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Placental growth factor (alone or in combination with soluble fms-like tyrosine kinase 1) as an aid to the assessment of women with suspected pre-eclampsia: systematic review and economic analysis

Addendum (15 September 2015)

Produced by Southampton Health Technology Assessments Centre

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This report contains information considered at the time of writing to be confidential. This is clearly identified as underlined text with yellow or blue highlighting: [redacted] or [redacted]

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Declared competing interests of authors

None

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1 ANALYSES REQUESTED FOR ADDENDUM

1.1 Base case cost effectiveness results with ICERs/dominant/dominated

This section reports the cost-effectiveness results for women presenting for assessment of suspected pre-eclampsia, prior to 35 weeks and between 35 and 37 weeks' gestation, using biomarker tests compared with standard clinical assessment (based on clinical signs, symptoms and findings) . Results for costs and QALYs are presented for each diagnostic strategy with incremental costs and QALYs calculated compared with the next best alternative (based on dominance and extended dominance).

Cost effectiveness results for suspected pre-eclampsia presenting before 35 weeks of gestation

The cost effectiveness results for women presenting for assessment of suspected pre-eclampsia prior to 35 weeks' gestation, using each diagnostic strategy, are presented in Table 1. In the base case, total costs vary between £6,048 for the Triage test to £8,945 for standard clinical assessment. Both strategies including biomarker tests are cost-saving compared with standard clinical assessment, with the cost reductions per patient varying between £2,896 for the Alere Triage PlGF test and £2,488 for the Roche Elecsys sFLt-1/PlGF ratio test. Total QALYs for each diagnostic strategy were similar, with no more than 0.00076 QALYs separating the most clinically effective diagnostic strategy and the least clinically effective diagnostic strategy for women suspected of pre-eclampsia before 35 weeks' gestation. The differences in HRQoL for this cohort of patients may not be clinically significant, and there is substantial uncertainty around the utility values. The base case indicates that including a biomarker test in the assessment of suspected pre-eclampsia, prior to 35 weeks' gestation, is cost-saving and may yield slightly better clinical outcomes.

Table 1 Fully incremental base case cost effectiveness results for women presenting before 35 weeks

Strategy	Costs		QALYs		ICER
	Total	Increment	Total	Increment	
Triage PlGF test	£6,048		0.39445		Dominant
Elecsys sFlt-1/PlGF ratio test	£6,456	£408	0.39434	-0.00011	Dominated by Triage PlGF test
Standard assessment	£8,945	£2,488	0.39368	-0.00066	Dominated by Elecsys sFlt-1/PlGF ratio test

Cost effectiveness results for suspected pre-eclampsia presenting between 35 and 37 weeks of gestation

In the base case analysis for women with suspected pre-eclampsia presenting between 35 and 37 weeks, the cost differences are much smaller than in women with suspected pre-eclampsia presenting

before 35 weeks, and there is no difference between any of the strategies in HRQoL. This is because HRQoL is dependent on the type of delivery in the model, and there are no differences between the strategies after 35 weeks. The Triage PlGF test is still the least costly diagnostic assessment, but the difference between the Triage PlGF test and the Elecsys sFlt-1/PlGF ratio test is now only £191, and standard assessment is only £365 more expensive than the Triage PlGF test. Results of the base case analysis for women presenting between 35 and 37 weeks are reported in Table 2.

Table 2 Fully incremental base case cost effectiveness results for women presenting between 35 and 37 weeks

Strategy	Costs		QALYs	
	Total	Increment	Total	Increment
Triage PlGF test	£3,393		0.3954	
Elecsys sFlt-1/PlGF ratio test	£3,584	£191	0.3954	0
Standard assessment	£3,758	£174	0.3954	0

1.2 Sensitivity analyses with lower tests costs

In this sensitivity analysis the Alere PlGF test costs are [redacted] to £40 and the Roche Elecsys sFlt-1/PlGF ratio test costs are [redacted] to £57.23. These cost values were those presented by the companies that market the tests upon request from NICE;[1;2] they were not the values used in the company submission models, and neither value includes the cost of the testing machine, central laboratory costs, or maintenance costs. These values only include the cost of the test medium. The EAG does not feel that these values are the most appropriate values to use in modelling. However, as Table 3 and Table 4 show, changing the cost of the tests makes little difference to the cost-effectiveness results, and had a similar type of effect to the analyses of doubling and trebling the test costs (reported in Table 69 and Table 76 in the EAG report).

Table 3 Alere PlGF ratio test cost = £40, Roche Elecsys sFlt-1/PlGF ratio test cost = £57.23 before 35 weeks' gestational age

Strategy	Costs		QALYs		ICER
	Total	Increment	Total	Increment	
Triage PlGF test	£6,038		0.39445		Dominant
Elecsys sFlt-1/PlGF ratio test	£6,449	£409	0.39434	-0.00011	Dominated by Triage PlGF test
Standard assessment	£8,945	£2,498	0.39368	-0.00066	Dominated by Elecsys sFlt-1/PlGF ratio test

Table 4 Alere PlGF ratio test cost = £40, Roche Elecsys sFlt-1/PlGF ratio test cost = £57.23 between 35 and 37 weeks' gestational age

Strategy	Costs		QALYs	
	Total	Increment	Total	Increment
Triage PlGF test	£3,383		0.3954	
Elecsys sFlt-1/PlGF ratio test	£3,576	£193	0.3954	0
Standard assessment	£3,758	£182	0.3954	0

1.3 Summary of cost effectiveness issues in the addendum

The primary driver of cost differences between the strategies is potential days in the neonatal intensive care unit. The false positive rate on the tests is likely to drive this key cost parameter in the model. Given that the EAG has been forced to assume that the prognostic sensitivity and specificity of the Alere Triage PlGF test and the diagnostic sensitivity and specificity of the Roche Elecsys sFlt-1/PlGF ratio test are directly comparable, there is a high degree of uncertainty in the structure of the comparison. Future head to head comparisons using both tests and assessing the same diagnostic or prognostic outcome may provide different sensitivity and specificity results. The EAG has no way of predicting what effect these new test accuracy results would have on cost-effectiveness for the Alere Triage PlGF test and the Roche Elecsys sFlt-1/PlGF ratio test compared to each other, but the EAG believes that both interventions are likely to be cost-saving compared to standard assessment. This belief is supported by clinical opinion describing standard assessment as being high sensitivity and low specificity, which matches the values provided by Schnettler and colleagues[3] that have been repeated in the EAG model. Additionally, every previously published model has shown cost savings versus standard assessment.[3-5] This gives credence to the external validity of the EAG model. All in confidence submissions for either test in this assessment [redacted] compared to standard assessment. [6-8] Given that the cost savings for both tests compared to standard assessment are due to increased specificity and the associated reduction in over-treatment in the EAG model, the cost-savings of the Alere Triage PlGF test and the Roche Elecsys sFlt-1/PlGF ratio test compared to standard assessment have good face validity. The most important uncertainty in the model is in the comparison of the two tests to each other, not in the comparison of the two tests to standard care.

2 REFERENCE LIST

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