Cxbladder Test

The **Cxbladder test** is a **non-invasive urine-based molecular diagnostic test** used to help detect or rule out **urothelial bladder cancer**. It measures the expression of specific messenger RNA (mRNA) biomarkers in urine and combines these with selected clinical risk factors to estimate the likelihood of bladder cancer.

Bladder cancer is most commonly **urothelial (transitional cell) carcinoma**. The classic presentation is **painless visible (macroscopic) haematuria**, although microscopic haematuria, irritative lower urinary tract symptoms, or recurrent "UTIs" without infection may also occur. Cystoscopy remains the diagnostic gold standard, but urine biomarker tests such as Cxbladder can help determine which patients are more or less likely to require invasive investigation.

Available Cxbladder tests

Test	Primary use	Typical clinical setting	Priority
Cxbladder Triage	Rule out bladder cancer in patients with haematuria	Initial evaluation of microscopic or visible haematuria	High
Cxbladder Detect	Detect bladder cancer	Patients being investigated for suspected cancer	High
Cxbladder Monitor	Surveillance after previous bladder cancer	Follow-up after treatment	High (selected patients)
Cxbladder Resolve (where available)	Further risk stratification	Intermediate-risk patients	Moderate

How it works

The test measures expression of **five mRNA biomarkers** shed into urine from bladder cells:

- **MDK (Midkine)**
- **HOXA13**
- **CDC2 (CDK1)**
- **IGFBP5**
- **CXCR2**

These molecular markers are analysed together with clinical information such as:

- Age
- Sex
- Smoking history
- Haematuria characteristics
- Previous urological history (depending on the test version)

The result is reported as **low**, **intermediate**, or **elevated risk**, rather than simply "positive" or "negative."

Diagnostic performance

Performance varies according to the version of the test and patient population.

Metric	Approximate performance
Sensitivity	~82–95% (higher for high-grade tumours)
Specificity	~60–85%
Negative predictive value	Often >95–97% in haematuria populations
Positive predictive value	Moderate; depends on cancer prevalence

The strongest value of Cxbladder is its **high negative predictive value**, meaning a negative result makes bladder cancer substantially less likely in appropriately selected patients.

Approximate likelihood ratios (vary by study):

Result	Approximate LR
Positive	LR+ ~2–5
Negative	LR− ~0.06–0.2

When it is used

High-yield indications

- Microscopic haematuria
- Visible haematuria
- Risk stratification before cystoscopy
- Surveillance following bladder cancer treatment

Not intended for

- Screening the general population
- Diagnosing other urinary tract cancers
- Replacing cystoscopy when there is a high clinical suspicion of cancer

Comparison with urine cytology

Feature	Cxbladder	Urine cytology
Detects low-grade cancer	Better	Poor
Detects high-grade cancer	Very good	Excellent
Sensitivity	Higher	Lower overall
Specificity	Moderate	Very high
Non-invasive	Yes	Yes

Comparison with cystoscopy

Cxbladder	Cystoscopy
Urine test	Endoscopic examination
No instrumentation	Invasive
No anaesthetic required	Often local anaesthetic
Cannot localise tumour	Direct visualisation
Cannot biopsy	Allows biopsy and tumour resection

Cxbladder is considered an **adjunct**, not a replacement, for cystoscopy when bladder cancer is strongly suspected.

Limitations

Limitation	Clinical relevance
Positive result does not confirm cancer	Requires cystoscopy and imaging
False positives can occur	Inflammation, recent instrumentation, or other urinary tract pathology may influence results
A negative result does not absolutely exclude cancer	Small or very early tumours may occasionally be missed
Availability	Not universally funded or available in all countries

Diagnostic pathway for haematuria

Investigation	Rationale	Priority
Urinalysis	Confirm haematuria; assess for infection or proteinuria	High
Urine culture	Exclude urinary tract infection	High
Serum creatinine (SI reference range: approximately **60–110 µmol/L**, laboratory-dependent)	Assess renal function before imaging	High
Full blood count (Hb: men **130–180 g/L**, women **115–165 g/L**, laboratory-dependent)	Assess for anaemia or infection	High
Cxbladder (selected patients)	Risk stratification for urothelial cancer	High
Flexible cystoscopy	Gold standard for bladder evaluation	High
CT urography	Evaluate upper urinary tract and stage disease	High
Urine cytology	Particularly useful for high-grade disease or carcinoma in situ	Moderate

Red flags

Urgent urological assessment is warranted for:

- Painless visible haematuria
- Persistent unexplained microscopic haematuria in high-risk individuals (e.g., older age, smoking history)
- Haematuria with a bladder mass on imaging
- Recurrent haematuria despite treatment of infection
- Constitutional symptoms (weight loss, anorexia)
- Hydronephrosis or impaired renal function
- Persistent irritative urinary symptoms without infection

Differential diagnoses

Diagnosis	Distinguishing features	Approximate LR
Urothelial bladder cancer	Painless haematuria, smoking history, filling defect on imaging	Positive Cxbladder: LR+ ~2–5
Urinary tract infection	Dysuria, frequency, positive culture	Positive urine culture strongly favours UTI
Nephrolithiasis	Colicky flank pain, haematuria, CT stone	Non-contrast CT highly sensitive
Renal cell carcinoma	Flank mass, haematuria, renal lesion on CT	CT findings strongly supportive
Benign prostatic hyperplasia	Lower urinary tract symptoms in older men	Clinical diagnosis; no specific LR
Prostate cancer	Elevated PSA, abnormal digital rectal examination	MRI and biopsy required for diagnosis
Glomerular disease	Proteinuria, dysmorphic red cells, casts	Dysmorphic RBCs increase likelihood of glomerular source

Prioritised diagnostic pathway

1. **Exclude urgent pathology:** visible haematuria, urinary obstruction, severe anaemia, renal impairment, or imaging evidence of malignancy.
2. **Assess for common causes:** urinalysis, urine culture, renal function, and history to identify infection, stones, or medical renal disease.
3. **Risk-stratify for urothelial cancer:** consider Cxbladder (where available) in appropriate haematuria patients.
4. **Definitive evaluation:** perform cystoscopy and upper urinary tract imaging (typically CT urography) when indicated, regardless of urine biomarker results if clinical suspicion remains high.
5. **Ongoing surveillance:** for patients with a history of bladder cancer, use cystoscopy with or without adjunctive tests such as Cxbladder Monitor according to specialist recommendations.