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

Dabrafenib-Trametinib
for BRAF V600E mutant anaplastic thyroid cancer
FMEC Responses to Questions from the Drug Programs

Table 1: Response Summary

Drug Program Implementation Questions	Clinical Expert Response (Clinical experts act as guest specialists for FMEC)	FMEC Response
Considerations for Initiation of Therapy		
Clarification was needed regarding the drug's place in therapy.	It was emphasized that patients with a confirmed diagnosis either through chemistry or rapid PCR testing should be eligible and offered treatment, even if they are undergoing other therapies, including palliative care or surgical procedures. The treatment should be integrated into overall management plan, especially in centers with limited access to multiple therapies. There was also expressed concern by the experts about the wording in the eligibility criteria regarding "no satisfactory local regional treatment options." The consensus was that this could cause confusion in peripheral centers, where it may be assumed that local regional treatment is possible, even if it is not. It was suggested that the criteria should focus on the patient's eligibility for systemic treatment without limiting them based on local /regional options. The experts expressed concern and suggested to not include the statement on "no satisfactory local regional treatment".	Defer to the clinical experts Refer to the initiation conditions listed in Table 1and the related implementation guidance within the recommendation report.
It is noted that the ROAR trial has an exclusion criterion for patients with prior treatment with BRAF and/or MEK inhibitors. However, patients were allowed to receive other treatments (e.g. chemotherapy, surgery, radiation therapy). How should patients with BRAF V600E mutant anaplastic thyroid cancer be managed if they have received any prior treatments?	Given the aggressive nature of the disease, patients can progress rapidly if treatment is not initiated as soon as possible, with the risk of fatality within days or weeks. Hence, the treatment approach should be multimodal in nature. This condition should be managed as an oncological emergency.	FMEC agrees with the clinical experts
Special Implementation Issues		
The drug plan raised the question on optimal timing and availability of molecular testing, specifically if it should be conducted at the time of diagnosis or as part of the eligibility assessment before treatment is initiated.	The clinical experts noted that while molecular testing for the BRAF mutation may not be universally available in all centers, particularly in smaller ones, there is an alternative immunohistochemical antibody approach. This approach uses a widely available antibody that is used for other conditions including colorectal cancers and melanomas, and is accessible and	Defer to the clinical experts. Refer to the initiation conditions listed in Table 1and the related implementation

Drug Program Implementation Questions	Clinical Expert Response (Clinical experts act as guest specialists for FMEC)	FMEC Response
It was noted that diagnostic testing for the BRAF mutation may not always be publicly funded in all Canadian jurisdictions, though it is funded in Ontario. Given the aggressive nature of the disease, there was also concern about the need for quick turnaround times for test results.	available in pathology departments across provinces. This method allows for a quicker turnaround time and provides rapid access to results in days rather than weeks. The antibody specifically detects the BRAF V600E mutation however does not offer the broader molecular analysis that would be provided for example by Next-Generation Sequencing (NGS).	guidance within the recommendation report.