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Multiple Technology Appraisal

Avatrombopag for treating thrombocytopenia in people with chronic liver disease needing a planned invasive procedure [ID3754]

Committee Papers

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SINGLE TECHNOLOGY APPRAISAL

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Contents:

The following documents are made available to consultees and commentators:

1. Addendum to the Assessment Report from Kleijnen Systematic Reviews

Any information supplied to NICE which has been marked as confidential, has been redacted. All personal information has also been redacted.

in collaboration with:

Erasmus School of Health Policy & Management

Maastricht University

Avatrombopag and lusutrombopag for treating thrombocytopenia in people with chronic liver disease needing an elective procedure

Addendum 2

Produced by	Kleijnen Systematic Reviews Ltd. in collaboration with Erasmus University Rotterdam (EUR) and Maastricht University
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Declared competing interests of the authors

None.

1. Results after the updated price for avatrombopag

In this addendum, the assessment group (AG) analyses the cost-effectiveness of lusutrombopag and avatrombopag versus established clinical management without thrombopoietin receptor agonists (no TPO-RA), for treating thrombocytopenia in people with chronic liver disease (CLD) requiring surgery.

The company communicated that the per mg price for avatrombopag would be £3.20, which would lead to a package price of £640 for 40mg pack (10x 20mg tablets, to be administered for patients with a platelet count of 40,000/μL to < 50,000/μL) and £960 for 60mg pack (15 x20mg tablets, to be administered for patients with a platelet count less than 40,000/μL).

The company suggested that the newly communicated avatrombopag prices would reflect the avatrombopag drug acquisition costs used in the AG base case (£800 for both subgroups) and therefore the cost-effectiveness results in the AG report would be still applicable. Even though this approach could be considered justifiable and would provide approximately similar results, it would not be technically accurate and therefore, in this addendum the actual drug acquisition costs, differentiated by subgroup (i.e. £640 for 40 mg, used in patients with a platelet count of 40,000/μL to < 50,000/μL and £960 for 60 mg, used in patients with a platelet count less than 40,000/μL), are used in the analysis.

To demonstrate the impact of the newly communicated avatrombopag prices, in this addendum the AG deterministic base case analysis, probabilistic sensitivity analysis and the scenario analyses with the highest impact on the incremental results will be reconducted using the newly communicated avatrombopag prices.

Since the cost-effectiveness analysis results generated unstable incremental cost effectiveness ratio (ICER) values in the original AG report, due to extremely small incremental life years (LYs) and incremental quality adjusted life years (QALYs), in this addendum, we focus on the incremental cost results and specifically the cost differences between lusutrombopag and avatrombopag.

From the subgroup analysis results, the overall (for the whole population) cost difference between avatrombopag and lusutrombopag will be calculated based on the percentages observed in the ADAPT trials as calculated in Table 1 below.

Table 1: Percentages of "<40,000/μl" subpopulation in the ADAPT trials

	N <40,000/μl	N 40,000/μl to <50,000/μl	% <40,000/μl
ADAPT-1	138	93	59.7
ADAPT-2	113	91	55.4
Overall % <40,000/μl			57.7

AG Base-case deterministic results

Base-case deterministic model results from the AG model with the new avatrombopag prices are shown in Table 2 below.

Table 2: Deterministic base-case discounted AG model results

Technologies	Total costs (£)	Total LYGs	Total QALYs	Incr. costs (£)	Incr. LYGs	Incr. QALYs	ICER (£/QALY)
Platelet count < 40,000 / μL Subgroup							

No TPO-RA	£2,320	7.3961	3.3626				
Lusutrombopag	£2,911	7.3961	3.3627	£592	0.00002	0.00017	£3,422,801
Avatrombopag 60 mg	£3,121	7.3961	3.3627	£209	-0.000006	-0.000079	Dominated
Platelet count 40,000- 50,000 / µL Subgroup							
No TPO-RA	£2,283	7.3961	3.3625				
Lusutrombopag	£2,907	7.3961	3.3625	£624	0.00002	0.000000007	£84,890,361,589
Avatrombopag 40 mg	£2,756	7.3961	3.3629	-£151	0.00000	0.00041	Dominant
ICER = incremental cost effectiveness ratio, Incr. = incremental, LYGs = life years gained, QALYs = quality-adjusted life years.							

