Table 24: Clinical evidence profile: Comparison 2.1. Dornase alfa versus placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dornase alfa	Placebo	Relative (95% CI)	Absolute		
Lung function: relative mean % change in FEV_1 (follow-up 10 days; range of scores: 0-100; Better indicated by higher values)												
Shah 1996	randomised trials	very serious [1]	no serious inconsistency	no serious indirectness	serious[7]	none	20	21	-	MD 13.17 higher (0.70 to 25.64 higher)	VERY LOW	CRITICAL
Lung function: relative mean % change in FEV_1 (follow-up 1 months; range of scores: 0-100; Better indicated by higher values)												
4 (Laube 1996, Ramsey 1993a, Ranasinha 1993,	randomised trials	very serious [3]	very serious[4]	no serious indirectness	serious[7]	none	121	127	-	MD 9.52 higher (0.59 to 18.46 higher)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dornase alfa	Placebo	Relative (95% CI)	Absolute	**Quality**	**Importance**
Shah 1995)												
Lung function: relative mean % change in FEV_1 (follow-up 3 months; range of scores: 0-100; Better indicated by higher values)												
2 (Amin 2011, McCoy 1996)	randomised trials[5]	very serious [6]	no serious inconsistency	no serious indirectness	serious[7]	none	175	144	-	MD 6.7 higher (3.72 to 9.67 higher)	VERY LOW	CRITICAL
Lung function: relative mean % change in FEV_1 (follow-up 6 months; range of scores: 0-100; Better indicated by higher values)												
1 (Fuchs 1994)	randomised trials	serious [8]	no serious inconsistency	no serious indirectness	serious[7]	none	322	325	-	MD 5.8 higher (4.41 to 7.19 higher)	LOW	CRITICAL
subgroup analysis based on disease severity: participants with moderate disease FEV_1 relative mean % change in FEV_1 (follow-up 1 months; range of scores: 0-100; Better indicated by higher values)												
3 (Laube 1996, Ramsey 1993a, Ranasinha 1993)	randomised trials	very serious [9]	no serious inconsistency	no serious indirectness	no serious imprecision	none	90	93	-	MD 14.32 higher (10.81 to 17.83 higher)	LOW	CRITICAL
subgroup analysis based on disease severity: participants with severe disease FEV_1 relative mean % change in FEV_1 (follow-up 1 months; Better indicated by higher values)												
1 (Shah 1995)	randomised trials	very serious [10]	no serious inconsistency	no serious indirectness	serious[7]	none	31	34	-	MD 2.8 lower (8.76 lower to 3.16 higher)	VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dornase alfa	Placebo	Relative (95% CI)	Absolute	Quality	Importance
subgroup analysis based on disease severity: participants with acute pulmonary exacerbation mean % change in FEV_1 (follow-up 1 months; range of scores: 0-100; Better indicated by higher values)												
1 (Wilmott 1996)	randomised trials	very serious[11]	no serious inconsistency	no serious indirectness	very serious[2]	none	43	37	-	MD 1 higher (13.93 lower to 15.93 higher)	VERY LOW	CRITICAL
Lung function: absolute mean % change in FEV_1 (follow-up 2 years; range of scores: 0-100; Better indicated by higher values)												
1 (Quan 2001)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	204	206	-	MD 3.24 higher (1.03 to 5.45 higher)	MODERATE	CRITICAL
Number of people experiencing exacerbations (follow-up 6 month)												
1 (Fuchs 1994)	randomised trials	serious[8]	no serious inconsistency	no serious indirectness	serious[12]	none	71/322 (22%)	89/325 (27.4%)	RR 0.81 (0.61 to 1.06)	52 fewer per 1000 (from 107 fewer to 16 more)	LOW	CRITICAL
Number of people experiencing exacerbations (follow-up 2 years)												
1 (Quan 2001)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[12]	none	40/236 (16.9%)	56/234 (23.9%)	RR 0.71 (0.49 to 1.02)	69 fewer per 1000 (from 122 fewer to 5 more)	MODERATE	CRITICAL
Number of days of IV antibiotic use (follow-up 3 months; Better indicated by lower values)												
1 (McCoy 1996)	randomised trials	serious[13]	no serious inconsistency	no serious indirectness	very serious[14]	none	158	162	-	MD 2.96 lower (7.29 lower to 1.37 higher)	VERY LOW	CRITICAL
Adverse events: haemoptysis (follow-up 1 months)												
2 (Rana	randomised trials				very serious[14]	none	4/71 (5.6%)	3/70 (4.3%)		10 more per 1000 (from	VERY LOW	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dornase alfa	Placebo	Relative (95% CI)	Absolute		
sinha 1993, Shah 1995)		very serious [15]	no serious inconsistency	no serious indirectness					RR 1.23 (0.20 to 7.63)	34 fewer to 284 more)		
								4.3%		10 more per 1000 (from 34 fewer to 285 more)		
Adverse events: haemoptysis (follow-up 6 months)												
1 (Fuchs 1994)	randomised trials	serious [8]	no serious inconsistency	no serious indirectness	very serious[14]	none	17/322 (5.3%)	21/325 (6.5%)	RR 0.82 (0.44 to 1.52)	12 fewer per 1000 (from 36 fewer to 34 more)	VERY LOW	IMPORTANT
Adverse events: voice alteration (follow-up 1 months)												
3 (Ramsey 1993a, Ranasinha 1993, Shah 1995)	randomised trials	very serious [16]	very serious[17]	no serious indirectness	very serious[14]	none	13/115 (11.3%)	3/118 (2.5%)	RR 2.79 (0.03 to 278.07)	46 more per 1000 (from 25 fewer to 1000 more)	VERY LOW	IMPORTANT
								0%		-		
Adverse events: voice alteration (follow-up 3 months)												
1 (McCoy 1996)	randomised trials	serious [13]	no serious inconsistency	no serious indirectness	no serious imprecision	none	28/158 (17.7%)	10/162 (6.2%)	RR 2.87 (1.44 to 5.71)	115 more per 1000 (from 27 more to 291 more)	MODERATE	IMPORTANT
Adverse events: voice alteration (follow-up 6 months)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dornase alfa	Placebo	Relative (95% CI)	Absolute		
1 (Fuchs 1994)	randomised trials	serious [8]	no serious inconsistency	no serious indirectness	very serious[14]	none	12/322 (3.7%)	7/325 (2.2%)	RR 1.73 (0.69 to 4.34)	16 more per 1000 (from 7 fewer to 72 more)	VERY LOW	IMPORTANT
Adverse events: voice alteration (follow-up 2 years)												
1 (Quan 2001)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[14]	none	26/236 (11%)	27/234 (11.5%)	RR 0.95 (0.57 to 1.59)	6 fewer per 1000 (from 50 fewer to 68 more)	LOW	IMPORTANT
Quality of life: change in QFQ-R parents (follow-up 3 months; range of scores: 0-100; Better indicated by higher values)												
1 (Amin 2011)	randomised trials[5]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	17		-	MD 5.45 lower (15.23 lower to 4.33 higher)	MODERATE	IMPORTANT
Quality of life: change in QFQ-R 14+ (follow-up 3 months; range of scores: 0-100; Better indicated by higher values)												
1 (Amin 2011)	randomised trials[5]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	17		-	MD 5.21 lower (15.5 lower to 5.08 higher)	MODERATE	IMPORTANT

