

Cystic Fibrosis: diagnosis and management

Appendix M

Main appendix document

Health economics quality assessment

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Draft for Consultation

*Developed by the National Guideline Alliance, hosted
by the Royal College of Obstetricians and
Gynaecologist*

Disclaimer

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Appendices

Appendix M: Health economics quality assessment

M.1 Airway clearance

Study identification		
M.P. McIlwaine, M. Richmond, J.L. Agnew, N. Alarie, L. Lands, M. Chilvers, F. Ratjen WS5.6 Cost-effectiveness of performing positive expiratory pressure versus high frequency chest wall oscillation. Journal of Cystic Fibrosis, Volume 13, Supplement 2, Page S11		
Guidance topic: Cystic Fibrosis		Question no: 6
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	PEP & HFCWO
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	Canada
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Unclear	Non-societal and direct health care inferred
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not considered
1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 1 year
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcome measure: cost of therapy & number of exacerbations
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Cost-benefit analysis alongside RCT
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Time horizon: 1 year
2.3 Are all important and relevant outcomes included?	Partly	QoL outcomes not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	From RCT
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	From RCT
2.6 Are all important and relevant costs included?	Partly	Lack of detail
2.7 Are the estimates of resource use from the best	Partly	From RCT

available source?		
2.8 Are the unit costs of resources from the best available source?	Unclear	Sources not reported
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	Difference in cost / difference in exacerbations calculable
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	No	Only point estimates reported
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Severe limitations		
Other comments:		
Are money-costs and 'benefits' which are savings of future money-costs evaluated? No		
Have all important and relevant costs and outcomes for each alternative been quantified in money terms? Yes, medical costs appear to include the cost of treating exacerbations, but limited details in conference paper		
Has at least 1 of net present value, benefit/cost ratio and payback period been estimated? No, only net present value. Equipment does not appear to be annuitised over the lifespan		
Were any assumptions of materiality made? No, all relevant costs appear to be included, but limited details in conference paper		

M.2 Monitoring pulmonary disease

Study identification		
Moodie et al. 2014. Costs of Bronchoalveolar Lavage-Directed Therapy in the First 5 Years of Life for Children with Cystic Fibrosis. <i>The Journal of Pediatrics</i> ; 165 (3), pages 564–569		
Guidance topic: Cystic Fibrosis		Question no: 9
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	BAL & standard therapy
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	Australia & New Zealand
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	Health care provider
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL and adverse events not considered
1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 5 years
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	All outcomes transformed into costs
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	Other sectors not stated
1.9 Overall judgement: Directly applicable		
Other comments: This study does not include the preferred measure of effects (QALYs), but is still thought to be useful for decision making given that all other criteria are applicable and the alternative outcome measure reported is unlikely to change the conclusions about cost-		

effectiveness.		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Cost benefit analysis alongside RCT
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon: 5 years
2.3 Are all important and relevant outcomes included?	Partly	QoL outcomes and adverse events not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	From RCT
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	From RCT
2.6 Are all important and relevant costs included?	Yes	Full details on costs provided
2.7 Are the estimates of resource use from the best available source?	Yes	From RCT
2.8 Are the unit costs of resources from the best available source?	Yes	From national databases
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	No	Cost-benefit analysis
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	SDs & 95% CIs reported
2.11 Is there any potential conflict of interest?	Partly	Tobramycin provided free by the manufacturer
2.12 Overall assessment: Minor limitations		
Other comments:		
Are money-costs and 'benefits' which are savings of future money-costs evaluated? No		
Have all important and relevant costs and outcomes for each alternative been quantified in money terms? Yes		
Has at least 1 of net present value, benefit/cost ratio and payback period been estimated? No, only net present value		
Were any assumptions of materiality made? No, all relevant costs included and described		
Study identification		
Etherington et al. 2008. Clinical impact of reducing routine susceptibility testing in chronic <i>Pseudomonas aeruginosa</i> infections in cystic fibrosis. <i>Journal of Antimicrobial Chemotherapy</i> ; 61, pages 425-7.		
Guidance topic: Cystic Fibrosis		Question no: 7
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	No	Number of routine susceptibility tests conducted on isolates of <i>pseudomonas aeruginosa</i> , frequency is not a comparison in the