Based on these subgroup analysis results, the overall cost difference between avatrombopag and lusutrombopag could be calculated as $£209 \times 0.577 + (-£151) \times (1 - 0.577) = £56.72$

Probabilistic sensitivity analysis results

Base-case results from the mean PSA runs from the AG model with the new avatrombopag prices are shown in Table 3 below.

Table 3: Mean PSA results

Technologies	**Total costs (£)**	**Total QALYs**	**Incr. costs (£)**	**Incr. QALYs**	**ICER (£/QALY)**
Platelet count < 40,000 / µL Subgroup					
no TPO-RA	£2,234	3.5704			
Lusutrombopag	£2,834	3.5705	£600	0.0002	£3,784,597
Avatrombopag 60 mg	£3,032	3.5705	£198	-0.0000	Dominated
Platelet count 40,000- 50,000 / µL Subgroup					
no TPO-RA	£2,185	3.5656			
Lusutrombopag	£2,809	3.5656	£624	0.0000	£446,071,715
Avatrombopag 40 mg	£2,660	3.5660	-£149	0.000	Dominant
ICER = incremental cost effectiveness ratio, Incr. = incremental, LYGs = life years gained, QALYs = quality-adjusted life years.					

Based on these subgroup analysis results, the overall cost difference between avatrombopag and lusutrombopag could be calculated as $£198 \times 0.577 + (-£149) \times (1 - 0.577) = £51.22$

Scenario analysis results

In this addendum, we only conducted scenarios from the AG report, which had a meaningful impact (>10%) on the incremental cost results. Therefore the following scenario analyses have been re-conducted.

1. Number of adult therapeutic doses (ATDs) per platelet transfusion
2. Cost of platelet transfusion

Number of adult therapeutic doses (ATDs) per platelet transfusion

Table 4: Scenario analysis – Number of ATDs per platelet transfusion

Platelet count <40,000/µL Subgroup												
No. ATDs	**Lusutrombopag**		**Avatrombopag 60 mg**		no TPO-RA		**Lus vs.** no TPO-RA			**Ava 60 mg vs.** no TPO-RA		
	Costs (£)	**QALYs**	**Costs (£)**	**QALYs**	**Costs (£)**	**QALYs**	**Incr. Costs (£)**	**Incr. QALYs**	**ICER (£)**	**Incr. Costs (£)**	**Incr. QALYs**	**ICER (£)**
[redacted]	£2,900	3.3627	£3,104	3.3627	£2,288	3.3626	£611	0.0002	£3,537,235	£816	0.0001	£8,660,996
[redacted] (AG BC)	£2,911	3.3627	£3,121	3.3627	£2,320	3.3626	£592	0.0002	£3,422,801	£801	0.0001	£8,502,309
[redacted]	£3,001	3.3627	£3,248	3.3627	£2,562	3.3626	£440	0.0002	£2,544,402	£686	0.0001	£7,284,219
3 (Sh BC)	£3,103	3.3627	£3,392	3.3627	£2,835	3.3626	£268	0.0002	£1,551,568	£557	0.0001	£5,907,443
Platelet count 40,000/µL to <50,000/µL Subgroup												
No. ATDs	**Lusutrombopag**		**Avatrombopag 40 mg**		no TPO-RA		**Lus vs.** no TPO-RA			**Ava 40 mg vs.** no TPO-RA		
	Costs (£)	**QALYs**	**Costs (£)**	**QALYs**	**Costs (£)**	**QALYs**	**Incr. Costs (£)**	**Incr. QALYs**	**ICER (£)**	**Incr. Costs (£)**	**Incr. QALYs**	**ICER (£)**
[redacted]	£2,898	3.3625	£2,751	3.3629	£2,255	3.3625	£643	0.00000001	£87,422,995,623	£496	0.0004	£1,197,912

