

# Lumella point-of-care test for assessing pre-eclampsia risk

Medtech innovation briefing

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[www.nice.org.uk/guidance/mib287](https://www.nice.org.uk/guidance/mib287)

## Summary

- The **technology** described in this briefing is the Lumella test. It is for assessing the risk of pre-eclampsia during pregnancy.
- The **innovative aspects** are that it is based on a novel biomarker (glycosylated fibronectin) that may have improved sensitivity and specificity compared with standard care. The test requires a finger prick blood sample (5 microlitres) and can be done in around 10 minutes.
- The intended **place in therapy** would be as an alternative to the placental growth factor (PIGF) test or soluble fms-like tyrosine kinase-1 (sFlt-1)/PIGF ratio test during pregnancy in women presenting with signs and symptoms of pre-eclampsia.
- The **main points from the evidence** summarised in this briefing are from 3 prospective observational studies including a total of 956 pregnant women. They show that Lumella has good diagnostic performance for detecting pre-eclampsia (area under the receiver-operating characteristic curve of 0.99), with a sensitivity of 0.98 and specificity of 0.93, at a glycosylated fibronectin cut-off value of 263 micrograms/ml.

- **Experts advised** that the test could improve result turnaround time and reduce hospital waiting time for people getting tested. This is because the test does not need to be done in a laboratory. All experts agreed that there is currently insufficient evidence to determine the test accuracy compared with standard care in the UK.
- **Key uncertainties** around the evidence or technology are that the studies included recommended biomarkers sFlt-1 and PIGF or PIGF alone. But the immunoassays used in the studies are not the commercial assays currently used in the NHS (Triage PIGF test and Elecsys immunoassay sFlt-1/PIGF ratio).
- The **cost** of a Lumella test kit is £50 per unit (excluding VAT). A standard care PIGF-based test costs around £40 to £60.

## The technology

The Lumella test (Diabetomics) is a point-of-care blood test used, together with other clinical and laboratory information, to assess the risk of pre-eclampsia in pregnancy. It works by detecting glycosylated fibronectin (GlyFn) in the blood and providing semi-quantitative measurements of the biomarker.

The Lumella test system comprises:

- a pre-eclampsia test cartridge
- a test reader that uses reflectance photometry to measure colour changes on a test cartridge

- accessories needed to do the test including:
  - lot-specific radiofrequency identification (RFID) card with RFID tag
  - single-use lancing device
  - capillary blood collection micropipette
  - vial containing sample buffer
  - alcohol wipe
  - bandage
  - sample transfer pipette.

All accessories are provided with each test kit and do not need to be purchased separately.

The test needs a finger prick blood sample (5 microlitres) and can be done at between 13 and 37 weeks of gestation. To do the test, the test cartridge is inserted into the reader and the diluted blood sample is applied to the cartridge. Test results are then displayed by the reader in 10 minutes. Results can also be printed by connecting the reader to a Bluetooth printer. The test can be transported, stored and done at room temperature.

## Innovations

The Lumella test is based on the novel biomarker GlyFn. The company states that compared with other currently used biomarkers (such as soluble fms-like tyrosine kinase-1 [sflT-1] and placental growth factor [PIGF] or PIGF alone), GlyFn is etiological to pre-eclampsia and maintains a linear progression throughout pregnancy. The company also claims that the test offers improved sensitivity and specificity over standard care tests. This would lead to a reduction in false positives and false negatives. The Lumella test requires a finger prick blood sample (5 microlitres). Other pre-eclampsia tests currently used in the NHS need a phlebotomy blood sample, which can be difficult to collect in some people. The test can also be transported and stored at room temperature. Other tests for pre-eclampsia need to be refrigerated and brought to room temperature before the test can be done. The Lumella test may improve patient experience and allow a more rapid turnaround time for results. The company states that Lumella is currently the only test that can be done within 10 minutes at room temperature.

## Current care pathway

Pre-eclampsia is usually diagnosed during routine antenatal appointments. This is based on blood pressure measurements and results of urine protein tests that are recommended at each routine antenatal visit to screen for the condition. The Triage PIGF test and the Elecsys immunoassay sFlt-1/PIGF ratio is also recommended to help rule out the condition in women presenting with suspected pre-eclampsia between 20 weeks and 34 weeks of pregnancy plus 6 days. If diagnosed with pre-eclampsia, women are usually referred to a specialist in hospital for further tests and more frequent monitoring. Depending on the severity of the condition, some women may be monitored as outpatients while others may need admission to hospital for closer monitoring or to have the condition managed in a critical care setting.