		protocol
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not considered
1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 6 months
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcome measure: cost savings from reduced resources
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Not applicable		
Other comments: Still considered relevant for decision making given that the Committee could make recommendations about the frequency of testing		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Not a cost-effectiveness analysis
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	No	Time horizon: 6 months
2.3 Are all important and relevant outcomes included?	Partly	QoL outcomes not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Partly	Before and after study
2.5 Are the estimates of relative intervention effects from the best available source?	Partly	Before and after study
2.6 Are all important and relevant costs included?	Partly	No detail regarding cost build up
2.7 Are the estimates of resource use from the best available source?	Partly	Before and after study, but resource use not described in detail
2.8 Are the unit costs of resources from the best available source?	Unclear	Sources not reported
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	No	Report cost savings from new protocol from consumable and staff time. Other clinical outcomes also reported.
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	No	Only point estimates reported
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Very serious limitations		
Other comments: Have all important and relevant costs and outcomes for each alternative been quantified, where appropriate? No, not all relevant costs and outcomes included Were any assumptions of materiality made to restrict the number of consequences considered?		

Unclear, insufficient detail regarding cost build-up
 Was an analysis of correlations between consequences carried out to help control for double counting? No
 Was there any indication of the relative importance of the difference consequence and suggested weighting of them? No
 Were there any theoretical relationships between consequences that could have been taken into account in determining weights? Final outcomes associated with a cost a QoL weight such as the duration of IV antibiotics
 Were the consequences considered one by one to see if a decision could be made based on a single consequence or a combination of a small number of consequences? No
 Were the consequences considered in subgroups of all consequences in the analysis to see if a decision could be made based on a particular subgroup? No
 Was an MCDA (multiple criteria decision analysis) or other published method of aggregation of consequences attempted?

M.3 Muocactive agents

Study identification

Suri R, Grieve R, Normand C, Metcalfe C, Thompson S, Wallis C, Bush A. "Effects of hypertonic saline, alternate day and daily rhDNase on healthcare use, costs and outcomes in children with cystic fibrosis." *Thorax*. 2002: Oct;57(10):841-6

Guidance topic: Cystic Fibrosis		Question no: 11
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	rhDNase & HS
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL and adverse events not considered
1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 12 weeks
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcomes associated with a resource use transformed into costs
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Cost benefit analysis alongside crossover trial
2.2 Is the time horizon sufficiently long to reflect all	Partly	Time horizon: 12

important differences in costs and outcomes?		week crossover trial
2.3 Are all important and relevant outcomes included?	Partly	QoL outcomes and adverse events not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	From randomised crossover trial
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	From randomised crossover trial
2.6 Are all important and relevant costs included?	Yes	Full details on costs provided
2.7 Are the estimates of resource use from the best available source?	Yes	From randomised crossover trial
2.8 Are the unit costs of resources from the best available source?	Yes	UK recognised sources
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	No	Cost-benefit analysis
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	95% CIs reported
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations		
Other comments:		
Are money-costs and 'benefits' which are savings of future money-costs evaluated? No		
Have all important and relevant costs and outcomes for each alternative been quantified in money terms? Yes		
Has at least 1 of net present value, benefit/cost ratio and payback period been estimated? No, only net present value		
Were any assumptions of materiality made? No, all relevant costs included and described		
Study identification		
Grieve R, Thompson S, Normand C, Suri R, Bush A, Wallis C. "A cost-effectiveness analysis of rhDNase in children with cystic fibrosis." <i>Int J Technol Assess Health Care</i> . 2003; 19(1):71-9.		
Guidance topic: Cystic Fibrosis		Question no: 11
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	rhDNase & HS
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL and adverse effects not considered
1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 12 weeks
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcomes associated with a resource use transformed into costs
1.8 Are costs and outcomes from other sectors fully and	Unclear	

