Canada's Drug and Health Technology Agency

Eltrombopag

CADTH Formulary Management Expert Committee Responses to Questions From the Drug Programs

Table 1: Response Summary

Drug program implementation questions	FMEC response
Considerations for initiation of therapy	
Can the drug be given again to patients who relapse after a course of therapy? If so, what would be the appropriate timing of re-treatment and how would the drug be dosed?	In the RACE trial, re-treatment was allowed for patients who experienced loss of response after response to initial therapy. However, the outcomes in the re-treated patient population were not reported separately. Therefore, FMEC is unable to provide a recommendation for the re-treated population due to lack of data specific to the subpopulation of re-treated patients in the pivotal trial. FMEC would leave re-treatment funding decisions to the drug plans' discretion.
Considerations for discontinuation of therapy	
How should clinically meaningful response be defined? What duration of treatment is appropriate for assessing response to therapy?	FMEC defers to clinical expertise in the management of SAA and vSAA. Therapy with eltrombopag may be considered up to 6 months to achieve CR. In the RACE trial, CR was defined as hemoglobin level greater than 10 g/dL, ANC count greater than 1.0×10^9/L, and platelet count greater than 100×10^9/L. PR was defined as no longer meeting the criteria for SAA and transfusion independency, with hemoglobin level greater than 8 g/dL, ANC count greater than 0.5×10^9/L, and platelet count greater than 20×10^9/L.
Considerations for prescribing of therapy	
Should treatment with eltrombopag only continue for 3 or 6 months, as was the case in the pivotal trial? If so, how should patients be subsequently managed?	FMEC defers to the clinical community with expertise in managing SAA and vSAA.

Drug program implementation questions	FMEC response
	The clinical expert consulted by CADTH for this review provided the following suggested guidance on duration of therapy with eltrombopag. Three types of response can be expected: no response, PR, and CR. Guided by the evidence, the study protocol of the pivotal trial, and their clinical experience, the clinical experts suggested the following in terms of treatment continuation or discontinuation. **At 3 months:** • No response: Continue IST + eltrombopag • PR: Continue IST + eltrombopag • CR: Discontinue eltrombopag and continue IST with cyclosporine **At 6 months:** • No response: Discontinue IST + eltrombopag • PR: Consider continuing IST and eltrombopag for another 3 months to 6 months • CR: Discontinue eltrombopag, continue IST, and taper cyclosporine as per institutional practice Some patients may be eligible for allo-HSCT if they have no response after 6 or more months of IST with eltrombopag. However, for the majority of patients, no alternative therapy is available. It was also noted that there is no definitive discontinuation timeline for partial responders to eltrombopag combination with IST within the Health Canada product monograph.

allo-HSCT = allogeneic hematopoietic stem cell transplant; ANC = absolute neutrophil count; CR = complete response; FMEC = CADTH Formulary Management Expert Committee; IST = immunosuppressive therapy; PR = partial response; SAA = severe aplastic anemia; vSAA = very severe aplastic anemia.