Canada's Drug and Health Technology Agency

Rivaroxaban Granules for Oral Suspension

FMEC Responses to Questions From the Drug Programs

Table 1: Response Summary

Drug program implementation questions	FMEC response
Considerations for initiation of therapy	
Can FMEC comment on rivaroxaban use without prior use of parenteral anticoagulation?	FMEC noted that there is no evidence to support this practice in the pediatric population. However, the adult algorithm allows for parenteral anticoagulation to be omitted.
Considerations for continuation or renewal of therapy	
Is it possible that patients may require re-treatment after successfully completing a treatment course?	FMEC agreed with the clinical experts for this review. Patients may require re-treatment after successfully completing a treatment course. Any patients with presence or recurrence of a risk factor may qualify for treatment (e.g., cancer, inflammatory bowel disease flares, rheumatology disorders that flare, nephrotic syndrome).
Is there a clear duration of therapy required by these patients? Would re-treatment, or long-term treatment, ever be necessary in these indications? If yes, in what condition would there be a need for long-term treatment in the pediatric population?	FMEC agreed with the clinical experts. The clinical experts indicated that the duration of therapy would be a standard of 3 months; however, patients may be treated for a shorter (i.e., 6 weeks) or longer (> 3 months) duration. Patients with no prior VTE, nonsevere VTE, provoked risk factor that has been resolved, or resolved thrombosis, and with very low risk of provoked DVT may be suited to a shorter treatment duration. A longer treatment duration may be warranted based on additional risk factors.
Considerations for discontinuation of therapy	
How is treatment response monitored? How is clot resolution assessed? Is there a need for imaging in clinical practice to determine the need for ongoing treatment? If so, would that need exist for all anticoagulants used in this patient population?	The clinical experts stated that the main clinical outcome of interest is to prevent extension, embolization, and recurrence of VTE events at follow-up. Radiographic resolution is not typically considered as the main clinical outcome, as persistent vein occlusion is frequent, and it does not affect the duration of treatment (taken from adult experience). FMEC agreed with the clinical experts. However, if complete resolution of VTE is documented by radiologic assessment, treatment may be discontinued earlier than planned based on individual patient circumstances.
Considerations for prescribing of therapy	
Who would be the appropriate prescribers of this medication? Pediatricians,	The clinical experts indicated that anticoagulants may not necessarily be initiated by pediatric hematologists. Almost all

Drug program implementation questions	FMEC response
pediatric hematologists, other? Will treatment always start in hospital? Will it ever originate while patients are in the community? What is the breakdown of hospital starts compared to community starts?	patients who are infants and young start in hospitals (except for a small number of children who start as outpatients), where they could be initiated in the emergency department at community hospitals, for example. Up to a third (20% to 30%) of older children would be starting in the hospital, while some may be started in a community settings (e.g., DVT caused by use of oral contraceptives). FMEC noted that subspecialists must be consulted for specific subgroups. Neonates should be treated by neonatal experts; patients with cancer may require input from a hematologist or oncologist.
Generalizability	
Is there potential for rivaroxaban use beyond VTE treatment or prevention of VTE recurrence?	The clinical experts consulted by CADTH provided some examples for off-label use. FMEC noted that this is beyond the scope of the current review.
Care provision issues	
Is there an opportunity for drug wastage considering the different size syringes and 14-day stability of reconstituted suspension?	FMEC agreed with the clinical experts, who outlined that the younger the patient, the smaller the dose they would require. Therefore, wastage would be expected.
System and economic issues	
How many patients would be anticipated to require rivaroxaban? Are most patients in this population group going to be candidates for rivaroxaban? Which treatment alternatives' (products) market share are likely to be replaced with rivaroxaban use for this population?	The experts noted that approximately 50% of patients would be anticipated to require rivaroxaban as rivaroxaban would be seen as an alternative for LMWH and not every patient would be a candidate (e.g., those with significant renal impairment). FMEC noted that rivaroxaban is an alternative to SOC anticoagulants and would be used in patients who meet the eligibility criteria of the EINSTEIN Jr trial.
Is posttreatment imaging a routine associated cost in this treatment population? Does it apply regardless of anticoagulation product?	FMEC agreed with the clinical experts who noted that posttreatment imaging is independent of the anticoagulation product.
Would the availability of rivaroxaban granules for suspension help facilitate discharge from the hospital or other care centres sooner?	FMEC agreed with the clinical experts who noted that the availability of rivaroxaban granules for suspension has the potential to help facilitate discharge from the hospital to other care centres sooner, but by only by a short amount of time.

DVT = deep vein thrombosis; FMEC = Formulary Management Expert Committee; LMWH = low molecular weight heparin; VTE = venous thromboembolic events; SOC = standard of care.