use molecular testing to help drive my patients' treatment plans.

Xpert® Bladder Cancer Detection
&
Xpert® Bladder Cancer Monitor

In Vitro Diagnostic Medical Device
Not all tests available in all countries.
Bladder Cancer Facts

By 2030, the annual incidence of bladder cancer is projected to increase to 219,000 (nearly double that of 2012).1

In Europe² Every Year
- 124,000 people are newly diagnosed with bladder cancer
- ~415,000 people live with bladder cancer
- More than 40,000 people die from the disease

The Incidence of Bladder Cancer is Increasing Because
- The risk of getting bladder cancer increases with age, and more Europeans are living longer
- The median age of diagnosis is ~70 years

75% of newly diagnosed patients have non-muscle invasive bladder cancer (NMIBC).³ Their 5 year survival chances are very good, but bladder cancer often recurs⁴ and patients need frequent monitoring.
Haematuria — Blood in the Urine

Blood in the urine is the most common symptom of bladder cancer.

- **4 out of 5** people with bladder cancer have some blood in their urine, however:
  - **80–90%** patients with gross haematuria do **NOT** have cancer
  - And over **95%** of patients with microhaematuria do **NOT** have cancer

Instead, the most common causes of haematuria are urinary tract infection, nephrolithiasis (stones), polycystic kidney disease, trauma, benign prostatic hyperplasia (BPH) in older men, or, in some cases, even vigorous exercise.

Sometimes, it can be difficult for doctors to decide who may have cancer and who might have a different condition.

Not knowing the cause of the haematuria leads to anxiety in the patient. A fast, non-invasive diagnostic test, could help you to decide on the best follow-up strategy.

**The Xpert® Bladder Cancer Detection and Monitor Tests from Cepheid**

- Offer you an additional test which could help to determine if your patient does or does not have bladder cancer.
- May help to increase the negative predictive value of cystoscopy, which could guide your choice of surveillance interval length between cystoscopies.
- Could help to improve your monitoring compliance rates in patients with bladder cancer by offering a non-invasive option to support your overall monitoring strategies.
Non-Invasive Tests for Two Clinical Applications

Detection

The non-invasive, urine based Xpert® Bladder Cancer Detection test could help you assess whether your patient presenting with haematuria is likely to have cancer or not.

The test detects the presence of bladder cancer in patients with haematuria suspected of having bladder cancer.

Monitoring

The non-invasive, urine based Xpert® Bladder Cancer Monitor test could help you decide if your bladder cancer patient has recurring cancer or remains cancer-free.

It detects the recurrence of bladder cancer in those who have previously been diagnosed and treated for bladder cancer.
How Do They Work?

Both are ‘non-invasive’ tests that measure the expression of five mRNA tumour markers in a voided urine sample.

The five mRNA tumour markers were:

- Selected for their presence and ability to distinguish bladder cancer cells from normal cells.
- Optimised to have a high sensitivity for high and low grade tumours.

The test automatically combines the results of the 5 tumour markers to give you an actionable NEGATIVE or POSITIVE result.

Although the two tests use the same markers, the analysis equation combining information from the markers and the cut off criteria are applied differently in the Detection and Monitor assay to optimise them for the different clinical setting. Both tests should be used in conjunction with other clinical measures to assess disease diagnosis and disease recurrence.
Understanding the concepts of sensitivity, specificity and negative predictive value helps to understand the value of these tests and of other diagnostic methods like cystoscopy and cytology.

**Sensitivity** — the percentage of people with bladder cancer who are correctly identified as having the condition (or the proportion of true positives that are correctly identified).

**Specificity** — the percentage of healthy people who are correctly identified as not having bladder cancer (or the proportion of true negatives that are correctly identified).
An increase in test sensitivity usually causes a decrease in test specificity. That means some patients might get positive test results but a cancer cannot be found by cystoscopy. Thus, there is a discrepancy between test results.

In some patients, these discrepant results are caused by **false positive results of the test**.

In other patients, these discrepant results might be caused by **false negative results by cystoscopy**.

**Negative Predictive Value (NPV)** — is an estimate of the probability that subjects with a negative screening test truly do not have the disease.

A high negative predictive value ensures that very few patients have a false negative test result.
Detection Test

The sensitivity was optimised to ensure that patients presenting with all stages and grades of bladder cancer stand the greatest chance of being detected.

Xpert® Bladder Cancer Detection exhibits high sensitivity and a high negative predictive value.

**Xpert® Bladder Cancer Detection**
**Performance vs. Cystoscopy/Histology**

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Low Grade</th>
<th>High Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>75.8%</td>
<td>52.2%</td>
<td>88.4%</td>
</tr>
<tr>
<td>Specificity (among patients with haematuria)</td>
<td>84.6%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

For complete performance information, please see the Xpert® Bladder Cancer Detection Package Insert: 301-2414, Rev. A

The NPV of Xpert® Bladder Cancer Detection is **97.8%**. This means that among those who had a negative test, the probability of being disease-free was **97.8%**.
Monitor Test

This test was optimised to detect recurrent tumours in patients who have already had bladder cancer. The performance for low and high grade tumours increases the likelihood of detecting the tumour regardless of grade.

Xpert® Bladder Cancer Monitor Performance vs. Cystoscopy/Histology

(N=257 study subjects) | Overall | Low Grade | High Grade |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>75.0%</td>
<td>63.2%</td>
<td>84.0%</td>
</tr>
<tr>
<td>Specificity (among patients with history of bladder cancer)</td>
<td>80.6%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

For complete performance information, please see the Xpert® Bladder Cancer Monitor Package Insert: 301-5933, Rev A

The NPV of Xpert® Bladder Cancer Monitor is 93.9%. This means that among those who have a negative monitoring test, the probability of being disease-free is 93.9%.
What Do I Need to Do Next?

The test is very simple for you and your patient. All the patient needs to do is provide a urine sample.

1. Obtain a urine sample of at least 4.0mL in the primary collection cup.
2. Obtain one Xpert® Urine Transport Reagent kit.
3. Invert cup 3 times to mix the urine.
4. Use the disposable transfer pipette provided in the Xpert Urine Transport Reagent kit in the pouch with the tube.
5. Insert the transfer pipette into the bottom of the urine cup.
6. Transfer approximately 4.0mL of urine so that the volume reaches the black line on the tube label.
7. Replace the cap on the Xpert Urine Transport Reagent tube and tighten securely. Label correctly and transfer to the GeneXpert® cartridge preparation area.

**NOTE:** Do not use the pipette from the assay kit.
Remember

Order a Detection test if...

...you have a patient present with haematuria whom you suspect may have bladder cancer, but has no previous history of bladder cancer

Order a Monitor test if...

...you have a previously diagnosed bladder cancer patient and you want to know if the cancer has recurred

+ use molecular testing to help drive my patients’ treatment plans.


Xpert® Bladder Cancer Detection and Monitor