Abbreviations: CFQ-R: cystic fibrosis questionnaire revised; CI: confidence interval; FEV_1: forced expiratory volume in 1 second; IV: intravenous; MD: mean difference; RR: risk ratio

1 The quality of the evidence was downgraded by due to unclear sequence generation, allocation concealment, blinding and reporting

2 The quality of the evidence was downgraded by 2 as the CI crossed 2 clinical MIDs

3 The quality of the evidence was downgraded by 2 due to unclear sequence generation, blinding, allocation concealment and reporting in 3 of the trials, and unclear blinding and reporting in the fourth trial

4 The quality of the evidence was downgraded by 1 due to high heterogeneity (I2=88%) . See sensitivity analysis.

5 Amin 2011: cross-over trial

6 The quality of the evidence was downgraded by 1 due to unclear sequence generation, blinding, allocation concealment and reporting in the 1 of the trial

7 The quality of the evidence was downgraded by 1 as the 95% CI crossed 1 clinical MID

8 The quality of the evidence was downgraded by 1 due to unclear blinding, allocation, concealment and reporting

9 The quality of the evidence was downgraded by 2 due to unclear sequence generation, blinding, allocation concealment and reporting in 2 of the trials, and unclear blinding and reporting in the third trial

10 The quality of the evidence was downgraded by 2 due to unclear sequence generation, blinding, allocation concealment and reporting

11 The quality of the evidence was downgraded by 2 due to unclear sequence generation, blinding, allocation concealment and reporting
12 The quality of the evidence was downgraded by 1 as the 95% CI crossed 1 default MID
13 The quality of the evidence was downgraded by 2 due to unclear randomization, blinding, allocation concealment and reporting
14 The quality of the evidence was downgraded by 2 as the 95% CI crossed 2 default MIDs
15 The quality of the evidence was downgraded by 2 due to unclear sequence generation, blinding, allocation concealment and reporting in both trials
16 The quality of the evidence was downgraded by 2 due to unclear blinding, allocation concealment and reporting in 2 of the trials, and unclear blinding and reporting in the third trial
17 The quality of the evidence was downgraded by 1 due to high heterogeneity (I2=85%)