Ivacaftor–tezacaftor–elexacaftor, tezacaftor–ivacaftor and lumacaftor–ivacaftor for treating cystic fibrosis [ID3834]

Addendum- Fully incremental scenario analysis table

October 2023

1.1 EAG scenario analyses – fully incremental results with dominated treatments removed

1.1.1 F/F population

	Absolute			Incremental			ICER	NHB
	Costs	QALYs	LYs	Costs	QALYs	LYs		
Base case								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 1: LT ppFEV$_1$ decline absolute reduction								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 2: Company's estimates of LT ppFEV$_1$ decline on modulator treatments								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
IVA/TEZ/ELX	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 3: LT ppFEV$_1$ decline of ELX/TEZ/IVA from CF Trust FA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 4: LT ppFEV$_1$ decline of ELX/TEZ/IVA and TEZ/IVA from EAG lower bounds								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 5: No separate PE treatment effect								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 6: PE treatment effect applied for extension study period								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	

TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 7: No discontinuation beyond the extension study period								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 8: Lower long-term CFTR modulator compliance								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 9: EQ-5D values from Acaster 2015*								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 10: Pulmonary exacerbation disutility applied for 14 days								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 11: CFQ-R utility values from company model								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 12: Carer QoL utility increment for ELX/TEZ/IVA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 13: 23% reduction in ECM medication costs when on CFTR modulators								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 14: 40% reduction in ECM medication costs when on CFTR modulators								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	

LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 15: 1.5% discount rate (costs and QALYs)†								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 16: No long-term ppFEV$_1$ decline in ELX/TEZ/IVA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
LUM/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

*Severity modifier of 1.2 applied. ICER for ELX/TEZ/IVA when not applied is £[redacted]

† Severity modifier of 1.2 applied. ICER for ELX/TEZ/IVA when not applied is £[redacted]

Abbreviations: ELX/TEZ/IVA, Elexacaftor/tezacaftor/ivacaftor; LUM/IVA, Lumacaftor/ivacaftor; TEZ/IVA, Tezacaftor/ivacaftor; QALY, quality adjusted life year; LY, life year; ICER, incremental cost effectiveness ratio; ECM, established clinical management; EQ-5D, Euroqol 5-dimension; PE, pulmonary exacerbation; ppFEV$_1$, percent predicted forced expiratory volume in 1 second; LT, long-term; FA, final analysis; CF, cystic fibrosis

1.1.2 F/MF population

	Absolute			Incremental			ICER	NHB
	Costs	QALYs	LYs	Costs	QALYs	LYs		
Base case								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 1: LT ppFEV$_1$ decline absolute reduction								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 2: Company's estimates of LT ppFEV$_1$ decline on modulator treatments								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
IVA/TEZ/ELX	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 3: LT ppFEV$_1$ decline of ELX/TEZ/IVA from CF Trust FA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 4: LT ppFEV$_1$ decline of ELX/TEZ/IVA and TEZ/IVA from EAG lower bounds								

ECM	[redacted]							
IVA/TEZ/ELX	[redacted]							
Scenario 5: No separate PE treatment effect								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 6: PE treatment effect applied for extension study period								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 7: No discontinuation beyond the extension study period								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 8: Lower long-term CFTR modulator compliance								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 9: EQ-5D values from Acaster 2015*								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 10: Pulmonary exacerbation disutility applied for 14 days								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 11: CFQ-R utility values from company model								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 12: Carer QoL utility increment for ELX/TEZ/IVA								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 13: 23% reduction in ECM medication costs when on CFTR modulators								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 14: 40% reduction in ECM medication costs when on CFTR modulators								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 15: 1.5% discount rate (costs and QALYs)†								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							
Scenario 16: No long-term ppFEV$_1$ decline in ELX/TEZ/IVA								
ECM	[redacted]							
ELX/TEZ/IVA	[redacted]							

*Severity modifier of 1.2 applied. ICER without a severity modifier is £[redacted]

† Severity modifier of 1.2 applied. ICER without a severity modifier is £[redacted]

Abbreviations: ELX/TEZ/IVA, Elexacaftor/tezacaftor/ivacaftor; LUM/IVA, Lumacaftor/ivacaftor; TEZ/IVA, Tezacaftor/ivacaftor; QALY, quality adjusted life year; LY, life year; ICER, incremental cost effectiveness ratio; ECM, established clinical management; EQ-5D, Euroqol 5-dimension; PE, pulmonary exacerbation; $ppFEV_1$, percent predicted forced expiratory volume in 1 second; LT, long-term; FA, final analysis; CF, cystic fibrosis

1.1.3 F/Gating population

	Absolute			Incremental			ICER	NHB
	Costs	QALYs	LYs	Costs	QALYs	LYs		
Base case								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 1: LT ppFEV$_1$ decline absolute reduction								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 2: Company's estimates of LT ppFEV$_1$ decline on modulator treatments								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
IVA/TEZ/ELX	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 3: LT ppFEV$_1$ decline of ELX/TEZ/IVA from CF Trust FA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 4: LT ppFEV$_1$ decline of ELX/TEZ/IVA and TEZ/IVA from EAG lower bounds								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 5: No separate PE treatment effect								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 6: PE treatment effect applied for extension study period								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 7: No discontinuation beyond the extension study period								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 8: Lower long-term CFTR modulator compliance								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 9: EQ-5D values from Acaster 2015*								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 10: Pulmonary exacerbation disutility applied for 14 days								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 11: CFQ-R utility values from company model								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 12: Carer QoL utility increment for ELX/TEZ/IVA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 13: 23% reduction in ECM medication costs when on CFTR modulators								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 14: 40% reduction in ECM medication costs when on CFTR modulators								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 15: 1.5% discount rate (costs and QALYs)†								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 16: No long-term ppFEV$_1$ decline in ELX/TEZ/IVA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