appropriately measured and valued?		
1.9 Overall judgement: Directly applicable		
Other comments: This study does not include the preferred measure of effects (QALYs), but is still thought to be useful for decision making given that all other criteria are applicable and the alternative outcome measure reported is unlikely to change the conclusions about cost-effectiveness.		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Results taken from crossover trial
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Time horizon: 12 week crossover
2.3 Are all important and relevant outcomes included?	Partly	QoL outcomes and adverse effects not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	From randomised crossover trial
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	From randomised crossover trial
2.6 Are all important and relevant costs included?	Yes	Full details on costs provided
2.7 Are the estimates of resource use from the best available source?	Yes	From randomised crossover trial
2.8 Are the unit costs of resources from the best available source?	Yes	UK recognised sources
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	ICER £ per 1% gain in FEV1
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	PSA
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations		
Other comments:		
Study identification		
Christopher F, Chase D, Stein K, Milne R.J. rhDNase therapy for the treatment of cystic fibrosis patients with mild to moderate lung disease. Clin Pharm Ther. 1999 Dec;24(6):415-26.		
Guidance topic: Cystic Fibrosis		Question no: 11
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	rhDNase
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	UK analysis based on US clinical effectiveness data
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not considered
1.6 Are all future costs and outcomes discounted appropriately?	Yes	Time horizon: lifetime
1.7 Is QALY used as an outcome, and was it derived using	No	LYG

NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).		
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	Risk of death dependent on FEV1
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Time horizon: 12 week crossover trial used to inform analysis
2.3 Are all important and relevant outcomes included?	Partly	QoL outcomes not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Partly	From US RCT
2.5 Are the estimates of relative intervention effects from the best available source?	Partly	From US RCT
2.6 Are all important and relevant costs included?	Partly	From US RCT
2.7 Are the estimates of resource use from the best available source?	Partly	From US RCT
2.8 Are the unit costs of resources from the best available source?	Yes	UK recognised sources
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	ICER cost per LYG
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	OWSA on FEV1 parameters and subgroup analysis
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Very serious limitations		
Other comments:		
Study identification		
Menzin J, Oster G, Davies L, Drummond MF, Greiner W, Lucioni C, Merot JL, Rossi F, vd Schulenburg JG, Sou��tre E. "A multinational economic evaluation of rhDNase in the treatment of cystic fibrosis." Int J Technol Assess Health Care. 1996; 12(1):52-61.		
Guidance topic: Cystic Fibrosis		Question no: 11
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	rhDNase
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	UK analysis based on US clinical effectiveness data
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not considered

1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 24 weeks
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Cost-benefit analysis
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Cost-benefit analysis
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Time horizon: 24 weeks
2.3 Are all important and relevant outcomes included?	Partly	QoL outcomes not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Partly	From US RCT
2.5 Are the estimates of relative intervention effects from the best available source?	Partly	From US RCT
2.6 Are all important and relevant costs included?	No	From US RCT adapted to UK setting, insufficient detail reported on translation, cost of rhDNase not included
2.7 Are the estimates of resource use from the best available source?	Partly	From US RCT adapted to UK setting, insufficient detail reported on translation
2.8 Are the unit costs of resources from the best available source?	Unclear	Cost of care taken from 3 UK CF centres
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	No	Cost-benefit analysis
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	No	Not assessed
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Very serious limitations		
Other comments:		
Are money-costs and 'benefits' which are savings of future money-costs evaluated? No		
Have all important and relevant costs and outcomes for each alternative been quantified in money terms? Unclear, cost of rhDNase not included		
Has at least 1 of net present value, benefit/cost ratio and payback period been estimated? No, only net present value		
Were any assumptions of materiality made? Unclear		
Study identification		
McIntyre AM. "Dornase alpha and survival of patients with cystic fibrosis." Hosp Med. 1999; 60(10):736-9.		
Guidance topic: Cystic Fibrosis		Question no: 11

Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	rhDNase
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Partly	UK analysis based on non-UK clinical effectiveness data
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Partly	Discount rate: 6% Time horizon: lifetime
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Cost-benefit analysis
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Cost-benefit analysis
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon: lifetime
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Partly	From non-UK studies
2.5 Are the estimates of relative intervention effects from the best available source?	Partly	From non-UK studies
2.6 Are all important and relevant costs included?	Unclear	CF costs categorised into mild, moderate or severe CF
2.7 Are the estimates of resource use from the best available source?	Unclear	From non-UK studies, insufficient detail on how CF care is costed according to severity
2.8 Are the unit costs of resources from the best available source?	Partly	Cost of care taken from a UK study (Robson 1992), based on severity
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	No	Cost-benefit analysis
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Improvement with rhDNase varied
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Very serious limitations		

Other comments:		
Are money-costs and 'benefits' which are savings of future money-costs evaluated? No		
Have all important and relevant costs and outcomes for each alternative been quantified in money terms? Unclear		
Has at least 1 of net present value, benefit/cost ratio and payback period been estimated? No, only net present value		
Were any assumptions of materiality made? Unclear		
Study identification		
Mannitol HTA		
Guidance topic: Cystic Fibrosis		Question no: 11
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	rhDNase & mannitol
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Yes	Time horizon: lifetime
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Yes	
1.9 Overall judgement: Applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon: lifetime
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	Patient level data
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	Patient level data, note the effect of mannitol was assumed to be the same in rhDNase users and non-users in the manufacturer's initial submission
2.6 Are all important and relevant costs included?	Yes	Patient level data
2.7 Are the estimates of resource use from the best available source?	Yes	Patient level data

2.8 Are the unit costs of resources from the best available source?	Yes	UK recognised sources
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	PSA
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: No limitations		

M.4 Antimicrobial agents

Study identification

Tappenden, P., Harnan, S., Uttley, L., Mildred, M., Walshaw, M., Taylor, C., Brownlee, K., The cost effectiveness of dry powder antibiotics for the treatment of *Pseudomonas aeruginosa* in patients with cystic fibrosis, *Pharmacoeconomics*, 32, 159-72, 2014

Guidance topic: Cystic Fibrosis		Question no: 13
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	Coli DPI vs. NT Tobi DPI vs. NT
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Yes	Time horizon: lifetime Discount rate: 3.5%
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Yes	
1.9 Overall judgement: Applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	Treatment switching occurs in clinical practice but no data on this
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon: lifetime and within trial analysis
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	From RCT

2.5 Are the estimates of relative intervention effects from the best available source?	Yes	From RCT
2.6 Are all important and relevant costs included?	Yes	Full details on costs provided
2.7 Are the estimates of resource use from the best available source?	Yes	From RCT
2.8 Are the unit costs of resources from the best available source?	Yes	From UK recognised sources
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	OWSA and PSA
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: No limitations		
Other comments:		
Study identification		
Tappenden,P., Harnan,S., Uttley,L., Mildred,M., Carroll,C., Cantrell,A., Colistimethate sodium powder and tobramycin powder for inhalation for the treatment of chronic Pseudomonas aeruginosa lung infection in cystic fibrosis: systematic review and economic model, Health Technology Assessment (Winchester, England), 17, v-xvii, 2013		
Guidance topic: Cystic Fibrosis		Question no: 13
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	Coli DPI vs. NT
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Yes	Time horizon: lifetime Discount rate: 3.5%
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Yes	
1.9 Overall judgement: Directly applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	Treatment switching occurs in clinical practice but no data on this
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon: lifetime and within trial analysis

2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	From RCT
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	From RCT
2.6 Are all important and relevant costs included?	Yes	Full details on costs provided
2.7 Are the estimates of resource use from the best available source?	Yes	From RCT
2.8 Are the unit costs of resources from the best available source?	Yes	From UK recognised sources
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	OWSA and PSA
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: No limitations		
Other comments:		
Study identification		
Iles, R., Legh-Smith, J., Drummond, M., Prevost, A., Vowler, S., Economic evaluation of Tobramycin nebuliser solution in cystic fibrosis, <i>Journal of Cystic Fibrosis</i> , 2, 120-8, 2003		
Guidance topic: Cystic Fibrosis		Question no: 13
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	NT
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not considered
1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 12 months
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcome measure: cost savings from reduced resources
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Directly applicable		
Other comments: This study does not include the preferred measure of effects (QALYs), but is still thought to be useful for decision making given that all other criteria are applicable and the alternative outcome measure reported is unlikely to change the conclusions about cost-effectiveness.		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no/unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Cost-benefit analysis

