Frequently Asked Questions

CADTH Therapeutic Review of Anti–Vascular Endothelial Growth Factor (Anti-VEGF) Drugs for Retinal Conditions

What is a Therapeutic Review?

Often, more than one drug is available to treat a condition, which gives patients, clinicians, and policy-makers several treatment options. But treatment options are complex and sometimes we know very little about how these drugs compare to each other. Is one safer, more effective, or more cost-effective than the others?

CADTH can answer some of these questions by conducting a Therapeutic Review of two or more drugs used to treat the same condition. We compare the best publicly available evidence on the clinical and cost-effectiveness, and the benefits and harms. The results are summarized in a science report that is considered by the CADTH Canadian Drug Expert Committee (CDEC) as it develops recommendations. Recommendations are provided to participating drug programs in Canada to help inform their reimbursement decisions, although how these drug plans implement such recommendations is at their discretion, because CDEC recommendations are non-binding.

Why did CADTH undertake this Therapeutic Review of anti-VEGF drugs for retinal conditions?

Until recently, only one drug (ranibizumab [Lucentis]) had been approved by Health Canada for a single indication (a retinal condition called wet age-related macular degeneration [AMD]), although another drug, bevacizumab (Avastin), has been used widely in practice to treat eye conditions despite not being approved for this use by Health Canada. The recent approval of a second anti-VEGF drug (aflibercept [Eylea]), and the expansion in the number of indications for both ranibizumab and aflibercept, necessitated this Therapeutic Review.

Did the public drug programs ask CADTH to undertake this Therapeutic Review?

The project was initially developed by CADTH in 2014, after CADTH received a request for a Rapid Response report on the intravitreal use of bevacizumab (Avastin). CADTH evaluated the potential pan-Canadian relevance of a Therapeutic Review of anti-VEGF drugs for the treatment of retinal conditions. CADTH developed a project proposal, and participating drug programs selected this topic for a Therapeutic Review.

Which drugs were included in the Therapeutic Review?

The following drugs were included in the Therapeutic Review, based on which anti-VEGF drugs are being used currently in Canada to treat eye conditions:

- Aflibercept (Eylea)
- Bevacizumab (Avastin)
- Ranibizumab (Lucentis)
Why did CADTH include an off-label comparator (Avastin) in the Therapeutic Review?
CADTH consulted with federal, provincial, and territorial drug programs, as well as clinical experts, to determine the most relevant interventions and comparators. The inclusion of bevacizumab (Avastin) in the scope of the Therapeutic Review was determined to be relevant based on:

- the long-standing intravitreal use of bevacizumab (Avastin) for the treatment of some retinal conditions in Canada and internationally
- new scientific evidence, including the recent publication of independently funded studies (for example, by the National Institute of Health) and Cochrane reviews of bevacizumab (Avastin), which allowed CADTH to compare bevacizumab (Avastin) with drugs that have formal indications for the treatment of retinal conditions.

Is inclusion of an “off-label” comparator within the mandate of CADTH?
Yes, the inclusion of an off-label use comparator is within the mandate of CADTH. In June 2015, the CADTH Therapeutic Review Framework and Process was updated to include drugs with “evidence-based expanded use.” This formalized the inclusion of relevant “off-label” treatments, which previously have been included in CADTH drug reviews where such treatments have been considered to be relevant.

Did CADTH review the safety concerns with Avastin in the absence of a Health Canada–approved indication?
Yes, safety-related outcomes were reviewed as part of our Therapeutic Review. As there is a dearth of high-quality clinical studies that have specifically addressed the relative safety of bevacizumab and other anti-VEGF drugs, in addition to a formal systematic review of the highest quality clinical evidence available, CADTH also undertook an assessment of the real-world safety of bevacizumab (Avastin) as a complement to the Therapeutic Review report. This evaluation included 17 observational studies and three systematic reviews of randomized controlled trials comparing bevacizumab (Avastin) with ranibizumab (Lucentis) and/or aflibercept (Eylea) and focused on ophthalmic as well as cardiovascular complications.

Are the recommendations biased in favour of Avastin due to cost?
No. The recommendations are based on an objective, systematic review of the comparative clinical and economic evidence as well as an economic evaluation of the three anti-VEGF drugs included in the Therapeutic Review. The Therapeutic Review was an evidenced-based review that adhered to the highest methodological standards, to avoid any bias for or against any of the anti-VEGF drugs.

When developing the recommendations, CDEC took into account feedback from three ophthalmologists with expertise in the treatment of retinal conditions, who acted as advisers during the project. CDEC also considered input from patients and patient groups, as well as other stakeholders, such as drug manufacturers, individual clinicians, and Health Canada.

How will the recommendations be implemented?
Recommendations will be communicated to participating drug programs through the CADTH website. Jurisdictional drug programs will consider these recommendations and other factors when developing or updating their reimbursement policies on anti-VEGF drugs for the treatment of retinal conditions.
Is Avastin approved or licensed in any country for treatment of retinal conditions?
Yes. On September 1, 2015, France’s national medicines regulator (l’Agence nationale de sécurité du médicament [ANSM]) granted a temporary authorization for use of bevacizumab (Avastin) for the treatment of wet AMD. The temporary authorization allows ANSM to recommend bevacizumab (Avastin) for indications that are not included within its regulatory approved use(s).

What about the decision in the UK stating that Avastin is unlicensed for wet AMD and that setting a policy for its routine use based on cost alone wouldn’t be prudent?
The decision in the UK was to not allow for an alternative treatment (bevacizumab, Avastin) to be used in an unlicensed population based on cost alone. This is due to a bureaucratic impasse in the UK: the National Institute for Health and Care Excellence (NICE) is unable to carry out a full appraisal of bevacizumab (Avastin) without the approval of the UK Department of Health, which has said that an appraisal is not necessary because an alternative licensed therapy is already available. Therefore, in the UK, there has been no complete appraisal of the clinical evidence that would determine the cost-effectiveness of bevacizumab (Avastin) when used in patients with wet AMD. Interestingly, an assessment of the safety of intravitreal injection of bevacizumab (Avastin) by NICE (not limited to patients with a specific retinal condition such as AMD) did not reveal any major differences between the harms associated with bevacizumab (Avastin) compared with those seen in patients treated with ranibizumab (Lucentis). The cost of bevacizumab (Avastin) was one consideration that was assessed in the CADTH Therapeutic Review, in addition to its relative clinical effectiveness and safety versus other anti-VEGF drugs administered intravitreally for the treatment of retinal conditions.
About CADTH
CADTH is an independent, not-for-profit organization responsible for providing Canada’s health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs and medical devices in our health care system.

CADTH receives funding from Canada’s federal, provincial, and territorial governments, with the exception of Quebec.

Ce document est également disponible en français.

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