The following publications have been identified as relevant to this care pathway:

- [NICE guideline on antenatal care](#)
- [NICE guideline on hypertension in pregnancy: diagnosis and management](#)
- [NICE diagnostics guidance on PIGF-based testing to help diagnose suspected pre-eclampsia.](#)

## Population, setting and intended user

The Lumella test is intended to be used with other clinical and laboratory information to assess the risk of pre-eclampsia during pregnancy, between 13 and 37 weeks. The company states that it can also be used at the bedside in hospitals to monitor patients.

Pre-eclampsia is a potentially serious condition that affects some pregnant women, usually during the second half of pregnancy (after 20 weeks) or soon after birth. It is characterised by new-onset high blood pressure (hypertension) and new or significant protein in the blood (proteinuria). Other symptoms include headache, visual disturbances, right upper quadrant abdominal (epigastric) pain, oedema (swelling of the hands, face or feet) and oliguria (low output of urine). If undiagnosed, pre-eclampsia can lead to complications such as eclampsia, HELLP syndrome (haemolysis, elevated liver enzymes and low platelets), stroke, organ dysfunction and blood clotting disorders. Women who develop pre-eclampsia during pregnancy may be at greater risk of cardiovascular disease in later life. Women with pre-eclampsia may have a higher risk of placental abruption (a

condition in which the placenta separates from the inner wall of the uterus before the baby is born). Pre-eclampsia can also affect the baby, increasing the risk of fetal growth restriction, low birth weight or preterm birth. In the UK, pre-eclampsia is estimated to affect up to 1 in 25 pregnancies. In the UK, mild pre-eclampsia affects about 6% of pregnancies. Severe cases develop in around 1% to 2% of pregnancies.

The Lumella test is likely to be used in secondary care and will be done by a midwife or obstetrician during routine antenatal appointments.

## Costs

### Technology costs

Each Lumella test kit costs £50 (excluding VAT) and includes 1 test cartridge and consumables needed to do the test. The reader is supplied free of charge with the first order. The initial purchase contains 10 test cartridges and a reader. The reader is not sold separately. It comes with a 1-year warranty, and can be replaced free of charge within the warranty period if damage is because of conditions within the warranty limits. The reader also comes with a calibration cartridge.

### Costs of standard care

A standard care PIGF-based test costs around £40 to £60. The Alere (Quidel) PIGF test also requires a reader that is priced at £1,400 ([NICE diagnostics guidance on PIGF-based testing to help diagnose suspected pre-eclampsia](#)). There may also be additional costs involved for laboratory instruments and service costs for the Roche Elecsys test. PIGF-based testing involves a blood draw, which requires a trained clinician to do. There are unlikely to be additional costs for phlebotomy with these tests because blood samples will have already been taken as part of standard clinical assessment.

## Resource consequences

Lumella has been launched in the UK but is not currently used in NHS clinical practice. The company states that the Lumella test is cheaper to purchase than standard care tests. Adopting the technology could be resource releasing because it is a point-of-care test that does not need to be done in a central laboratory. The test is simple to do and can be done by midwives during routine antenatal appointments. Some women having standard care

tests may need an overnight hospital stay while waiting for test results. The company states that Lumella could reduce hospital stays because test results are available within 15 minutes. There is currently no published evidence to support this claim. [NICE diagnostics guidance on PIGF-based testing](#) assumed that 10% of women having assessment for suspected pre-eclampsia using the Elecsys immunoassay sFlt-1/PIGF ratio will need an overnight stay while waiting for test results. If the Triage PIGF test is used in a near-patient setting in a midwife-led day-case unit it is assumed that no one needs to be admitted overnight while waiting for test results. There are no anticipated practical difficulties or changes in facilities and infrastructure associated with adopting this technology. Training is provided by the company's UK team at no additional cost. The company states that they have 2 training videos and are developing an online training program and certification.

## Regulatory information

The Lumella test is CE-marked as an in vitro diagnostic medical device (In Vitro Diagnostic Directive; general category).

## Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

The test is intended to be used during pregnancy. Pre-eclampsia is more common in women with pre-existing diabetes. Diabetes may be considered a disability under the Equality Act 2010. Women over 40 have a higher risk of developing pre-eclampsia than women under 40. The Lumella test may be appropriate for people who do not identify as women but are pregnant. Pregnancy, disability, age, sex and gender reassignment are protected characteristics under the Equality Act 2010.

## Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [interim process and methods statement for medtech innovation briefings](#). This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the

technology. Further information about how the evidence for this briefing was selected is available on request by contacting [mibs@nice.org.uk](mailto:mibs@nice.org.uk).

## Published evidence

Three studies are summarised in this briefing, involving a total of 956 pregnant women. All studies were prospective, non-randomised observational studies.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

## Overall assessment of the evidence

The current published evidence for Lumella is limited to 3 prospective observational studies. All studies were funded or supported by the company and some of the authors were employees or shareholders of the company.

Across all 3 studies, glycosylated fibronectin (GlyFn) showed good biomarker performance to detect pre-eclampsia. The reported area under the receiver-operating characteristic curve (AUROC) for GlyFn was between 0.94 and 0.99, and numerically higher than that reported for other pre-eclampsia biomarkers tested (soluble fms-like tyrosine kinase-1 [sFlt-1] and placental growth factor [PlGF], sFlt-1, PlGF and PAPP2). Only 1 of the studies evaluated GlyFn biomarker performance primarily using the commercially available Lumella test (Nagalla et al. 2020). In this study (n=798), the Lumella test had a sensitivity of 98.5% and a specificity of 92.8% (at a threshold of 263 microgram/ml GlyFn or higher). The other 2 studies mainly used a GlyFn plate immunoassay but showed that the performance (AUROC) was similar to the Lumella point-of-care test using a small subset of samples.

The studies included recommended biomarkers sFlt-1 and PlGF or PlGF alone but the immunoassays used in the studies are not the commercial assays currently used in the NHS (Triage PlGF test and Elecsys immunoassay sFlt-1/PlGF ratio). Studies were done in India, Finland and Switzerland. There is currently no evidence in an NHS setting. Further evidence comparing the diagnostic accuracy of the Lumella test with standard care testing in the NHS is needed. Future research evaluating the impact of the test on clinical outcomes and resource use compared with standard care testing would also be helpful.

## **Nagalla et al. (2020)**

### **Study size, design and location**

Prospective, multicentre observational study of 798 pregnant women in India. Of these, 469 tested as normotensive with no proteinuria, 135 had pre-eclampsia and 194 had gestational hypertension at 20 weeks or more of pregnancy.

### **Intervention and comparators**

The Lumella test compared with immunoassays for sFlt-1, PIGF, and PAPP2.

### **Key outcomes**

The Lumella test showed the highest test performance, followed by PAPP2, PIGF and sFlt-1. AUROC values were 0.99 (95% confidence interval [CI] 0.98 to 0.99) with the Lumella test, 0.96 (95% CI 0.94 to 0.98) with PIGF, 0.86 (95% CI 0.83 to 0.89) with sFlt-1 and 0.96 (95% CI 0.94 to 0.97) with PAPP2. Overall and relative biomarker performance were not different between early- and late-onset pre-eclampsia or between non-severe and severe pre-eclampsia.

### **Strengths and limitations**

The study included a relatively large number of people and had well-defined inclusion and exclusion criteria. However, the study was done in India which may limit the generalisability of results to the NHS. The prevalence of pre-eclampsia in the study was 17%, higher than that reported in the UK. The study does however present diagnostic accuracy data based on a theoretical prevalence of 5% or 7%. All people in the study had new-onset hypertension and were being evaluated for pre-eclampsia so results may not be generalisable to a screening population of women with no symptoms. Although Lumella was compared with immunoassays for other biomarkers, the study did not use standard care tests in the NHS (Triage PIGF test and Elecsys immunoassay sFlt-1/PIGF ratio). The study was funded by the company and a number of the authors are either employees or shareholders of the company.



## Rasanen et al. (2015)

### Study size, design and location

Prospective observational study including 107 pregnant women from 2 centres in Finland.

### Intervention and comparators

GlyFn immunoassay compared with other pre-eclampsia biomarkers (PIGF, sFlt-1 and PIGF/sFlt-1 ratio). The diagnostic accuracy of the GlyFn immunoassay was also compared with that of the point-of-care GlyFn test (Lumella version 1.0).

