assessment should include serial lung functions taken during the trial on at least 3 occasions ie 2½, 4½ and 6 months, impact on hospitalisation, infective exacerbations, antibiotic use etc.
- (b) Dornase alfa therapy should cease if there is not general agreement of benefit, as there is always the possibility of harm from unnecessary use.

- (c) Maintenance of FEV1 at greater than or equal to 7.5% above original baseline.

9. Reassessment

Reassessment at 1 month and 6 months should be undertaken when clinically stable.

10. Long Term Treatment

After completion of the six month trial, patients are eligible for continuation on long term therapy.

To be eligible for continued treatment, the following criteria must be met:

- (a) patient consent and willingness to continue with treatment is required. This requires a formal assessment by the physician that in their opinion, and in the opinion of the patient (or the patient's family, in the case of paediatric patients) that DN'ase is continuing to produce worthwhile benefits. Such an assessment should include impact of hospitalisation, infective exacerbations, IV antibiotic use, out-patient visits, height, weight etc.
- (b) serial lung functions taken at 3 monthly intervals and regular reviews by physician;
- (c) provision of the formal assessments and lung function tests to the Panel is a requirement of continued supply. A request would be made asking the patient to allow this information to be included in the national CF database.

11. Appeal Procedure

- (a) In the first instance, an appeal is to be referred directly to the CF DN'ase Advisory Panel. The Panel is to consider that appeal within a reasonable time and is to provide a summary of that appeal to PHARMAC with the Panel's report for the relative month. The Panel is to provide PHARMAC with such further details in relation to any such appeal as it may reasonably request.
- (b) If after considering an appeal by an applicant under clause 11(a), the Panel upholds its decision not to grant the applicant subsidised access to dornase alfa, then the Panel is, via the Panel Co-ordinator, to advise the applicant of his or her right of appeal to an appeal committee against the determination of the Panel.
- (c) It is intended that the appeal committee will consist of a member of the Pharmacology and Therapeutics Advisory Committee and a person nominated by each of the New Zealand branch of, the Thoracic Society of Australia and New Zealand and/or the Respiratory Committee of the NZ Paediatric Society.

12. Review Criteria

These guidelines for use will be reviewed by the Panel with the objective of

ensuring, to the extent possible, optimum and fair allocation of dornase alfa. The guidelines for use may not be amended by the Panel unless it has consulted with PHARMAC in connection with the proposed amendment and the amendment has been approved by both PTAC and PHARMAC's board of directors.

Application and consent forms for one month trial, six month trial and initial 12 month supply of dornase alfa (Pulmozyme)

Please send applications to:

CF Advisory Panel Coordinator
 PHARMAC
 P O Box 10-254
 WELLINGTON

Phone: 04 460 4990
 Facsimile: 04 460 4995
 Email: cfpanel@pharmac.govt.nz

Complete this section when applying for a one month assessment and, if details have changed, when applying for continuation of therapy for six months.

Patient Details – patient sticker is acceptable			
Surname:			
First Name/s:			
NHI No:			
D.O.B:			
Address:			
Phone No:	Home:	Work:	Mobile:

Applying physician:		Date:
Practice Address:		
Phone:		
Fax:		
Email:		

General Practitioner:	
Address:	
Phone:	
Fax:	

Designated pharmacy: (hospital or equivalent HP1)	
Address:	
Phone:	
Fax:	

Patient history

Morbidity:	
Number of hospital admissions in the last 12 months for respiratory complications:	
Number of courses of IV antibiotics in the last 12 months:	
Outpatient visits:	
Number of outpatient visits in last 12 months:	

Management:			
Chest Physiotherapy		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Frequency:		<input type="checkbox"/> < once daily	
		<input type="checkbox"/> once-twice daily	
		<input type="checkbox"/> > twice daily	
Other therapies:			
Inhaled Antibiotic		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Long term macrolide		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Hypertonic saline	- Current therapy	<input type="checkbox"/> Yes	<input type="checkbox"/> No
	- Previous Trial	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Other comments

Pulmonary function

Measurement of lung function must be conducted by trained and experienced technicians and conform to the ATS criteria for lung function testing.

Date of Application: _____ / _____ / _____

Ethnicity: _____

Patient Details – patient sticker is acceptable	
Patient name:	_____
NHI No:	_____
D.O.B:	_____

One month trial – Baseline lung function				
Baseline data: FEV₁ measurements must be within 10% (mean FEV₁ +/- 5%) and all measurements should be taken within a 6 week period. If reversible airway obstruction is present, results should be measured post bronchodilator.				
Visit date	_____	_____	_____	_____
Age*	_____	_____	_____	_____
Height*	_____	_____	_____	_____
Weight*	_____	_____	_____	_____
FEV ₁ (L)	_____	_____	_____	_____
FEV ₁ (% predicted)	_____	_____	_____	_____
FVC (L)	_____	_____	_____	_____
FVC (% predicted)	_____	_____	_____	_____
*Age, height and weight required in children each time; single age and height for adults.				

