Canada's Drug Agency
L'Agence des médicaments du Canada

Dabrafenib-Trametinib for Low Grade Gliomas

FMEC Responses to Questions from the Drug Programs

Table 1: Response Summary

Drug Program Implementation Questions	Clinical Expert Response (Clinical Experts Acts Guest Specialists for FMEC)	FMEC Response
Considerations for Initiation of Therapy		
Note that testing for BRAF V600 mutation may be used in clinical trials. However, testing for BRAF V600 mutation may not be funded in all jurisdictions. (Funded in Ontario)	This is a comment from the drug plans to inform FMEC deliberations.	FMEC acknowledges this information.
Health Canada approved indication (LGG and HGG) – dabrafenib in combination with trametinib: • The treatment of pediatric patients 1 year of age and older with low-grade gliomas (LGG) with a BRAF V600E mutation who require systemic therapy • The treatment of pediatric patients 1 year of age and older with high-grade glioma (HGG) with a BRAF V600E mutation who have received at least one prior radiation and/or chemotherapy treatment	The clinical experts indicated that both Health Canada approved indications are populations with unmet needs. Pediatric patients 1 year of age and older with LGG and BRAF V600E mutation who require systemic therapy are included in the current review of dabrafenib-trametinib. However, patients 1 year of age and older with HGG and BRAF V600E mutation who have been previously treated are considered by the experts to be outside the scope of the current evidence review.	FMEC agrees with the experts.
Special Implementation Issues		
There are populations outside the indication or reimbursement request but are of interest to jurisdictions. The following drug-indication has been raised by jurisdictions with unmet needs: *Trametinib monotherapy: for 2nd line or greater therapy in low grade with residual or progressive disease with known non-V600 BRAF alterations*	The clinical experts expressed that they were aware of patients with LGG and with residual or progressive disease and with known non-V600 BRAF mutations to be treated with trametinib monotherapy, indicating that there is a phase II study that will be published by clinicians in Canada shortly (TRAM-01 study). Additionally, the experts pointed out that they were aware of a publication of selumetinib monotherapy (also a MEK inhibitor like trametinib) in second-line treatment of LGG that was published in Lancet Oncology (Selumetinib in Children with BRAF-Aberrant or Neurofibromatosis type 1-Associated Recurrent, Refractory or Progressive Low-Grade Glioma: a Multi-Center Phase II Trial - PMC	This is outside the scope of the current review
While not for the same indication, there are two other FMEC reviews (trametinib for LGOC, dabrafenib-trametinib for BRAF V600E ATC) using the drug(s) being reviewed for this current request. There	This is a comment from the drug plans to inform FMEC deliberations.	FMEC acknowledges this information.

Drug Program Implementation Questions	Clinical Expert Response (Clinical Experts Acts Guest Specialists for FMEC)	FMEC Response
may be opportunities to negotiate the same drug(s) for these files at the same time.		

ATC = anaplastic thyroid cancer; BRAF = proto-oncogene B-Raf; FMEC = Formulary Management Expert Committee; HGG = high-grade glioma; LGG = low grade gliomas; LGOC = low-grade ovarian cancer.