28 February 2025

CXBLADDER INCORPORATED INTO AUA CLINICAL GUIDELINE

- *New AUA microhematuria guideline incorporates language for urine-based biomarkers in appropriately counseled intermediate-risk patients*
- *Guideline specifically mentions Cxbladder Triage as the only urine biomarker with 'Grade A' evidence*
- *Intermediate-risk patients represent an estimated 70%* [1] *of those presenting with microhematuria*

DUNEDIN, New Zealand – Cancer diagnostics company Pacific Edge (NZX, ASX: PEB) today announces the American Urological Association (AUA) has included Cxbladder Triage as the standard of care in an amendment to its clinical guideline for the management of patients presenting with microhematuria.[2]

In a major amendment to the 2020 AUA microhematuria guideline[3], the Panel has incorporated language for the use of urine-based biomarkers for intermediate-risk patients. It specifically mentions Cxbladder Triage as the only urine-based biomarker test that has 'Grade A' evidence from a randomized controlled trial (the STRATA Study[4]) in support of this recommendation. Intermediate-risk patients represent a large cohort (estimated at 70%) of microhematuria patients, and future evidence being generated in Pacific Edge's CREDIBLE Study for the next generation test Triage Plus is designed to apply beyond the intermediate-risk hematuria patients.

The guideline states: "In appropriately counseled intermediate-risk patients who want to avoid cystoscopy and accept the risk of forgoing direct visual inspection of the bladder urothelium, clinicians may offer urine cytology or validated urine-based tumor markers (Table 5 included in this release) to facilitate the decision regarding utility of cystoscopy. Renal and bladder ultrasound should still be performed in these cases."

The AUA amendment specifically references the latest evidence generated from the STRATA Study following its publication in the Journal of Urology in May 2024. The study demonstrated in a randomized controlled trial, a first for any urine biomarker, that Cxbladder Triage could safely and effectively reduce cystoscopies by as much as 59% without missing tumors. This result paves the way for future Cxbladder products such as Cxbladder Triage Plus to be demonstrate equivalent or better performance than Cxbladder Triage for future guideline acceptance.

As a consequence of the new guideline, Pacific Edge anticipates an uplift in demand for Cxbladder tests as more clinicians in the US and around the world begin to observe this updated

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[1] Changes to the risk-stratification criteria for low, intermediate and high-risk categories have been made as part of the guideline update and increases the percentage of patients that are expected to be classified as intermediate risk up to 70% of the population presenting with microhematuria, according to Pacific Edge's estimate.

[2] Blood in urine that is revealed in tests, though not visible to the naked eye

[3] Barocas DA, Lotan Y, Matulewicz RS, Raman JD, Westerman ME, Kirkby E, Pak L, Souter L. Updates to Microhematuria: AUA/SUFU Guideline (2025). *J Urol*. doi: 10.1097/JU.0000000000004490.

[4] Lotan et al. (2024). A Multicenter Prospective Randomized Controlled Trial Comparing Cxbladder Triage to Cystoscopy in Patients With Microhematuria. The Safe Testing of Risk for Asymptomatic Microhematuria Trial. The Journal of Urology Vol 212 1-8 Jul 2024.

guideline and incorporate the tests into care pathways for the evaluation and management of patients presenting with microhematuria.

Pacific Edge also expects to leverage the guideline language in its ongoing policy dialogue with Medicare Administrative Contractor Novitas and the Centers for Medicare and Medicaid services over the 'Genetic Testing in Oncology: Specific Tests' (L39365) local coverage determination (LCD). The LCD released on 9 January 2025 threatens to end Medicare coverage of Cxbladder on 24 April 2025.

Under current legislation, MACs are required to consider consensus statements and/or guidelines in determining coverage. Pacific Edge will inform Novitas of the new guideline and expects to use the AUA guideline and the evidence on which it is based for a formal reconsideration of the LCD.

Pacific Edge Chief Medical Officer Dr Tamer Aboushwareb said: "The inclusion of Cxbladder Triage in the AUA guideline for the management of microhematuria is a significant milestone for Pacific Edge. While the guideline does not mandate the use of Cxbladder Triage, they are authoritative, reinforcing best practice within the urological industry and supporting greater adoption of Cxbladder in hematuria evaluation.

"Cxbladder is the only test supported by a Grade A evidence from the AUA Guideline panel and the update reflects the strength of the evidence supporting Triage and will help to reduce the burden of unnecessary cystoscopies in patients of lower risk, resulting in less patient discomfort and less morbidity, and improved access to care by reducing wait times," Dr Aboushwareb said.