### Key outcomes

There were 45 women with normotension and 62 who were diagnosed with pre-eclampsia. Compared with women with normotension, women with pre-eclampsia had significantly high levels of GlyFn in the first semester which remained high throughout pregnancy ( $p < 0.01$ ). All biomarkers tested were associated with pre-eclampsia status ( $p < 0.01$ ). The AUROC was 0.99 (95% CI 0.98 to 1.00) for GlyFn, 0.96 (95% CI 0.89 to 1.00) for sFlt-1, 0.94 (95% CI 0.86 to 1.00) for PIGF and 0.98 (95% CI 0.94 to 1.00) for sFlt-1/PIGF ratio. At a cut-off value of 176.4 micrograms/ml, GlyFn had a sensitivity of 0.97 (95% CI 0.85 to 1.00) and a specificity of 0.93 (95% CI 0.66 to 1.00). With an estimated population prevalence of 5% for pre-eclampsia, the positive predictive value was 47% (95% CI 23% to 72%) and the negative predictive value was 89% (95% CI 80% to 98%). Increased GlyFn levels were statistically significantly associated with length of pregnancy, birthweight, blood pressure, uric acid and alanine transaminase ( $p \leq 0.01$ ). The point-of-care GlyFn test (Lumella) showed similar diagnostic performance to the plate assay (AUROC of 0.93; 95% CI 0.85 to 1.00). Authors state that it outperformed the plate assay for the ability to distinguish between mild and severe pre-eclampsia (AUROC 0.78 compared with 0.68).

### Strengths and limitations

The study included a small number of people, and the primary outcomes were measured using a GlyFn plate assay, not the commercially available Lumella test. The Lumella test was compared with the plate assay using a small subset of samples, but it is not clear from the study how many this was. There were 13 people who were unable to be assessed for sFlt-1 because of the large serum sample needed. The PIGF assay was only done in 57 people because of inadequate serum sample. The study was funded by the company

and some of the authors are employees or shareholders of the company, or consultants for the company.

## Huhn et al. (2020)

### Study size, design and location

Prospective, single-centre observational study of 151 pregnant women with risk factors for, or clinical signs and symptoms of, pre-eclampsia in Switzerland.

### Intervention and comparators

GlyFn immunoassay compared with other biomarkers for pre-eclampsia (including PAPP2, PlGF, and sFlt-1). The diagnostic accuracy of the GlyFn immunoassay was also compared with that of the point-of-care GlyFn test (Lumella).

### Key outcomes

Serum samples were collected from women between 20 and 37 weeks of pregnancy. There were 32 out of 151 women (21%) who developed a clinical diagnosis of pre-eclampsia within 4 weeks. All biomarkers exhibited good classification performance (GlyFn AUROC 0.94, 91% sensitivity, 86% specificity; PAPP2 AUROC 0.92, 87% sensitivity, 77% specificity; PlGF AUROC 0.90, 81% sensitivity, 83% specificity; sFlt-1 AUROC 0.92, 84% sensitivity, 91% specificity). The GlyFn immunoassay and the rapid point-of-care test showed a correlation of  $r=0.966$ .

### Strengths and limitations

The study's primary outcomes were measured using the GlyFn plate immunoassay and not the point-of-care Lumella test. The Lumella test was compared with the GlyFn immunoassay only in a small subset of randomly selected samples (25 control and 25 cases). The study was not able to test the diagnostic accuracy of the biomarkers in pre-existing proteinuria without hypertension. The diagnostic performance of the biomarkers in late-onset pre-eclampsia was not evaluated by the study. The study used simplified cut-off values for the biomarkers that may need validating in different populations before being integrated into clinical practice. The study was partly supported by the company.

## Sustainability

The company states that compared with standard care the Lumella test has a lower environmental impact. It states that adopting the test may help to reduce the need for people to travel if the test is done locally by midwives. The company also states that the test reader uses less energy than the instruments needed to process standard care tests. There is no published evidence to support these sustainability claims.

## Recent and ongoing studies

Glycosylated fibronectin test in first trimester to predict chances of preeclampsia. Trial identifier: CTRI/2021/04/033066. Status: not yet recruiting (last modified on 20 April 2021). Indication: unspecified pre-eclampsia. Device: Lumella. Date: trial was registered on 23 April 2021 with planned date of first enrolment of 30 April 2021. Country: India.

The company also states that a retrospective study of 6,546 people is planned at the Prince of Wales hospital in Hong Kong to evaluate the effectiveness of Lumella as a first trimester screening test for pre-eclampsia. The samples for this study are from the ASPIRE trial ([Rolnik et al. 2017](#)), which was a multicentre randomised trial of women screened for pre-eclampsia at 11 to 13 weeks of pregnancy.

## Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 3 experts were familiar with similar tests for pre-eclampsia, but none had used this particular technology before.

