Panitumumab

Formulary Management Expert Committee Responses to Questions From the Drug Programs

Table 1: Response Summary

Drug program implementation questions	Clinical expert response	FMEC response
Considerations for initiation of therapy		
Can panitumumab be used with another "backbone chemotherapy" instead of modified FOLFOX, which was used in the clinical trials?	As per the clinical experts, panitumumab can be used with another backbone chemotherapy.	FMEC defers to the clinical experts' response.
In PARADIGM, left-sidedness was defined as "primary tumours occupying a left-sided site, including the descending colon, sigmoid colon, rectosigmoid, and rectum." What would be the generally accepted definition of "left-sided" disease?	As per the clinical experts, it would be reasonable to include "transverse colon" in the definition of "left sided" to allow flexibility for clinicians. They also noted that only 5% of patients will have tumour in the transverse colon.	FMEC agrees with the clinical experts that transverse colon can be included in the definition of left-sided disease.
PARADIGM was conducted in 197 sites in Japan. Canada's population is made up of diverse ethnicities. Can the results of PARADIGM be generalized to the Canadian population?	As per the clinical experts, the population in the PARADIGM study can be generalized to patients living in Canada.	From other studies there is no reason to believe the disease is different in the patient population in Canada. FMEC defers to the clinical experts' response.
Participants previously treated with oxaliplatin in the adjuvant or neoadjuvant setting were excluded in the PARADIGM study. Is this practice consistent with Canadian clinical practice?	As per the clinical experts, in clinical practice, patients previously treated with oxaliplatin in the adjuvant or neoadjuvant setting would not be excluded from treatment with an EGFR inhibitor. Instead, they would receive irinotecan-based backbone chemotherapy.	FMEC defers to the clinical experts' response.
Patients treated with panitumumab in PARADIGM were able to access an EGFR inhibitor (panitumumab [26.3%] or cetuximab [5.4%]) in subsequent lines of treatment. Currently, re-treatment with an EGFR inhibitor for mCRC may not be funded in all Canadian jurisdictions. Should re-treatment with an EGFR inhibitor be considered in the new treatment algorithm resulting from this review?	As per the clinical experts, re-treatment could be an evolving area: there is emerging data with ctDNA technology that if *RAS* variant clones have been eliminated with another treatment, then re-treatment could be beneficial. In the era of genomic-based medicine, consideration of re-treatment with an EGFR inhibitor would be important to address the	This question is out of scope for this review: FMEC did not evaluate re-treatment or subsequent lines of therapy.

Drug program implementation questions	Clinical expert response	FMEC response
	potential needs of patients as they are treated with a subsequent line of therapy.	
Considerations for continuation or renewal of therapy		
Imaging tests (e.g., CT, MRI) were done at enrolment, every 8 weeks for the first 2 years, and every 12 weeks thereafter. Does the frequency of imaging reflect current Canadian practice?	As per the clinical experts, imaging is only done every 2 to 3 months in Canada.	Imaging should be done as per standard of care for the centre. CT resources are limited in many centres and provinces. Scanning every 8 weeks for 2 years may not be achievable.
Considerations for prescribing of therapy		
In the PARADIGM trial, panitumumab 6 mg/kg is given every 2 weeks, and this aligns with the dosing frequency of mFOLFOX6. However, if in clinical practice, panitumumab can be generalized to be used with other chemotherapy, such as XELOX or AVEX, these chemotherapy backbones are administered every 3 weeks. Therefore, to reduce clinic visits, is there any evidence to support panitumumab to be given every 3 weeks?	As per the clinical experts, there is evidence and practice of giving cetuximab (another EGFR inhibitor) and panitumumab every 3 weeks.	Dose adjustments were not considered as part of the FMEC review.
Special implementation issues		
At the time of implementation, for a time-limited basis, some patients who are being treated with bevacizumab-chemotherapy for first-line mCRC may wish to switch to panitumumab chemotherapy based on discussion with treating clinicians if they otherwise would meet panitumumab eligibility criteria. Can there be a time frame?	As per the clinical experts, a time-limited opportunity to switch from first-line bevacizumab (for those who did not have a contraindication to bevacizumab) to first-line panitumumab may be reasonable if panitumumab is funded as first-line therapy (as per this review).	This decision can be left to the discretion of the physician.
Currently, access to later-line (e.g., second or third line) bevacizumab with or without chemotherapy is only funded in some provinces. However, patients in the PARADIGM study were able to access bevacizumab in subsequent lines of treatment (44.6%). Should access to later lines of bevacizumab therapy be considered in the new treatment algorithm resulting from this review?	As per the clinical experts, consideration for access to a later line of bevacizumab therapy would be important to improve treatment choices and for patients to benefit from both therapies.	The use of bevacizumab in the second-line setting was not reviewed and is out of scope for this review. An update to the provisional funding algorithm is recommended.

EGFR = epidermal growth factor receptor; FMEC = Formulary Management Expert Committee; mCRC = metastatic colorectal carcinoma.