*Severity modifier of 1.2 applied. ICER without a severity modifier is £[redacted]

† Severity modifier of 1.2 applied. ICER without a severity modifier is £[redacted]

Abbreviations: ELX/TEZ/IVA, Elexacaftor/tezacaftor/ivacaftor; LUM/IVA, Lumacaftor/ivacaftor; TEZ/IVA, Tezacaftor/ivacaftor; QALY, quality adjusted life year; LY, life year; ICER, incremental cost effectiveness ratio; ECM, established clinical management; EQ-5D, Euroqol 5-dimension; PE, pulmonary exacerbation; ppFEV$_1$, percent predicted forced expiratory volume in 1 second; LT, long-term; FA, final analysis; CF, cystic fibrosis

1.1.4 F/RF population

	Absolute			Incremental			ICER	NHB
	Costs	QALYs	LYs	Costs	QALYs	LYs		
Base case								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 1: LT ppFEV$_1$ decline absolute reduction								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 2: Company's estimates of LT ppFEV$_1$ decline on modulator treatments								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 3: LT ppFEV$_1$ decline of ELX/TEZ/IVA from CF Trust FA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 4: LT ppFEV$_1$ decline of ELX/TEZ/IVA and TEZ/IVA from EAG lower bounds								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 5: No separate PE treatment effect								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 6: PE treatment effect applied for extension study period								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 7: No discontinuation beyond the extension study period								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Scenario 8: Lower long-term CFTR modulator compliance								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 9: EQ-5D values from Acaster 2015								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 10: Pulmonary exacerbation disutility applied for 14 days								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 11: CFQ-R utility values from company model								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 12: Carer QoL utility increment for ELX/TEZ/IVA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 13: 23% reduction in ECM medication costs when on CFTR modulators								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 14: 40% reduction in ECM medication costs when on CFTR modulators								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 15: 1.5% discount rate (costs and QALYs)*								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Scenario 16: No long-term ppFEV$_1$ decline in ELX/TEZ/IVA								
ECM	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	-	-
TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
ELX/TEZ/IVA	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

*Severity modifier of 1.2 applied. ICER without severity modifier for ELX/TEZ/IVA is £[redacted]

Abbreviations: ELX/TEZ/IVA, Elexacaftor/tezacaftor/ivacaftor; LUM/IVA, Lumacaftor/ivacaftor; TEZ/IVA, Tezacaftor/ivacaftor; QALY, quality adjusted life year; LY, life year; ICER, incremental cost effectiveness ratio; ECM, established clinical management; EQ-5D, Euroqol 5-dimension; PE, pulmonary exacerbation; $ppFEV_1$, percent predicted forced expiratory volume in 1 second; LT, long-term; FA, final analysis; CF, cystic fibrosis

1.2 QALY shortfall estimates using EAG base-case with 1.5% discount rate

	F/F	F/MF	F/Gating	F/RF
Mean age (years)	20.15	20.91	20.71	28.61
Female (%)	51	51	52	55
QALYs with CF	[redacted]	[redacted]	[redacted]	[redacted]
QALYs without CF	34.91	34.51	34.51	31.11
Abs. shortfall	[redacted]	[redacted]	[redacted]	[redacted]
Prop. shortfall	[redacted]	[redacted]	[redacted]	[redacted]
QALY weight	1.2	1.2	1.2	1.2

Abbreviations: F/F, *F508del* homozygous; MF, minimal function; RF, residual function; CF, cystic fibrosis; QALY, quality adjusted life year

1.3 Additional EAG model validation

The EAG noted the concerns raised during the stakeholder engagement process about the reliability of the EAG's model. As an additional quality assurance step, the EAG used the Company's preferred parameter estimates and assumptions for ELX/TEZ/IVA within the EAG model. This could only be compared to the Company's originally submitted model with list prices and age of patients aged 6+ as the EAG had not received an updated model following stakeholder engagement. As the EAG model was not built to be an exact replicate of the Company's model, it would be expected that there would be some differences that cannot be accounted for in how the model has been set up. The results shown below compare the Company's preferences and inputs used in the EAG model versus the Company's own model results. As shown, although there are some differences in costs in both the ECM and ELX/TEZ/IVA arms between the two models, the results are largely similar and resulting ICERs broadly comparable, providing evidence of reliability of the EAG model.

Table 1. Comparison of company model results for ELX/TEZ/IVA (originally submitted, list price) versus Company preferences and inputs applied in EAG model

	F/F population		F/MF population		F/gating population		F/RF population	
	EAG model with company preferences	Company model	EAG model with company preferences	Company model	EAG model with company preferences	Company model	EAG model with company preferences	Company model
ECM LYs*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ECM QALYs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ECM costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA LYS*	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA QALYS	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ELX/TEZ/IVA costs	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ICER (no severity modifier)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

*Undiscounted

Abbreviations: F/F, *F508del* homozygous; MF, minimal function; RF, residual function; EAG, evidence review group; QALY, quality adjusted life year; ECM, established clinical management; ELX/TEZ/IVA, Elexacaftor/tezacaftor/ivacaftor; ICER, incremental cost effectiveness ratio; LY, life years