

URO17 for detecting bladder cancer

Medtech innovation briefing

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Summary

- The **technology** described in this briefing is URO17. It is a urine-based biomarker test to detect bladder cancer in people with symptoms of bladder cancer. It is also used to monitor for recurrence during treatment follow up.
- The **innovative aspect** is that it is a non-invasive diagnostic tool that detects bladder cancer based on the novel biomarker keratin 17 (K17). It can help stratify patients with suspected bladder cancer and prioritise them for further secondary care investigations during the COVID-19 pandemic.
- The intended **place in therapy** would be used alongside cystoscopy as an alternative to other urine-based tests.
- The **main points from the evidence** summarised in this briefing are from 2 prospective studies including a total of 156 people with suspected bladder cancer. They show that URO17 had a sensitivity of 100% in detecting bladder cancer with a specificity of 60% to 93%.

- The **key uncertainty** around the evidence is that it is from only 2 studies, 1 of which is an abstract. Further studies are needed to validate results when the test is used to help initial diagnosis, and to provide evidence for when it is used to monitor for recurrence. Longer-term data on larger populations and data from comparisons with other urinary biomarker tests would be helpful.
- The **cost** of URO17 is £110 per test (excluding VAT).

The technology

URO17 is a urine test for detecting bladder cancer in people with symptoms associated with malignancy, including blood in the urine (haematuria) or lower urinary tract symptoms. It is also indicated for detecting urogenital cancer recurrence in the urogenital tract during treatment follow up.

URO17 is an immunocytochemistry-based test that detects the presence of the oncoprotein keratin 17 (K17), which is a member of cytokeratin family of proteins. There is evidence suggesting that K17 is associated with poor prognosis in tumorigenesis of malignancies such as cervical, endometrial and lung. Studies also found that K17 is expressed in urothelial cancer and suggested that K17 is a highly accurate biomarker for underlying biopsy-confirmed urothelial cancer ([Babu et al. 2018](#); [Babu et al. 2020](#)).

The company notes that the diagnostic utility of URO17 in people who have had Bacillus Calmette-Guerin (BCG) or radical radiotherapy is not conclusive. There is an ongoing study in this patient group.

Innovations

URO17 is an in-vitro diagnostic test based on a novel biomarker for bladder cancer. The company notes that, unlike other urine-based tests, the URO17 assay can test people with visible or invisible haematuria. This means that people with early-stage cancers could be identified as early as possible.

It is a non-invasive test. Currently dipstick tests check the urine for traces of blood. People with a positive result are referred on for invasive procedures such as cystoscopy to get a definitive diagnosis. URO17 could help rule out cancer, or flag it up, at the first stage, reducing unnecessary invasive procedures and hospital visits.

Current care pathway

Diagnosis

Bladder cancer is usually identified from blood visible in the urine or found during urine testing. Emergency admission is also a common way for bladder cancer to present, and is often associated with a poor prognosis. The prevalence of the condition and the nature of its management make bladder cancer one of the most expensive cancers for the NHS.

Cystoscopy is the standard investigation for suspected bladder cancer and for treatment follow up. Urinary biomarkers are only recommended in the context of a clinical research study.

If abnormalities are found during cystoscopy, white-light-guided transurethral resection of bladder tumour (TURBT) is recommended. If muscle-invasive bladder cancer is suspected at cystoscopy, CT or MRI staging should be considered before TURBT. TURBT should be done or supervised by a urologist experienced in the procedure. It should be done with:

- photodynamic diagnosis
- narrow band imaging
- cytology or
- a urinary biomarker test (such as UroVysion using fluorescence in-situ hybridisation, ImmunoCyt or a nuclear matrix protein 22 test).

Random biopsies of normal-looking urothelium during TURBT should not be taken unless there is a specific clinical indication (for example, to investigate positive cytology that is not otherwise explained). The size and number of tumours found during TURBT should be recorded.

Monitoring after treatment

Periodic cystoscopy should be offered to patients after treatment for non-muscle-invasive bladder cancer and after radical radiotherapy for muscle-invasive bladder cancer. The frequency depends on the severity and risk of bladder cancer.

Urinary biomarkers and cytology can be offered with cystoscopy for all patients except

those with low-risk bladder cancer. If someone's muscle-invasive bladder cancer has been treated with radical cystectomy or radical radiotherapy, they should also be offered annual upper-tract imaging and CT of the abdomen, pelvis and chest. This should be 6 months, 12 months and 24 months after treatment to monitor for local and distant recurrence. Anyone with haematuria or other urinary symptoms and a history of non-muscle-invasive bladder cancer should be urgently referred to urological services.

