Table 48: Clinical evidence profile: Comparison 7. Itraconazole *versus* placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Itraconazole**	**Placebo, 24-week treatment**	**Relative (95% CI)**	**Absolute**		
Lung function (follow-up mean 24 weeks; measured with: percentage change in FEV_1 predicted from baseline ; range of scores: 0-100; Better indicated by higher values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	18	17	-	MD 4.94 lower (15.33 lower to 5.45 higher)	VERY LOW	CRITICAL
Lung function (follow-up mean 48 weeks; measured with: percentage change in FEV_1 predicted from baseline; range of scores: 0-100; Better indicated by higher values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	18	17	-	MD 3.71 lower (-13.26 to 20.28)	VERY LOW	CRITICAL
Time to next pulmonary exacerbation (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[4]	none	0/18 (0%)	0/17 (0%)	adjHR 1.34 (0.57 to 3.14)	-	VERY LOW	CRITICAL
proxy: number of patients with an exacerbation requiring antibiotics (follow-up mean 24 weeks; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Itraconazole	Placebo, 24-week treatment	Relative (95% CI)	Absolute		
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[5]	none	12/18 (66.7%)	7/18 (38.9%)	RR 1.71 (0.88 to 3.33)	276 more per 1000 (from 47 fewer to 906 more)	VERY LOW	IMPORTANT
proxy: number of patients with an exacerbation requiring AB (follow-up mean 48 weeks; Better indicated by lower values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[5]	none	15/18 (83.3%)	11/18 (61.1%)	RR 1.36 (0.89 to 2.08)	220 more per 1000 (from 67 fewer to 660 more)	VERY LOW	IMPORTANT
proxy: number of patients with an exacerbation admitted to hospital (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	3/18 (16.7%)	3/17 (17.6%)	RR 0.94 (0.22 to 4.05)	11 fewer per 1000 (from 138 fewer to 538 more)	VERY LOW	IMPORTANT
proxy: number of patients with an exacerbation admitted to hospital (follow-up mean 48 weeks; Better indicated by lower values)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Itraconazole	Placebo, 24-week treatment	Relative (95% CI)	Absolute		
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	4/18 (22.2%)	3/17 (17.6%)	RR 1.26 (0.33 to 4.82)	46 more per 1000 (from 118 fewer to 674 more)	VERY LOW	IMPORTANT
Quality of life – CFQ-R all domains (follow-up mean 24 weeks; range of scores: 0-100; Better indicated by higher values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	not calculable[7]	none	18	17	-	No significant differences	VERY LOW	IMPORTANT
Quality of life - CFQ-R respiratory domain (follow-up mean 24 weeks; range of scores: 0-100; Better indicated by higher values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	not calculable[7]	none	18 (mean: 3.76)	17 (mean: 4.77)	MD 1.01	p-value= 0.87	VERY LOW	IMPORTANT
Minor adverse events: increased dyspnoea (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	2/18 (11.1%)	2/16 (12.5%)	RR 0.89 (0.14 to 5.6)	14 fewer per 1000 (from 108 fewer	VERY LOW	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Itraconazole	Placebo, 24-week treatment	Relative (95% CI)	Absolute		
										to 575 more)		
Minor adverse events: rash (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	2/18 (11.1%)	1/16 (6.3%)	RR 1.78 (0.18 to 17.8)	49 more per 1000 (from 51 fewer to 1000 more)	VERY LOW	IMPORTANT
Minor adverse events: hyperglycaemia (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	1/18 (5.6%)	0/16 (0%)	RR 2.68 (0.12 to 61.58)	-	VERY LOW	IMPORTANT
Minor adverse events: flu-like illness (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	3/18 (16.7%)	0/16 (0%)	RR 6.26 (0.35 to 112.7)	-	VERY LOW	IMPORTANT
Minor adverse events: diarrhoea (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	0/18 (0%)	1/16 (6.3%)	RR 0.3 (0.01 to 6.84)	44 fewer per 1000	VERY LOW	IMPORTANT

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Itraconazole	Placebo, 24-week treatment	Relative (95% CI)	Absolute		
2012)										(from 62 fewer to 365 more)		
Minor adverse events: conjunctivitis (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	0/18 (0%)	1/16 (6.3%)	RR 0.3 (0.01 to 6.84)	44 fewer per 1000 (from 62 fewer to 365 more)	VERY LOW	IMPORTANT
Major adverse events: haemoptysis (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron 2012)	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	2/18 (11.1%)	1/16 (6.3%)	RR 1.78 (0.18 to 17.8)	49 more per 1000 (from 51 fewer to 1000 more)	VERY LOW	IMPORTANT
Major adverse events: spontaneous pneumothorax (follow-up mean 24 weeks; Better indicated by lower values)												
1 (Aaron	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[6]	none	1/18 (5.6%)	0/17 (0%)	RR 2.84 (0.12 to 65.34)	-	VERY LOW	IMPORTANT

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Itraconazole	Placebo, 24-week treatment	Relative (95% CI)	Absolute	Quality	Importance
2012)												

Abbreviations: CFQ-R: cystic fibrosis questionnaire reviewed; CI: confidence interval; FEV_1: forced expiratory volume in 1 second; MD: mean difference; RR: risk ratio
1 The quality of the evidence was downgraded by 1 due to unclear allocation, data reporting and sample size
2 The quality of the evidence was downgraded by 1 due to indirectness, as the therapeutic dosages were not achieved in 2/3 of the participants
3 The quality of the evidence was downgraded by 2 as the 95% CI crossed 2 clinical MIDs.
4 The quality of the evidence was downgraded by 2 as the 95% CI crossed the null effect and it is very wide. The study in underpowered to detect differences between groups.
5 The quality of the evidence was downgraded by 1 as the 95% CI crossed 1 default MID.
6 The quality of the evidence was downgraded by 2 as the 95% CI crossed 2 default MIDs
7 Not calculable, as no data was provided in the study.