One and six month trial review data – please resubmit this form and any relevant correspondence				
	One month trial review	Six month trial		
		2/12 review	4/12 review	6/12 review
Visit date	_____	_____	_____	_____
Age*	_____	_____	_____	_____
Height*	_____	_____	_____	_____
Weight*	_____	_____	_____	_____
FEV ₁ (L)	_____	_____	_____	_____
FEV ₁ (% predicted)	_____	_____	_____	_____
FVC (L)	_____	_____	_____	_____
FVC (% predicted)	_____	_____	_____	_____
*Age, height and weight required in children each time; single age and height for adults.				

Application for one month trial

Applying/Prescribing physician/paediatrician to complete:

Completed application form enclosed.	<input type="checkbox"/>
Signed patient consent included.	<input type="checkbox"/>
I acknowledge that this application for a trial of Pulmozyme, if approved, will be valid for one month and that I will have to reapply after 3 weeks for ongoing therapy for this patient.	<input type="checkbox"/>
I agree to ensure that Pulmozyme will be administered according to the guidelines.	<input type="checkbox"/>
I acknowledge that if there is insufficient response to therapy, subsidy for ongoing therapy will not be forthcoming.	<input type="checkbox"/>

Signed: _____

Date: ____/____/____

Note: Retesting of the patient at the appropriate time and prompt forwarding of information to the Cystic Fibrosis Advisory Panel Coordinator is necessary in order to avoid delays in reassessment of application and to avoid any unnecessary interruption of treatment.

Note: If the patient is unwell (acutely/subacutely) towards the end of the one or six month period and is not able to complete the required reassessment measurements, it is necessary to inform the Panel immediately.

Consent form – One month trial

Patient (or guardian) to complete:

I agree that further clinical data may be required by the Cystic Fibrosis Advisory Panel.	<input type="checkbox"/>
I acknowledge that, if approved for initial assessment, this is a one month trial after which the trial will end and I will be reassessed. I acknowledge that if there is not sufficient response to therapy after the one month trial, subsidy for ongoing therapy will not be forthcoming. I am aware that evidence from clinical trials suggests that the likelihood of having a beneficial response to justify ongoing provision of Pulmozyme is less than 50%.	<input type="checkbox"/>
I agree to my hospital number and details of my local hospital pharmacy (or equivalent) being given to Roche NZ for the sole purpose of supplying Pulmozyme for one month.	<input type="checkbox"/>

Signed: _____

Date: ____/____/____

Application for six month trial

Applying/Prescribing physician/paediatrician to complete

Completed application form enclosed.	<input type="checkbox"/>
Signed patient consent included.	<input type="checkbox"/>
I acknowledge that if approval for continuation is given, reassessment is required at or before 6 months from the approval date.	<input type="checkbox"/>
I agree to ensure that Pulmozyme is administered according to the guidelines. I acknowledge that if there is not sufficient ongoing response to therapy, subsidy for further ongoing therapy will not be forthcoming.	<input type="checkbox"/>

Signed: _____

Date: ____/____/____

Note: Retesting of the patient at the appropriate time and prompt forwarding of information the CF Advisory Panel Coordinator is necessary in order to avoid delays in reassessment of application and to avoid any unnecessary interruption of treatment.

Note: If the patient is unwell (acutely/subacutely) towards the end of the one or six month period and is not able to complete the required reassessment measurements, it is necessary to inform the CF Advisory Panel Coordinator immediately.

Note: If treatment is suspended or discontinued for any reason, please notify the CF Advisory Panel Coordinator immediately.

Consent form – Six month trial

Patient (or guardian) to complete

I acknowledge that, if approval for continuation is given, reassessment must occur at or before 6 months from approval date. I acknowledge that if there is not sufficient response to therapy that subsidy for ongoing therapy will not be forthcoming after the initial 6 months. I realise that it is difficult to estimate what my chances of continuation are.

Signed: _____

Date: ____/____/____

Application to continue long term therapy

Applying/Prescribing physician/paediatrician to complete

I acknowledge treatment with Pulmozyme continues to provide worthwhile benefits for this patient.	<input type="checkbox"/>
I acknowledge that if approval for long term therapy is given, reassessments are required at 3 monthly intervals or more frequently from the approval date, and that these assessments will be provided on an annual basis to the CF Advisory Panel Coordinator.	<input type="checkbox"/>
I agree to provide records of patient progress that include impact on hospitalisations, infective exacerbations, IV antibiotic use, and indices of nutrition including height and weight with centiles.	<input type="checkbox"/>
I agree to ensure that Pulmozyme is administered according to the guidelines.	<input type="checkbox"/>

Signed: _____

Date: ____/____/____

Note: Retesting of the patient at the appropriate times and prompt forwarding of these assessments to the CF Advisory Panel Coordinator is necessary in order to avoid delays in reassessment of application and to avoid any unnecessary interruption of treatment.

Note: If treatment is suspended or discontinued for any reason, please notify the CF Advisory Panel Coordinator immediately.