Pacific Edge Chief Executive Dr Peter Meintjes said: "We are very pleased that Cxbladder Triage has been acknowledged with its inclusion in the AUA guideline. This is an outstanding result for patients across the US, and a reflection of the role genomic tests now play in the standard of care for bladder cancer patients as they have already done for prostate, breast, colon and other cancers.

"Importantly, while the AUA Guideline language is currently focused on Cxbladder Triage for intermediate-risk microhematuria patients, we now have a strong foundation for the future inclusion of Cxbladder Triage Plus for a wider range of patient types given its superior performance characteristics[5]. Additionally, any competing product or service will have to complete their own randomized clinical trial to establish the same Grade A evidence, fortifying our first-mover advantage."

Dr Meintjes concluded: "The acknowledgement of Cxbladder in the AUA guideline reinforces how we create value for investors, i.e. with the continued commitment to generating the highest quality clinical evidence within a framework of AV, CV and CU, and with the appropriate end points and statistically significant sample sizes. Importantly, creating value for investors through evidence development is a core expertise that Pacific Edge can repeat for Cxbladder Triage Plus, for Monitor Plus and products beyond bladder cancer."

View the amended AUA Clinical Guidelines for the Management of Microhematuria here:
https://www.auanet.org/guidelines-and-quality/guidelines/microhematuria

[5] Lotan et al., (2022). Urinary Analysis of FGFR3 and TERT Gene Mutations Enhances Performance of Cxbladder Tests and Improves Patient Risk Stratification. The Journal of Urology, 10-1097.

Table 5: Reported Negative Predictive Values for the Detection of Bladder Cancer Using the Available Urine Cytology and Urine-Based Biomarkers

Assay[A]	Hematuria Population	Total Patients (n)	Reported Negative Predictive Value	AUA Strength of Evidence[B]
CxBladder Resolve	MH and GH	Total n=548; MH n=289	99.8%[98]	B
CxBladder Triage	MH[C]	n=390	99%;[97] 95%CI: 95 to 100%[D]	A
	MH and GH	Total n=571; MH n=185	100%;[99] 95%CI: 94 to 100%[E]	C
NMP22 BladderChek (qualitative)	MH	n=876	95% - 100%[100-102]	C
Urine cytology	MH	n=513	95.0% - 98.7%[100, 103, 104]	C
	MH and GH	Total n=4,497; MH n=1,743	89.5%[F] - 96.0%[77, 105-107]	C
UroVysion	MH and GH	Total n=828; MH n=384	97%[105]	C
Xpert	MH and GH	Total n=1,152; MH n=597	98.0% - 99.6%[105, 106]	C

A. To be included in the table, NPV for the assay was reported in a purely MH population or MH patients comprised ≥25% of total hematuria population. All studies included ≥100 microhematuria patients.
B. Strength of evidence in relation to reported NPV. Refer to Table 1 for strength of evidence definition and methodology.
C. The RCT[97] is the only identified study designed to evaluate use of a urine-based biomarker to guide evaluation.
D. NPV for detection of high-grade disease[97], 100%; 95%CI: 97 to 100%. NPV for lower risk patients, 100%; 95%CI: 94 to 100%.
E. NPV reported for MH subgroup.[99]
F. NPV of 89.5%[107] reported for detection of bladder cancer and UTUC.

Released for an on behalf of Pacific Edge by Grant Gibson, Chief Financial Officer.

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OVERVIEW

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Pacific Edge Limited (NZX/ ASX: PEB) is a global cancer diagnostics company leading the way in the development and commercialization of bladder cancer diagnostic and prognostic tests for patients presenting with hematuria or surveillance of recurrent disease. Headquartered in

Dunedin, New Zealand, the company provides its suite of Cxbladder tests globally through its wholly owned, and CLIA certified, laboratories in New Zealand and the USA.

Cxbladder: www.cxbladder.com

Cxbladder is a urine-based genomic biomarker test optimized for the detection and surveillance of bladder cancer. The Cxbladder evidence portfolio developed over the past 14 years includes more than 20 peer reviewed publications for primary detection, surveillance, adjudication of atypical urine cytology and equivocal cystoscopy. Cxbladder is the focal point of numerous ongoing and planned clinical studies to generate an ever-increasing body of clinical utility evidence supporting adoption and use in the clinic to improve patient health outcomes. Cxbladder has been trusted by over 4,400 US urologists in the diagnosis and management of more than 100,000 patients, including the option for in-home sample collection. In New Zealand, Cxbladder is accessible to 75% of the population via public healthcare and all residents have the option of buying the test online.