Givosiran for treating acute hepatic porphyria [ID1549]

Highly Specialised Technologies

Evaluation Programme

Addendum #1

ERG base case and scenario analyses using the newly approved PAS for givosiran

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Produced by

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1. INTRODUCTION

The purpose of this addendum is to provide the results of the ERG base case and scenario analyses following the approval of the PAS discount for givosiran (confirmed to the ERG in correspondence with NICE on 19/04/2021).

The analyses reported herein update the results tables provided in Section 6.2 and 6.3 of the ERG report. The analyses incorporate the corrections made to the company model by the ERG, in addition to the ERG's preferred assumptions as they are stated in the report. Please note that the PAS now approved for givosiran was included in the ERG's scenario analyses incorporating the assumptions for the proposed managed access agreement (MAA) for givosiran. This addendum therefore only provides an update to the ERG analyses that did not incorporate these assumptions.

2. EXPLORATORY AND SENSITIVITY ANALYSES UNDERTAKEN BY THE ERG

The results of the ERG's scenario analyses updated to include the new PAS are summarised below in Table 1.

Table 1: ERG exploratory analyses (excluding MAA assumptions)

Preferred assumption	Section in ERG report	Incremental costs (£)	Incremental QALYs	£/QALY (ICER)	% change from company base case
ERG corrected company base-case	*5.1.1*	[redacted]	9.32	[redacted]	-
Scenario 1: Givosiran efficacy					
a) Clinical efficacy based on ENVISION and OLE data (TPs frozen after 18 months)	*6.2.1.1*	[redacted]	8.36	[redacted]	[redacted]
b) Clinical efficacy extrapolated to Year 3 (TPs frozen after 3 years)		[redacted]	9.26	[redacted]	[redacted]
c) ENVISION efficacy assumed to be maintained up to 18 months (OLE data not considered)		[redacted]	8.56	[redacted]	[redacted]
Scenario 2: BSC efficacy data from ENVISION extended to 18 months	*6.2.1.2*	[redacted]	9.14	[redacted]	[redacted]
Scenario 3: ToT extrapolation					
a) KM curve until 18 months and Log-normal for extrapolation beyond	*6.2.1.3*	[redacted]	9.32	[redacted]	[redacted]
b) Gompertz		[redacted]	9.30	[redacted]	[redacted]
Scenario 4: Health state utility values					
a) Utilities based on EQ-5D data from ENVISION	*6.2.1.4*	[redacted]	5.11	[redacted]	[redacted]

Preferred assumption	Section in ERG report	Incremental costs (£)	Incremental QALYs	£/QALY (ICER)	% change from company base case
b) Recurrent and severe ENVISION utilities adjusted by ERG		[redacted]	5.66	[redacted]	[redacted]
c) AHP utilities based on RRMS values in Hawton et al[1])		[redacted]	9.02	[redacted]	[redacted]
Scenario 5: 10% of patients assumed to require treatment after age of menopause onset	*6.2.1.5*	[redacted]	9.31	[redacted]	[redacted]
Scenario 6: The per cycle probability of menopause onset based on mean age from UK Women's cohort study[2] (fitting a normal distribution).	*6.2.1.6*	[redacted]	9.31	[redacted]	[redacted]
Scenario 7: Proportion hospitalised for acute attack reduced to 50%	*6.2.1.7*	[redacted]	9.32	[redacted]	[redacted]
Scenario 8: Opioid addiction costs removed	*6.2.1.8*	[redacted]	9.32	[redacted]	[redacted]
Scenario 9: Proportion female reduced to 82%	*6.2.1.9*	[redacted]	9.30	[redacted]	[redacted]
Scenario 10: Starting cohort mean age reduced to 30 years	*6.2.1.10*	[redacted]	10.71	[redacted]	[redacted]
Scenario 11: Time horizon reduced to 15 years	*6.2.1.11*	[redacted]	5.12	[redacted]	[redacted]
Scenario 12: Severe health state 'switched off'	*6.2.1.12*	[redacted]	8.24	[redacted]	[redacted]
Scenario 13: Patients treated with givosiran require monitoring prior (and once monthly for first 6 months)	*6.2.1.13*	[redacted]	9.32	[redacted]	[redacted]

Abbreviations: AHP, acute hepatic porphyria; BSC, best supportive care; EQ-5D, EuroQol 5-dimensions questionnaire; ERG, Evidence Review Group; ICER, incremental cost-effectiveness ratio; KM, Kaplan-Meier; MAA, managed access agreement; OLE, open label extension; QALY, quality adjusted life year; RRMS, relapsing-remitting multiple sclerosis; ToT, time on treatment; TPs, transition probabilities

3. ERG PREFERRED ASSUMPTIONS

The results of the ERG base case updated to include the PAS for givosiran are provided below in Table 2.

Table 2: ERG preferred base case (excluding MAA assumptions)

Preferred assumption	Section in ERG report	Cumulative ICER £/QALY
Company base-case	*5.1.1*	[redacted]
Scenario 1: Givosiran transition probabilities based on OLE data (frozen at 18 months)	*4.2.6 and 6.2.3*	[redacted]
Scenario 3: ToT extrapolated using piecewise approach (KM curve + log Normal cure)	*4.2.8 and 6.2.3*	[redacted]
Scenario 4c: AHP utilities based on RRMS values in Hawton et al[1]	*4.2.9.3 and 6.2.3*	[redacted]
Scenario 6: The per cycle probability of menopause onset based on mean age from UK Women's cohort study[2] (fitting a normal distribution).	*4.2.7 and 6.2.3*	[redacted]
Scenario 8: Opioid addiction costs removed	*4.2.9.6 and 4.2.9.6*	[redacted]

Abbreviations: AHP, acute hepatic porphyria; ERG, Evidence Review Group; ICER, incremental cost-effectiveness ratio; KM, Kaplan-Meier; MAA, managed access agreement; OLE, open-label extension; QALY, quality adjusted life year; RRMS, relapsing-remitting multiple sclerosis; ToT, time on treatment; UK, United Kingdom

4. CONCLUSIONS OF THE COST-EFFECTIVENESS SECTION

Based on the ERG preferred base case results including the PAS for givosiran (and excluding MAA assumptions), givosiran resulted in an ICER of [redacted], based on an incremental cost of [redacted] and an incremental QALY gain of 8.20. As noted in the ERG report, the ERG considered that there remains a significant amount of uncertainty surrounding the clinical efficacy of givosiran, and that longer term HRQoL and clinical efficacy data would be useful in addressing the limitations and uncertainties identified within this technology appraisal.