## Level of innovation

One expert said the test was a minor variation to standard care and would be offered as another biomarker test for pre-eclampsia in addition to the 4 already available. Two experts said that the test was novel and of uncertain safety and efficacy. One of these experts said that if the diagnostic accuracy is as described then the test appears to be

highly innovative. They added that there are few tests that have a high positive predictive value for pre-eclampsia. Two experts said that the test could replace standard care, if shown to have comparable efficacy. One expert said they were not aware of any other competing technologies and that Lumella is the only glycosylated fibronectin test for pre-eclampsia they are aware of. Two experts noted that other tests are available for pre-eclampsia. One of these experts said that most alternative tests need laboratory testing, but the Quidel Triage placental growth factor (PIGF) test can be done using near-patient testing with results available in 15 minutes.

## Potential patient impact

The experts noted that Lumella is a point-of-care test that could offer more rapid turnaround time for test results and quicker triage in suspected pre-eclampsia. One expert highlighted that standard care tests need to be processed in a laboratory and test results can sometimes take several hours. One expert said the test may provide greater reassurance for people because of the high positive predictive value. Women at high risk of or suspected to have pre-eclampsia were identified as people who would particularly benefit from the test. One expert said that the test may also be used to exclude pre-eclampsia in a larger cohort of women with hypertension.

## Potential system impact

Two experts said that Lumella could change the current care pathway. One of these experts said the main system benefit is how quickly the test result is returned. They added that this may help to reduce the hospital waiting time for people being tested and even reduce hospital attendance if testing can be done in the community. The expert also noted that finger prick testing is technically easier than phlebotomy and therefore a trained phlebotomist would not be needed to do the test. One expert did not think that the test would change the current pathway that uses PIGF-based testing. Two experts said the cost of adopting the technology would be similar to standard care. One expert said that the cost of implementing the test would be the same as standard care but cost saving in outcomes may be seen. This is because the test appears to have a higher accuracy and therefore fewer false positive and false negative results. Most of the experts agreed that little to no changes to existing facilities would be needed to adopt the test and minimal training would be needed. One expert said that point-of-care testing approval and maintenance would be needed and could be a barrier to adoption.

## General comments

None of the experts were aware of any NHS centres using the test. Two experts said there were no practical or usability issues of the technology. Two experts thought that the test could be done at most or all district general hospitals while 1 said they could not predict this at present. When asked about the size of the eligible population, one expert estimated 50,000 people. One expert estimated between 3% and 5% of 700,000 women per year and another estimated 5% to 7% of pregnant women. One expert said there is no risk of adverse events or harm to patients, while 2 said the risk would be low if the test efficacy is proven. All experts noted that there was insufficient evidence to determine the test accuracy compared with standard care in the UK. One expert said that the accuracy and positive or negative predictive values need to be confirmed. They also said that the available evidence comes from studies with a small sample size and that larger sized studies are needed. One expert noted that a prospective head-to-head comparison with standard care would be needed. One expert also noted the lack of published economic analyses on the technology.

## Patient organisation comments

The organisation stated that a new biomarker for pre-eclampsia would be welcomed, but for it to be adopted the test will need to outperform current pre-eclampsia tests. The organisation noted that the size of current studies for Lumella is smaller than expected for this type of test. It stated that any test shown to be quick and easy to do that provides a definitive diagnosis should be considered by healthcare professionals. They added such a test will likely reassure patients and ensure clinical care can be directed to those who need it most. The organisation noted that biomarker tests for pre-eclampsia are excellent tools, but that uptake of these tests has been minimal despite the success when they have been implemented. They stated that there appears to be some resistance from clinicians and commissioners, which they feel is a concern.

## Expert commentators

The following clinicians contributed to this briefing:

- Andrew H Shennan, professor of obstetrics, King's College London, did not declare any interests.

- Jenny Myers, clinical professor, University of Manchester, longstanding interest in diagnostic markers for pre-eclampsia. Author of several papers investigating diagnostic markers (non-financial professional interest).
- Manu Vatish, professor of obstetrics, University of Oxford. Has published several manuscripts on placental growth factor (PIGF)-based diagnostic biomarkers in the areas of clinical effectiveness, health economics, clinical guidance. Has been PIGF-based testing national champion for the NHS Accelerated Access Collaborative.

The patient organisation Action on Pre-eclampsia (APEC) contributed to this briefing.

## Development of this briefing

This briefing was developed by NICE. The [interim process and methods statement for medtech innovation briefings](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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