2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Partly	Time horizon: 12 months
2.3 Are all important and relevant outcomes included?	Partly	QoL outcomes not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Partly	Before and after study
2.5 Are the estimates of relative intervention effects from the best available source?	Partly	Before and after study
2.6 Are all important and relevant costs included?	Partly	Insufficient detail
2.7 Are the estimates of resource use from the best available source?	Partly	Before and after study, but resource use not described in detail
2.8 Are the unit costs of resources from the best available source?	Unclear	Not all sources reported
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	No	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	No	95% CIs reported
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Serious limitations		
Other comments:		
Are money-costs and 'benefits' which are savings of future money-costs evaluated? No		
Have all important and relevant costs and outcomes for each alternative been quantified in money terms? Yes		
Has at least 1 of net present value, benefit/cost ratio and payback period been estimated? No, only net present value		
Were any assumptions of materiality made? None implied		
Study identification		
Schechter, M. S., Trueman, D., Farquharson, R., Higuchi, K., Daines, C. L., Inhaled Aztreonam Lysine versus Inhaled Tobramycin in Cystic Fibrosis. An Economic Evaluation, Annals of the American Thoracic Society, 12, 1030-8, 2015		
Guidance topic: Cystic Fibrosis		Question no: 13
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no/unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	Aztreonam vs. NT
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	No	US
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes and no	Stated but inappropriate – US third party payer
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	
1.6 Are all future costs and outcomes discounted appropriately?	Yes	Time horizon: lifetime Discount rate: 3.0%
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	Yes	

1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	Cost sources not described
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	Yes	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon: 3 years
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	From RCT with an open label extension
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	But note estimates of effectiveness not reproducible
2.6 Are all important and relevant costs included?	Unclear	Insufficient detail
2.7 Are the estimates of resource use from the best available source?	Unclear	Insufficient detail
2.8 Are the unit costs of resources from the best available source?	Unclear	Insufficient detail and US based sources
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	Scenario analysis, univariate and PSA
2.11 Is there any potential conflict of interest?	Partly	Supported by Gilead Sciences
2.12 Overall assessment: Serious limitations		
Other comments:		

M.5 Service configuration

Study identification		
Wolter, J. M., Bowler, S. D., Nolan, P. J., McCormack, J. G., Home intravenous therapy in cystic fibrosis: a prospective randomized trial examining clinical, quality of life and cost aspects, <i>European Respiratory Journal</i> , 10, 896-900, 1997		
Guidance topic: Cystic Fibrosis		Question no: 16
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	Home IV vs. hospital IV
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	Australia
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Partly	Includes costs borne by participants (societal perspective)
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Yes	

1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 5 years
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Cost-consequence analysis, but quality of life assessed
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	Cost-consequence analysis alongside RCT
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Unclear	Time horizon not defined, 1 course of IV inferred
2.3 Are all important and relevant outcomes included?	Yes	
2.4 Are the estimates of baseline outcomes from the best available source?	Yes	From small RCT
2.5 Are the estimates of relative intervention effects from the best available source?	Yes	From small RCT
2.6 Are all important and relevant costs included?	Yes	Full details on costs provided
2.7 Are the estimates of resource use from the best available source?	Yes	From small RCT
2.8 Are the unit costs of resources from the best available source?	Yes	From national databases
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	No	Could be calculated from data reported
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	SDs reported but sensitivity analysis not performed
2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Serious limitations		
Other comments:		
Have all important and relevant costs and outcomes for each alternative been quantified, where appropriate? Yes		
Were any assumptions of materiality made to restrict the number of consequences considered? None reported		
Was an analysis of correlations between consequences carried out to help control for double counting? No		
Was there any indication of the relative importance of the difference consequence and suggested weighting of them? No		
Were there any theoretical relationships between consequences that could have been taken into account in determining weights? Final outcomes associated with a cost a QoL weight such as the number of hospital admissions		
Were the consequences considered one by one to see if a decision could be made based on a single consequence or a combination of a small number of consequences? No		
Were the consequences considered in subgroups of all consequences in the analysis to see if a decision could be made based on a particular subgroup? No		
Was an MCDA (multiple criteria decision analysis) or other published method of aggregation of consequences attempted? No		

