Enhanced Visualization Methods for First Transurethral Resection of Bladder Tumour in Suspected Non-muscle-invasive Bladder Cancer: Recommendation

Final Recommendation

- Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding hexaminolevulinate hydrochloride as an adjunct to white light during first transurethral resection of bladder tumour for suspected non-muscle-invasive bladder cancer
- Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends against publicly funding narrow band imaging as an adjunct to white light during first transurethral resection of bladder tumour for suspected non-muscle-invasive bladder cancer

Rationale for the Recommendation

The Ontario Health Technology Advisory Committee has reviewed the findings of the health technology assessment[1] and agreed that using hexaminolevulinate hydrochloride (HAL) as an adjunct to white light during first transurethral resection of bladder tumour (TURBT) likely improves important patient outcomes such as reducing bladder cancer recurrence and increasing recurrence-free survival. Committee members also agreed the evidence supports the safety of using HAL as an adjunct to white light during TURBT. In contrast, there was little to no difference in the rate of cancer recurrence between narrow band imaging (NBI) when used as an adjunct to white light during first TURBT and TURBT guided by white light alone. No evidence on the effect of NBI as an adjunct to white light during first TURBT on recurrence-free survival was identified. In considering the economic evidence, the committee agreed that HAL as an adjunct to white light for first TURBT was cost-effective and that the cost-effectiveness of NBI as an adjunct to white light during first TURBT was likely uncertain.

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Decision Determinants for Enhanced Visualization Methods for First Transurethral Resection of Bladder Tumour in Suspected Non-muscle-invasive Bladder Cancer

Decision Criteria	Subcriteria	Decision Determinants Considerations
Overall clinical benefit How likely is the health technology/intervention to result in high, moderate, or low overall benefit?	**Effectiveness** How effective is the health technology/intervention likely to be (taking into account any variability)?	HAL-guided TURBT likely reduces the rate of recurrence at 12 mo and 4 y and increases 5-y recurrence-free survival when compared with TURBT guided by white light alone (GRADE: Moderate). NBI-guided TURBT likely results in little to no difference in the rate of recurrence at 12 mo when compared with TURBT guided by white light alone (GRADE: Moderate). No evidence on the effect of NBI-guided TURBT on recurrence-free survival was identified. Based on an indirect comparison, there may be little to no difference in recurrence rates between HAL-guided TURBT and NBI-guided TURBT (GRADE: Low).
	Safety How safe is the health technology/ intervention likely to be?	The use of HAL-guided or NBI-guided TURBT is likely safe (GRADE: Moderate).
	Burden of illness What is the likely size of the burden of illness pertaining to this health technology/intervention?	The projected estimate of new bladder cancer cases in Ontario in 2020 was 4,450 (3,400 males and 1,050 females). About 75% of newly diagnosed cases are NMIBC.[2]
	Need How large is the need for this health technology/intervention?	White light is the standard method for visualizing tumours during first TURBT. If some tumours remain unseen or not fully excised, they may progress to a higher grade over time or invade the muscle of the bladder. Enhancing visualization methods during first TURBT to identify tumours can maximize the benefit of the procedure, as approximately one-third of cancers recur at 12 mo when white light is used alone.