[redacted] (AG BC)	£2,907	3.3625	£2,756	3.3629	£2,283	3.3625	£624	0.00000001	£84,890,361,589	£473	0.0004	£1,143,006
[redacted]	£2,980	3.3625	£2,798	3.3629	£2,499	3.3625	£481	0.00000001	£65,449,720,055	£299	0.0004	£721,546
3 (Sh BC)	£3,062	3.3625	£2,844	3.3629	£2,743	3.3625	£320	0.00000001	£43,476,444,487	£101	0.0004	£245,180
AG = assessment group, ATD = adult therapeutic dose, BC = base-case, ICER = incremental cost effectiveness ratio, iDFS = invasive disease-free survival; Incr. = incremental, QALY = quality-adjusted life year, Sh = Shionogi												

Based on the subgroup analysis results above, the overall cost difference between avatrombopag and lusutrombopag were calculated to be in the range of £56.10 and £74.12.

Cost of platelet transfusion

Table 5: Scenario analysis – Cost of platelet transfusion

Platelet count <40,000/µL Subgroup												
Cost PT	**Lusutrombopag**		**Avatrombopag 60 mg**		**No TPO-RA**		**Lus vs. No TPO-RA**			**Ava 60 mg vs. No TPO-RA**		
	Costs (£)	**QALYs**	**Costs (£)**	**QALYs**	**Costs (£)**	**QALYs**	**Incr. Costs (£)**	**Incr. QALYs**	**ICER (£)**	**Incr. Costs (£)**	**Incr. QALYs**	**ICER (£)**
£313.83 (BC)	£2,911	3.3627	£3,121	3.3627	£2,320	3.3626	£592	0.0002	£3,422,801	£801	0.0001	£8,502,309
£517.28	£2,991	3.3627	£3,233	3.3627	£2,533	3.3626	£458	0.0002	£2,649,449	£700	0.0001	£7,429,890
£812.61	£3,106	3.3627	£3,395	3.3627	£2,842	3.3626	£264	0.0002	£1,527,976	£553	0.0001	£5,874,727
Platelet count 40,000/µL to <50,000/µL Subgroup												
Cost PT	**Lusutrombopag**		**Avatrombopag 40 mg**		**No TPO-RA**		**Lus vs. No TPO-RA**			**Ava 40 mg vs. No TPO-RA**		

	Costs (£)	QALYs	Costs (£)	QALYs	Costs (£)	QALYs	Incr. Costs (£)	Incr. QALYs	ICER (£)	Incr. Costs (£)	Incr. QALYs	ICER (£)
£313.83 (BC)	£2,907	3.3625	£2,756	3.3629	£2,283	3.3625	£624	0.00000001	£84,890,361,589	£473	0.0004	£1,143,006
£517.28	£2,971	3.3625	£2,793	3.3629	£2,473	3.3625	£498	0.00000001	£67,774,610,741	£320	0.0004	£771,948
£812.61	£3,064	3.3625	£2,845	3.3629	£2,749	3.3625	£316	0.00000001	£42,954,304,853	£97	0.0004	£233,861
BC = base-case, ICER = incremental cost effectiveness ratio, iDFS = invasive disease-free survival; Incr. = incremental, PT = platelet transfusion, QALY = quality-adjusted life year												

Based on the subgroup analysis results above, the overall cost difference between avatrombopag and lusutrombopag were calculated to be in the range of £56.72 and £74.12.

Concluding remarks

The reconducted cost-effectiveness analyses based on the new avatrombopag prices are largely in line with the original analyses in the AG report. Even though avatrombopag led to smaller total costs compared to lusutrombopag in the platelet count 40,000/µL to <50,000/µL subgroup, the overall cost difference between avatrombopag and lusutrombopag, calculated from the total cost estimates from the subgroup analyses and the percentages obtained from the ADAPT trials are within the range of £50 and £75 (higher for avatrombopag). This cost difference might be regarded asnegligible when compared to the total cost estimates.