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

- [NICE guideline on bladder cancer](#)
- [European Association of Urology \(EAU\) guideline on non-muscle-invasive bladder cancer](#)

Population, setting and intended user

URO17 is intended to be used as a diagnostic tool to help identify people with haematuria or lower urinary tract symptoms with a suspicion of bladder cancer. It is also intended for monitoring recurrence in the urogenital tract during treatment follow up.

The company proposition originated from a UK urologist saying that 85% of haematuria cases identified in primary care are not malignant when investigated in secondary care. Also that there are currently long waiting lists for urology assessment because of COVID-19 restrictions. URO17 could be used to stratify patients on waiting lists to prioritise cases, as well as avoiding potentially unnecessary hospital visits for other patients during the COVID-19 pandemic.

Costs

Technology costs

The cost of the URO17 test is £110 per test (excluding VAT).

Costs of standard care

Costs per test (excluding VAT) are:

- diagnostic flexible cystoscopy (HRG code LB72A, 19 years and over) from £229 to £258
- cytology £7 (currency code DAPS01, cytology).

This includes the cost of consumables and healthcare professionals' time. Costs are based on [2020/21 hospital resource group \(HRG\) tariffs](#) and [2018/19 national schedule of reference costs](#).

Resource consequences

The cost of investigating haematuria is significant, in large part because of the cost of the cystoscopy. In the UK investigating people with haematuria who do not have bladder cancer was estimated in 2008 at £100 million, a third of the total cost of managing non-muscle-invasive bladder cancer ([Abogunrin et al. 2011](#)). This could be offset with a low-cost diagnostic test. Causes of haematuria and risk of bladder cancer vary. Investigations can reveal no identifiable cause, infection, benign causes or urological cancers.

URO17 is being introduced into the NHS but is not yet widely used. The test has the potential to be resource releasing if using it results in earlier diagnosis and treatment because of more accurate detection of bladder cancer. However, false-positive results could have cost and resource consequences by leading to further testing. Using the test to monitor patients during follow up may lead to an initial increase in resource use in this setting. Minimal to no training is needed, and no changes to facilities or infrastructure are needed to adopt the technology because urinalysis is already used routinely.

Regulatory information

URO17 is CE-marked as an in-vitro diagnostic medical device.

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.

Bladder cancer is more common in men than women; 72% of cases in the UK are in men,

and 28% are in women. Despite a lower incidence of bladder cancer in women, rates of survival are considerably lower for women than for men. It mainly affects older people with the highest incidence rates in people aged 90 and over ([Cancer Research UK, 2015](#)). People of European family origin have a much higher risk of developing bladder cancer than those of African American, Hispanic or Asian family origin. People with cancer are protected under the Equality Act 2010 from the point of diagnosis.

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.

Published evidence

Two prospective studies involving 156 people under investigation for urothelial cancer are summarised in this briefing.

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

Overall assessment of the evidence

Overall, the quantity of evidence for URO17 is limited. There was 1 prospective study, and an abstract by the same author. The study populations of both studies may overlap.

The main study was at just 1 centre. Further studies at multiple sites are needed to validate the results when the test is used for initial diagnosis, and to provide evidence for when it is used to monitor for recurrence. Longer-term data, and data comparing it to other urinary biomarker tests would be helpful.

Vasdev et al. (2020)

Study size, design and location

A prospective blinded validation trial of 71 people due to have a biopsy because of suspected urothelial tract cancer. The author noted that people included had likely already had flexible cystoscopy before study recruitment.

Intervention and comparator

URO17 compared with biopsy histology.

Key outcomes

In people with no previously diagnosed bladder cancer (n=71), URO17 was shown to have a sensitivity of 100% and a specificity of 92.6%. Cystoscopy and biopsy were used as the reference standard. The positive predictive value was 0.957 and negative predictive value was 1. URO17 was positive in all people with urothelial malignancy regardless of grade or stage. No interobserver variability was identified between the 2 pathologists reporting the URO17 results. URO17 was positive in all of 28 people with malignancy confirmed by histology and in 35 of 36 people with malignancy detected by radiological imaging (97.2%).

Strengths and limitations

The study was in just 1 hospital.

Vasdev et al. (2020) [an abstract]

Study size, design and location

A validation study of 85 people having cystoscopic investigations for urothelial tract cancer.

Intervention and comparator

URO17 compared with biopsy histology.