Decision Criteria	Subcriteria	Decision Determinants Considerations
Patient preferences and values How likely is adoption of the health technology/intervention to be congruent with patient preferences and values and with ethical or legal standards?	**Patient preferences and values** Do patients have specific preferences, values, or needs related to the health condition, health technology/ intervention, or life impact that are relevant to this assessment? (Note: The preferences and values of family members and informal caregivers are to be considered as appropriate.)	Patients value the outcomes reported in the clinical evidence including tumour recurrence rate, recurrence-free survival, safety, tumour progression, and adverse events. Patients' preferences are unlikely to influence the selection of particular types of equipment in a clinical setting. Patients would likely prefer techniques to improve these outcomes.
	Autonomy, privacy, confidentiality, and/or other relevant ethical principles as applicable Are there concerns regarding accepted ethical or legal standards related to patient autonomy, privacy, confidentiality, or other ethical principles that are relevant to this assessment? (Note: The preferences and values of the public are to be considered as appropriate.)	Using HAL-guided or NBI-guided TURBT is not expected to impact relevant ethical principles, patient autonomy, or privacy.
Equity and patient care How could the health technology/ intervention affect equity of access and coordination of patient care?	**Equity of access or outcomes** Are there disadvantaged populations or populations in need whose access to care or health outcomes might be improved or worsened that are relevant to this assessment?	The incidence rate of bladder cancer is higher in men and in people with lower socioeconomic status. There may also be gender inequalities in the promptness of diagnosis of bladder cancer.[3]
	Patient care Are there challenges in the coordination of care for patients or other system-level aspects of patient care (e.g., timeliness of care, care setting) that might be improved or worsened that are relevant to this assessment?	Identifying and removing all tumours can help patients avoid future intensive treatments, including surgery, due to undetected tumours that become invasive.

Decision Criteria	Subcriteria	Decision Determinants Considerations
Cost-effectiveness How efficient is the health technology/ intervention likely to be?	**Economic evaluation** How efficient is the health technology/intervention likely to be?	At willingness-to-pay values of $50,000 and $100,000 per QALY gained, HAL-guided TURBT is likely to be cost-effective (69.1% and 74.6% probability of being cost-effective, respectively), compared with NBI-guided TURBT and TURBT using white light alone. Our model suggested that the most likely estimate of the incremental cost-effectiveness ratio is $12,618 per QALY gained for HAL-guided TURBT compared with NBI-guided TURBT.
Feasibility of adoption into health system How feasible is it to adopt the health technology/intervention into the Ontario health care system?	**Economic feasibility** How economically feasible is the health technology/intervention?	The additional cost of a HAL-guided TURBT compared with TURBT using white light alone is approximately $800. In addition, costs and savings related to disease monitoring, treatments, and progression are expected to be incurred over time. We estimated that the annual budget impact to Ontario of publicly funding HAL-guided TURBT over the next 5 years will range from an additional $0.6 million in y 1 to $2.5 million in y 5, for a total 5-y budget impact of $7.8 million.
	Organizational feasibility How organizationally feasible is it to implement the health technology/ intervention?	HAL-guided TURBT requires additional or replacement capital equipment. Additional nursing resources are required for the instillation of HAL into the bladder before surgery. Some hospitals in Ontario are already using HAL-guided TURBT.

Abbreviations: GRADE, Grading of Recommendations, Assessment, Development and Evaluation; HAL, hexaminolevulinate hydrochloride; mo, month(s); NBI, narrow band imaging; NMIBC, non-muscle-invasive bladder cancer; TURBT, transurethral resection of bladder tumour; QALY, quality-adjusted life-year; y, year(s).

Note: In this table, we use the terms “HAL-guided” and “NBI-guided” to refer to the use of these technologies as adjuncts to white light to better visualize tumours in the bladder. These technologies do not replace the use of white light, they complement it.

References

(1) Ontario Health. Enhanced visualization methods for first transurethral resection of bladder tumour in suspected non-muscle-invasive bladder cancer: a health technology assessment. Ont Health Technol Assess Ser [Internet]. 2021 Aug;21(12):1–123. Available from: https://www.hqontario.ca/evidence-to-improve-care/health-technology-assessment/reviews-and-recommendations/enhanced-visualization-methods
(2) Brenner DR, Weir HK, Demerse AA, Ellison LF, Louzado C, Shaw A, et al. Projected estimates of cancer in Canada 2020. Can Med Assoc J. 2020:192(9):F199-205.
(3) Dobruch J, Daneshmand S, Fisch M, Lotan Y, Noon AP, Resnick MJ, et al. Gender and bladder cancer: a collaborative review of etiology, biology, and outcomes. Eur Urol. 2016:69(2)300-10.

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