

5-Aminolevulinic Acid Hydrochloride (5-ALA)–Guided Surgical Resection of High-Grade Gliomas: Health Quality Ontario Recommendation

DRAFT RECOMMENDATION

- Health Quality Ontario, under the guidance of the Ontario Health Technology Advisory Committee, recommends publicly funding 5-aminolevulinic acid hydrochloride (5-ALA) for guiding maximal surgical resection of high-grade gliomas, conditional on Health Canada approval of the technology

RATIONALE FOR THE RECOMMENDATION

The Ontario Health Technology Advisory Committee has reviewed the findings of the health technology assessment.¹ Ontario Health Technology Advisory Committee members noted that 5-ALA may provide benefit through the improved extent of tumour resection and potential improvement in progression-free survival. While the committee noted that there was considerable uncertainty in the clinical evidence, they also considered the disease severity and the poor prognosis for patients with high-grade gliomas and noted that the budget impact for 5-ALA was relatively small. Ontario Health Technology Advisory Committee members also considered the lived experience of a patient with high-grade glioma who described their experience of 5-ALA–guided surgical resection.

Based on these considerations, Health Quality Ontario decided to recommend public funding for 5-ALA–guided surgical resection of high-grade gliomas. The committee recognized the importance of Health Canada regulations for drugs and medical devices. Therefore, the recommendation to publicly fund this technology was made conditional on the technology receiving approval for use by Health Canada.

Given the uncertainty around clinical benefit and potential adverse events, the committee noted that clinicians should discuss this treatment with their patients during treatment planning, including the potential for neurological deficits after surgery.

Decision Determinants for 5-ALA–Guided Surgical Resection of High-Grade Gliomas

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)?	5-ALA may improve the extent of resection of high-grade gliomas compared with white-light microscopy (GRADE: Low). There is a potential improvement in overall survival with 5-ALA; however, results are imprecise, with the confidence interval including the possibility of no difference in survival (Grade: Low). 5 ALA-guided resection may improve 6-month progression-free survival, although results are highly uncertain (GRADE: Very low).
	Safety How safe is the health technology/intervention likely to be?	The safety of 5-ALA was evaluated by the United States Food and Drug Administration, and the drug was subsequently approved for use in 2017. 5-ALA is contraindicated in people with hypersensitivity to 5-ALA or porphyrins, or with porphyria. The impact of 5-ALA on overall and neurological adverse events was inadequately reported and is highly uncertain. However, no significant differences were observed in overall or neurological adverse events with 5-ALA relative to standard care. There was greater short-term neurological deterioration based on the National Institutes of Health Stroke Scale with 5-ALA compared to standard surgical treatment (GRADE: Very low).
	Burden of illness What is the likely size of the burden of illness pertaining to this health technology/intervention?	High-grade gliomas affect approximately 3 to 5 per 100,000 people.
	Need How large is the need for this health technology/intervention?	Maximal surgical resection is recommended for high-grade gliomas. Standard surgical resection with neuronavigation and white-light microscopy is challenging because it can be difficult for the surgeon to differentiate brain tumour from normal brain tissue, or because the tumour is near tissue that is responsible for neurological function.
Patient preferences and values How likely is adoption of the health technology/intervention to be congruent with patient preferences and values, and ethical or legal standards?	Patient preferences and values Do patients have specific values, preferences, or needs related to the health condition, health technology/intervention, or life impact that are relevant to this assessment? (Note: The values and preferences of family and informal caregivers are to be considered as appropriate.)	The participant we interviewed valued the use of 5-ALA and the impact it had on patient decision-making for brain tumour resection. The patient valued the accuracy that 5-ALA may provide for the visualization of brain tumours.
	Autonomy, privacy and confidentiality and/or other relevant ethical principles if applicable Are there concerns regarding accepted ethical or legal standards related to patient autonomy, privacy, confidentiality, or other ethical principles or values that are relevant to this assessment? (Note: The values	No issues related to patient autonomy, privacy, or confidentiality were identified.

Decision Criteria	Subcriteria	Decision Determinants Considerations
	and preferences of the public are to be considered as appropriate.)	
Equity and coordination of 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? Patient care Are there challenges in the coordination of care for patients and other system-level aspects of patient care (i.e., timeliness of care, setting of care etc.) that might be improved or worsened that are relevant to this assessment?	Access to 5-ALA is currently inequitable across Ontario because it is available only at hospitals with surgeons trained in the use of 5-ALA, and who have received approval to use it through Health Canada's Special Access Programme. Only a few surgical centres and surgeons are currently using 5-ALA for resections of high-grade gliomas in Ontario. No issues related to challenges in the coordination of care for patients and other system-level aspects of patient care were identified.
Cost-effectiveness How efficient is the health technology/intervention likely to be?	Economic evaluation How efficient is the health technology/intervention likely to be?	We did not conduct a primary economic evaluation because no high-quality clinical evidence was identified. Therefore, we did not estimate the cost-effectiveness of 5-ALA in Ontario.
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? Organizational feasibility How organizationally feasible is it to implement the health technology/intervention?	The cost of 5-ALA is \$2,265 per vial. In addition, costs related to the purchase of fluorescence modules (at the assumed price of \$71,810) are expected to be incurred over time. We estimated that the annual budget impact of publicly funding 5-ALA in Ontario over the next 5 years would range from about \$930,000 in year 1 to \$1,765,000 in year 5 (for a total budget impact of \$7,500,000 over this period). Six neuro-oncology surgical sites in Ontario perform most of the surgical resections of high-grade gliomas in the province. Half of these sites have the required infrastructure (i.e., fluorescence module) and trained neurosurgeons to perform 5-ALA-guided surgical resection. All sites are equipped with surgical microscopes compatible with the required modules, which can be purchased separately. Newer models of microscopes used in neurosurgery come fully integrated with the fluorescence module. In addition, 5-ALA certified training has been, and continues to be, offered by the manufacturer in various locations across Ontario.

Abbreviations: 5-ALA, 5-aminolevulinic acid hydrochloride.

REFERENCE

(1) TBA

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