CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

Rivaroxaban

Indication: Venous thromboembolic events

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SX0750
Name of the drug and Indication(s)	Rivaroxaban For the treatment of VTE and prevention of VTE recurrence in term neonates, infants and toddlers, children and adolescents < 18 years old, after at least 5 days of initial parenteral anticoagulation treatment.
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	☐
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	X☐
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
Please identify the specific text from the recommendation and provide a rationale for requesting a change in recommendation.

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
Please provide details regarding the information that requires clarification.
b) Reimbursement conditions and related reasons
Please provide details regarding the information that requires clarification. Clarification is required to confirm if all sub-criteria listed under reimbursement condition 1.3 need to be met by an individual patient.
c) Implementation guidance

Please provide high-level details regarding the information that requires clarification. You can provide specific comments in the draft recommendation found in the next section. Additional implementation questions can be raised here.

Outstanding Implementation Issues

In the event of a positive draft recommendation, drug programs can request further implementation support from CADTH on topics that cannot be addressed in the reimbursement review (e.g., concerning other drugs, without sufficient evidence to support a recommendation, etc.). Note that outstanding implementation questions can also be posed to the expert committee in Feedback section 4c.

Algorithm and implementation questions
1. Please specify sequencing questions or issues that should be addressed by CADTH (oncology only)
1. 2.
2. Please specify other implementation questions or issues that should be addressed by CADTH
1. 2.
Support strategy
3. Do you have any preferences or suggestions on how CADTH should address these issues?
May include implementation advice panel, evidence review, provisional algorithm (oncology), etc.

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SX0750-000 - SR0750-000
Brand name (generic)	XARELTO® (rivaroxaban)
Indication(s)	Venous Thromboembolic Events (VTE)
Organization	Bayer Inc.
Contact information[a]	Name: Andrew Kuo

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐

Bayer agrees with the CADTH recommendation for rivaroxaban granules for oral suspension, and the supporting rationale, which includes the clinical evidence of rivaroxaban providing comparable efficacy and safety to low molecular weight heparin (LMWH) for pediatric patients with VTE from the EINSTEIN-Jr trial.[1] Bayer is also in agreement with CADTH's conclusion that there remains a "significant unmet need in the treatment of VTE in the pediatric population, especially with options that are more convenient (e.g. oral liquid formulation) and requires less monitoring (e.g. no routine bloodwork requirement)" and that rivaroxaban granules for oral suspension has the potential to lead to "improvements in QoL [quality of life] associated with less injection and monitoring…".

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

Overall, Bayer submits that the committee considered most of the input provided by Bayer. However, Bayer disagrees with the inclusion of dabigatran as a relevant comparator for rivaroxaban in the pediatric population. As stated in previous input provided by Bayer, dabigatran does not have a Health Canada-approved indication for children, is not recommended by clinical practice guidelines, or commonly used in the Canada treatment landscape for the treatment of VTE and prevention of VTE recurrence in the pediatric population.[2,3] As such, dabigatran is not a relevant comparator in the pediatric setting.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

The reasons for the recommendation are clearly stated.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐

The implementation issues have been clearly articulated and adequately addressed in the recommendation.

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒

The reimbursement conditions and associated rationale are not clearly stated in the recommendation. The Implementation guidance for Reimbursement Condition #1 stipulates that "for specific subpopulations such as cancer related VTE, unprovoked VTE, children under 2 years where there is less clinical evidence of safety, a pediatric subspecialist should be involved (refer to condition 2 – prescribing)". However, Reimbursement Condition #2 states that "Rivaroxaban granules for oral suspension must be initiated by, or in consultation with, a pediatric hematologist or other pediatric subspecialist(s) with experience in managing anticoagulation". There is a lack of clarity in whether the involvement of a pediatric hematologist or other pediatric subspecialist(s) is recommended only in the subpopulations specified in the implementation guidance or for the entire population included in Reimbursement Condition #1.

Bayer highlights the following relevant statements by clinical experts consulted for this review as it pertains to this point: "anticoagulants may not necessarily be initiated by a pediatric hematologist. Almost all patients who are infants and young children start in hospitals…, where they could be initiated in the emergency department at community hospitals" and "Up to a third (20% to 30%) of older children would be starting in the hospital, while some may be started in community settings (e.g. DVT caused by use of oral contraceptives)". Based on these statements from the clinical experts consulted, Bayer disagrees with Reimbursement Condition #2, as current clinical processes in the initiation of anticoagulants may not necessarily involve a pediatric hematologist or other subspecialist. The requirement to involve a pediatric hematologist or other pediatric subspecialist(s) may lead to inequitable access to rivaroxaban granules for oral suspension depending on the clinical setting (e.g. community hospitals, community settings) where such specialists may not be readily available.

[a] CADTH may contact this person if comments require clarification.

References:

1) Male C, Lensing AWA, Palumbo JS, et al. Rivaroxaban compared with standard anticoagulants for the treatment of acute venous thromboembolism in children: a randomised, controlled, phase 3 trial. Lancet Haematol. 2020;7(1):e18-e27. PubMed
2) Monagle P, Chan AKC, Goldenberg NA, et al. Antithrombotic therapy in neonates and children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e737S-e801S.
3) PRADAXA (Dabigatran) 75 mg, 110 mg and 150 mg capsules, Oral [product monograph]. Burlington (ON): Boehringer Ingelheim Canada Ltd.; 2017.