Study identification		
Thornton, J., Elliott, R. A., Tully, M. P., Dodd, M., Webb, A. K., Clinical and economic choices in the treatment of respiratory infections in cystic fibrosis: comparing hospital and home care, Journal of Cystic Fibrosis, 4, 239-47, 2005		
Guidance topic: Cystic Fibrosis		Question no: 16
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	Home IV vs. hospital IV, but not exclusive
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not considered
1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 1 year
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	ICER reported. Outcome measure: FEV1
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Directly applicable		
Other comments: This study does not include the preferred measure of effects (QALYs), but is still thought to be useful for decision making given that all other criteria are applicable and the alternative outcome measure reported is unlikely to change the conclusions about cost-effectiveness.		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon: 1 year
2.3 Are all important and relevant outcomes included?	Yes	QoL outcomes not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Partly	From retrospective observational study
2.5 Are the estimates of relative intervention effects from the best available source?	Partly	From retrospective observational study
2.6 Are all important and relevant costs included?	Yes	Details provided
2.7 Are the estimates of resource use from the best available source?	Yes	From retrospective observational study
2.8 Are the unit costs of resources from the best available source?	Yes	Recognised UK databases
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	Yes	Difference in FEV1 / difference in cost
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Yes	95% Cis reported and probabilistic analysis performed

2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations		
Other comments:		
Study identification		
Elliott, R. A., Thornton, J., Webb, A. K., Dodd, M., Tully, M. P., Comparing costs of home- versus hospital-based treatment of infections in adults in a specialist cystic fibrosis center, <i>International Journal of Technology Assessment in Health Care</i> , 21, 506-10, 2005		
Guidance topic: Cystic Fibrosis		Question no: 16
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5)	Yes/partly/no /unclear/NA	Comments
1.1 Is the study population appropriate for the review question?	Yes	People with CF
1.2 Are the interventions appropriate for the review question?	Yes	Home IV vs. hospital IV, but not exclusive
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	Yes	UK
1.4 Are the perspectives clearly stated and are they appropriate for the review question?	Yes	NHS
1.5 Are all direct effects on individuals included, and are all other effects included where they are material?	Partly	HRQoL not considered
1.6 Are all future costs and outcomes discounted appropriately?	NA	Time horizon: 1 year
1.7 Is QALY used as an outcome, and was it derived using NICE's preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).	No	Outcome measure: Cost
1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?	Unclear	
1.9 Overall judgement: Partially applicable		
Other comments:		
Section 2: Study limitations (the level of methodological quality)	Yes/partly/no /unclear/NA	Comments
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	NA	
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	Yes	Time horizon: 1 year
2.3 Are all important and relevant outcomes included?	Yes	QoL outcomes not considered
2.4 Are the estimates of baseline outcomes from the best available source?	Partly	From retrospective observational study
2.5 Are the estimates of relative intervention effects from the best available source?	Partly	From retrospective observational study
2.6 Are all important and relevant costs included?	Yes	Details provided
2.7 Are the estimates of resource use from the best available source?	Yes	From retrospective observational study
2.8 Are the unit costs of resources from the best available source?	Yes	Recognised UK databases
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	No	Could be calculated from data reported
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	Partly	95% CIs reported

2.11 Is there any potential conflict of interest?	No	
2.12 Overall assessment: Minor limitations		
Other comments:		
Are money-costs and 'benefits' which are savings of future money-costs evaluated? No		
Have all important and relevant costs and outcomes for each alternative been quantified in money terms? Yes		
Has at least 1 of net present value, benefit/cost ratio and payback period been estimated? No, only net present value		
Were any assumptions of materiality made? None implied		