Consent form – Long term therapy

Patient (or guardian) to complete:

I consent to relevant clinical information being forwarded by my specialist to the Cystic Fibrosis Advisory Panel for the purposes of this application and subsequent long term applications, and understand that the information is used to evaluate my eligibility for continuing supply of Pulmozyme.	<input type="checkbox"/>
I understand that information contained in my applications is held securely by the Cystic Fibrosis Advisory Panel Coordinator. This information will be provided to the Cystic Fibrosis Advisory Panel and, when necessary, to PHARMAC staff and a PHARMAC review committee. This information may also be released to my specialist and my general practitioner on request.	<input type="checkbox"/>
I understand that I have the right to access and correct any personal information contained in any of my application form/s for funding of Pulmozyme.	<input type="checkbox"/>
PHARMAC may, from time to time, review funding of Pulmozyme.	<input type="checkbox"/>

Signed: _____

Date: ____/____/____

Renewal Application for Funding of dornase alfa (Pulmozyme)

Please send applications to:

CF Advisory Panel Coordinator
 PHARMAC
 P O Box 10-254
 WELLINGTON

Phone: 04 460 4990
 Facsimile: 04 460 4995
 Email: cfpanel@pharmac.govt.nz

Patient Details – patient sticker is acceptable			
Surname:			
First Name/s:			
NHI No:			
D.O.B:			
Address:			
Phone No:	Home:	Work:	Mobile:
Applying physician:			Date:
Practice Address:			
Phone:			
Fax:			
Email:			

Serial data				
Visit date				
Age*				
Height*				
Weight*				
FEV ₁ (L)				
FEV ₁ (% predicted)				
FVC (L)				
FVC (% predicted)				
*Age, height and weight required in children each time; single age and height for adults.				

Morbidity:		
Number of hospital admissions in the last 12 months for respiratory complications:		
Number of courses of IV antibiotics in the last 12 months:		
Outpatient visits:		
Number of outpatient visits in last 12 months:		
Compliance:		
To the best of your knowledge, is this patient compliant with Pulmozyme therapy?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Does this patient wish to continue with Pulmozyme therapy?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Do you consider that this patient continues to derive benefit from Pulmozyme therapy?		<input type="checkbox"/> Yes	<input type="checkbox"/> No
If yes to the question above, benefit is in terms of:			
Respiratory secretions are easier to remove		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Lung function has improved / maintained		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Exacerbation rate has reduced		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Other:	<hr/> <hr/> <hr/>		

Has Pulmozyme has been discontinued for any period (temporary or permanent) over the last 12 months?		<input type="checkbox"/> Yes	<input type="checkbox"/> No
If Yes, please provide details:	<hr/> <hr/> <hr/>		

Management:			
Chest Physiotherapy		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Frequency:		<input type="checkbox"/> < once daily	
		<input type="checkbox"/> once-twice daily	
		<input type="checkbox"/> > twice daily	
Other therapies:			
Inhaled Antibiotic		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Long term macrolide		<input type="checkbox"/> Yes	<input type="checkbox"/> No
Hypertonic saline		- Current therapy	
		<input type="checkbox"/> Yes	<input type="checkbox"/> No
		- Previous Trial	
		<input type="checkbox"/> Yes	<input type="checkbox"/> No

Other comments:

Application to continue long term therapy

Applying/Prescribing physician/paediatrician to complete

I acknowledge treatment with Pulmozyme continues to provide worthwhile benefits for this patient.	<input type="checkbox"/>
I acknowledge that if approval for long term therapy is given, reassessments are required at 3 monthly intervals or more frequently from the approval date, and that these assessments will be provided on an annual basis to the CF Advisory Panel Coordinator.	<input type="checkbox"/>
I agree to provide records of patient progress that include impact on hospitalisations, infective exacerbations, IV antibiotic use, and indices of nutrition including height and weight with centiles.	<input type="checkbox"/>
I agree to ensure that Pulmozyme is administered according to the guidelines.	<input type="checkbox"/>

Signed: _____

Date: ____/____/____

Note: Retesting of the patient at the appropriate times and prompt forwarding of these assessments to the CF Advisory Panel Coordinator is necessary in order to avoid delays in reassessment of application and to avoid any unnecessary interruption of treatment.

Note: If treatment is suspended or discontinued for any reason, please notify the CF Advisory Panel Coordinator immediately.

Consent form – Long term therapy

Patient (or guardian) to complete:

I consent to relevant clinical information being forwarded by my specialist to the Cystic Fibrosis Advisory Panel for the purposes of this application, and understand that the information is used to evaluate my eligibility for continuing supply of Pulmozyme.	<input type="checkbox"/>
I understand that the information contained in my application is held securely by the Cystic Fibrosis Advisory Panel Coordinator. This information will be provided to the Cystic Fibrosis Advisory Panel and, when necessary, to PHARMAC staff and a PHARMAC review committee. This information may also be released to my specialist and my general practitioner on request.	<input type="checkbox"/>
I understand that I have the right to access and correct any personal information contained in any of my application form/s for funding of Pulmozyme.	<input type="checkbox"/>
PHARMAC may, from time to time, review funding of Pulmozyme.	<input type="checkbox"/>

Signed: _____

Date: ____/____/____