Responses to L39365 Evidentiary Review Regarding Cxbladder Tests

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Conclusions of LCD

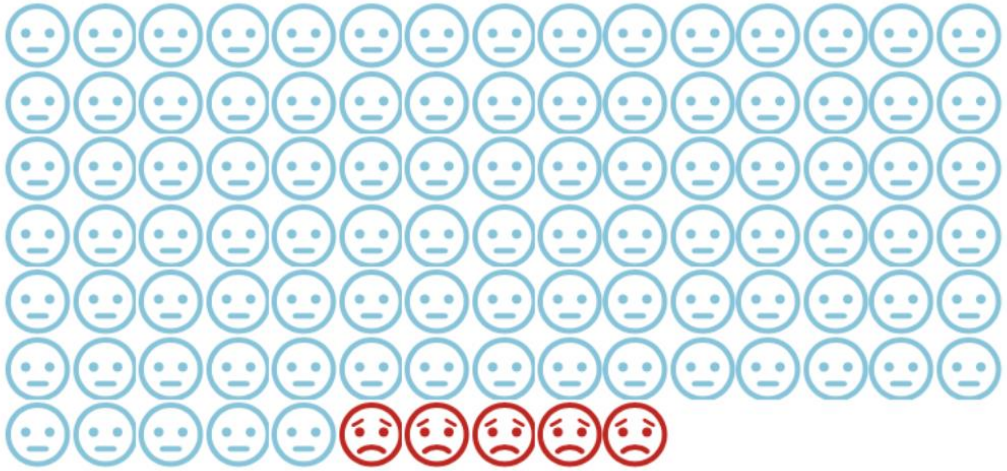
- L39365 concluded that Cxbladder diagnostic tests are not medically reasonable or necessary
- The supporting analysis demonstrates a lack of understanding of the Cxbladder tests, their purpose, their use, and indeed the evaluation and management of hematuria and Non-muscle invasive bladder cancer (NMIBC)
- Removal of coverage for these tests will lead to direct harm to Medicare covered patients, increase cost of care born by taxpayers, and waste resources (procedure and Operating Room time) leading to decreased access to care

Cxbladder tests (Triage, Detect) address need for cystoscopy in patients with hematuria

- 7 million patients with hematuria in USA per year
- AUA guidelines mandate cystoscopy for most, specifically to look for bladder pathology
- About 95% of these cystoscopies have no cancer diagnosis and could be avoided
- Cxbladder tests are genomic, performed on voided urine and are designed to have a high negative predictive value (97-98%) and rule out rate (70-80%)

5%

Up to 5% of microhematuria patients will have a urothelial cancer. 95% have unnecessary cystoscopy



29%

Cxbladder can spare 83% of patients who don't have tumors a normal cystoscopy and increase cancer detection rate of cystoscopy by almost 6x

Cxbladder Monitor and NMIBC Surveillance

- Patients with NMIBC require regular surveillance cystoscopy, sometimes for life
- Cxbladder Monitor has high NPV (97%)
- In the first 3-5 years of surveillance a negative test can de-intensify surveillance by 50%
- Beyond 3-5 years a negative test can be used in place of cystoscopy

Cystoscopy

- Outpatient, local anesthetic, some cannot tolerate
- Uncomfortable
- Complications include urinary tract infection, worsened hematuria, urethral trauma including false passage and stricture formation
- Increased risk in Medicare population with higher prevalence of BPH, implanted devices and artificial joints

Comments on Negative Feedback from the Previous Review

- Criticizes tests for high false positive rates
- Criticizes tests for not identifying other cancer types
- Criticizes development studies for being company sponsored
- Criticizes and denies for funding 3 tests that don’t exist commercially
- Criticizes studies for male bias
- Criticizes studies for short follow up

High False Positive Rate

- These are high NPV diagnostic tests designed to rule out patients with a very low risk of urothelial cancer, not rule in or diagnose urothelial cancer
- The clinical decision from a negative test is to omit or postpone a cystoscopy, the clinical decision to a positive test is to follow AUA guidelines
- There is no added burden to the patient of a false positive test

Cxbladder doesn’t identify other cancers

- The sole purpose of these tests is reducing the need for unnecessary workup (i.e. cystoscopy) that is done ONLY to search for bladder cancer
- Kidney cancers are not diagnosed by cystoscopy but by imaging
- Prostate cancer is not diagnosed by cystoscopy but by tumor markers, imaging and biopsy

Studies were company funded

- These tests were developed and are performed only by Pacific Edge
- Company sponsorship is standard practice throughout pharma, device and diagnostics development
- Published utility studies (Davidson x2, Li) were done completely independent of Pacific Edge

Cxbladder Resolve, Enhanced Triage, Enhanced Detect

- These products are criticized for insufficient data, specifically called out to not be covered, and their weaknesses used to strengthen the case against the other Cxbladder tests (Detect, Monitor, Triage)
- These are in development and NOT commercially available
- They are currently in use in several clinical trials with 1000’s of patients
- To "pre-emptively" deny coverage for tests that are in development should not be used as a criteria to deny coverage for the other tests that ARE commercially available

Studies Criticized for Male Bias

- Urothelial cancer is a disease of older men, with incidence 3-4x higher than women
- The sex and age distribution of our study populations reflect the true real world incidence

Studies had insufficient follow up

- Cxbladder tests inform the decision for cystoscopy at the time they are done
- They are neither prognostic or predictive for risk of developing cancer in the future
- Follow up was more than adequate to support the intended use

Genetic Testing for Oncology

- The inclusion criteria for this LCD is either the diagnosis of cancer or suspicion of cancer using histologic or cytologic evidence
- Hematuria is neither histologic or cytologic evidence
- 95% of hematuria patients don’t have cancer
- Cxbladder Detect and Cxbladder Triage are NOT considered screening tests as the patient population is symptomatic (hematuria)
- This LCD should not be applied to Cxbladder Triage and Detect as they are used to help rule out cancer as part of the diagnostic workup

Recommendations

- The arguments used to deny coverage to the commercially available Cxbladder tests are incorrect and not justified
- Access to Cxbladder Triage and Cxbladder Detect should be maintained for the Medicare population and removed from non-coverage as they fall out of the scope of the LCD
- Cxbladder Monitor should retain coverage under this LCD due to its utility in the Medicare population
- All mention and non-coverage comments with regards to products that are not commercially available should be removed from the LCD

Conclusion

- Cxbladder Triage, Detect, and Monitor perform exactly as designed
  - Noninvasive tests with a high NPV to reduce the need for unnecessary cystoscopy in patients with suspected urothelial carcinoma, a patient cohort heavily weighted to the Medicare population

- Lack of access to this technology by Medicare patients will lead to
  - More unnecessary cystoscopy procedures
  - Increased patient morbidity
  - Increased costs to Medicare
  - Increased opportunity costs as resources for outpatient and operating room procedures are wasted on cases that could have been avoided without harm to the patient