Key outcomes

URO17 had a sensitivity of 100% and a specificity of 60.5%. The results of a sub-analysis to determine confounding factors showed a sensitivity of 100% and specificity of 88.25%, with a negative predictive value of 1 and a positive predictive value of 0.93. URO17 was positive in all people with bladder cancer and no urothelial malignancy were found in any person with a negative URO17 result. The authors noted that there is a 5-year study to examine its diagnostic utility in people who have had Bacillus Calmette-Guerin (BCG) therapy.

Strengths and limitations

This is a cross-sectional study. Strengths and limitations have not been assessed because limited information was reported in the abstract.

Sustainability

This is a single-use test.

Recent and ongoing studies

The Welsh Accelerate Programme at Cardiff University is evaluating URO17 for detecting bladder cancer and its economic effects on the NHS.

There is ongoing work led by Mr Vasdev on using URO17 as a home test for surveillance of the backlog of people with bladder cancer during the COVID-19 pandemic.

The company notes there are studies in the US and European countries to assess the diagnostic accuracy of URO17.

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.

Four experts were familiar with or had used this technology before.

Level of innovation

Two experts thought URO17 is a newly emerging biomarker urine test for bladder cancer based on detecting the keratin 17 (K17) protein. One noted that URO17 had better diagnostic accuracy than other biomarker tests. For example, the sensitivity of ADXBLADDER ranges from 44% to 73% with a specificity between 66% and 71%; the sensitivity of EpiCheck is 64% with a specificity of 82%. Another expert said that the technology is a minor variation because it uses a different biomarker to other urine-based tests. The remaining expert did not think that the URO17 test was innovative, adding that there are many other urine-based tests to help diagnose bladder cancer.

Potential patient impact

The potential benefits identified by the experts included: improved identification of people with suspected bladder cancer based on its diagnostic utility, and avoiding unnecessary invasive cystoscopy. The experts thought that the test could be used to evaluate visible or non-visible haematuria, but cystoscopy remains standard care. Two experts were not convinced by the claimed benefits of the technology over traditional cytology, adding that initial cystoscopy would still be needed to assess other potential causes of haematuria, and that there is currently a lack of robust data to support the use of the URO17 test in routine clinical practice.

One expert considered that the URO17 test could be useful during the COVID-19 pandemic in managing the waiting list for cystoscopy by identifying and prioritising high-risk patients.

Potential system impact

The main system benefit identified by the experts was better identification of people with bladder cancer, potentially leading to a release of resource because of reduced cystoscopy. One felt it was too early to say what the system benefits would be, but that there might be a significant impact if the diagnostic accuracy of URO17 was proven. All the experts believed adopting the technology would change the current care pathway if more robust data were to support its diagnostic accuracy.

URO17 is a laboratory-based assay, and most of the experts did not think any substantial changes to infrastructure or facilities were needed because biomarker assay testing is

commonplace. All thought that the test would be relatively easy to use with a simple learning curve. No safety concerns or regulatory issues around the test were raised by the experts, although one noted that bladder cancer diagnosis would be delayed if the test performance was substandard.

General comments

The experts were aware of a number of biomarker urine tests for bladder cancer, but none is widely used in routine clinical practice. One explained that the main reason biomarker tests have not been adopted in practice is that the early data reporting high diagnostic accuracy often did not reflect how the test worked in clinical practice. Two experts thought it was too early to support the widespread use of URO17 in routine clinical practice in the NHS because of limited evidence. Most agreed that large-scale, multicentre studies are essential to improve the evidence base for the test.

One expert added that longer-term studies are needed on using URO17 for people who have had Bacillus Calmette-Guerin (BCG) or radiotherapy.

Expert commentators

The following clinicians contributed to this briefing:

- Rakesh Heer, consultant surgeon and chair of urology, Newcastle Urology, Freeman Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust. Did not declare any interests.
- John D Kelly, professor of uro-oncology, Division of Surgery and Interventional Science, University College London. Professor Kelly was the chief investigator for testing the MCM5 biomarker and UroMark for detecting bladder cancer.
- Sanjeev Madaan, consultant urological surgeon, Darent Valley Hospital, Dartford; visiting professor, Canterbury Christ Church University. Did not declare any interests.
- Nikhil Vasdev, consultant urological and robotic surgeon and associate medical director for cancer services, East and North Hertfordshire NHS Trust. Mr Vasdev is the chief investigator of the URO17 test in Europe. He received funding from KDX Diagnostics for the URO17 study in the East and North Hertfordshire NHS Trust.

Development of this briefing

This briefing was developed by NICE. The [interim process and methods statement](#) 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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