Table 21: Modified-Release HC tablet vs Standard Glucocorticoid

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[Isidori/Mixed] Modified-Release hydrocortisone	standard glucocorticoid	Relative (95% CI)	Absolute (95% CI)		
Change in BMI from baseline												
1	randomised trials	serious[a]	not serious	serious[b]	serious[c]	none	43	35	-	MD **1.6 kg/m2 lower** (2.7 lower to 0.5 lower)	⊕◯◯◯ Very low	CRITICAL
Change in bodyweight from baseline												
1	randomised trials	serious[a]	not serious	serious[b]	serious[d]	none	43	35	-	MD **4 kg lower** (6.64 lower to 1.36 lower)	⊕◯◯◯ Very low	CRITICAL
Change in HbA1c from baseline												
1	randomised trials	serious[a]	not serious	serious[b]	serious[e]	none	43	35	-	MD **0.3 % lower** (0.44 lower to 0.16 lower)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**[Isidori/Mixed] Modified-Release hydrocortisone**	**standard glucocorticoid**	**Relative (95% CI)**	**Absolute (95% CI)**		
Change in AddiQoL from baseline												
1	randomised trials	very serious[f]	not serious	serious[b]	serious[g]	none	43	35	-	MD **5 out of 10 (AddiQoL score). higher** (0.89 higher to 9.11 higher)	⨁◯◯◯ Very low	CRITICAL
Change in infections [flu or flu-like events in 6 months] from baseline												
1	randomised trials	serious[a]	not serious	serious[b]	serious[h]	none	43	35	-	MD **0.8 flu or flu-like events. lower** (1.52 lower to 0.08 lower)	⨁◯◯◯ Very low	CRITICAL
Change in total cholesterol from baseline												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[Isidori/Mixed] Modified-Release hydrocortisone	standard glucocorticoid	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious[a]	not serious	serious[b]	serious[i]	none	43	35	-	MD **1 mg/dL lower** (14.76 lower to 12.76 higher)	⊕◯◯◯ Very low	CRITICAL
Serious adverse events												
1	randomised trials	serious[a]	not serious	serious[b]	very serious[j]	none	0/43 (0.0%)	2/35 (5.7%)	**OR 0.10** (0.01 to 1.73)	**51 fewer per 1,000** (from 57 fewer to 38 more)	⊕◯◯◯ Very low	CRITICAL

Explanations

a. Downgraded by 1 increment as the majority of evidence was of high risk of bias due to bias arising from the randomisation process [single-blind study design, allocation not concealed from patients].
b. Downgraded by 1 increment because of population indirectness. Population includes people with both primary and secondary AI [50% of population have secondary AI]
c. Downgraded by 1 increment as confidence interval crossed 1 MID (+/- 1.165)
d. Downgraded by 1 increment as confidence interval crossed 1 MID (+/- 2.91)
e. Downgraded by 1 increment as confidence interval crossed 1 MID (+/- 0.145)

f. Downgraded by 2 increments as the majority of evidence was of high risk of bias due to bias arising from the randomisation process [single-blind study design, allocation not concealed from patients] and measurement of the outcome [risk of measurement bias in patient-reported outcome].
g. Downgraded by 1 increment as confidence interval crossed 1 MID (+/- 4.365)
h. Downgraded by 1 increment as confidence interval crossed 1 MID (+/- 0.8)
i. Downgraded by 1 increment as confidence interval crossed 1 MID (+/- 13.1)
j. Downgraded by 2 increments as the confidence interval crossed two MIDS (0.8 to 1.25 default MID)