Rivaroxaban (Xarelto®) for the prevention of atherothrombotic complications in adult patients with coronary artery disease

Summary of recommendations by *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 4 March 2019

Zorginstituut Nederland carried out an assessment of medicinal product rivaroxaban (Xarelto®), whereby they came to the following conclusion.

In a letter dated 9 October 2018 (CIBG-18-07012), the Minister of Health, Welfare and Sport (VWS) asked *Zorginstituut Nederland* to amend the conditions for rivaroxaban (Xarelto®). The *Zorginstituut* has completed its assessment.

Rivaroxaban is available in the form of 2.5 mg, 10 mg, 15 mg and 20 mg film-coated tablets. This product is already included in the Medicine Reimbursement System (GVS) for use in the prevention of thrombosis in elective knee and hip surgery and for use in the prevention of cerebrovascular accidents (CVA) and systemic embolisms in adults with non-valvular atrium fibrillation. Rivaroxaban is also included in the GVS for the prevention of atherothrombotic complications in adult patients after an acute coronary syndrome (ACS) and for the indication venous thromboembolism (VTE). List 2 conditions apply for these indications.

Registered indication
The manufacturer requested to extend the existing List 2 conditions for rivaroxaban, administered simultaneously with acetylsalicylic acid (ASA), for the prevention of atherothrombotic complications in adult patients with coronary artery disease (CAD) or symptomatic peripheral arterial disorder (PAD) with a high risk of ischaemic events.
The recommended dose amounts to 2.5 mg twice daily.

Conclusion on therapeutic value
Zorginstituut Nederland concludes that, for the prevention of atherothrombotic complications in adult patients with coronary artery disease (CAD) or symptomatic peripheral arterial disease (PAD), with a high risk of ischaemic events, the therapeutic value of rivaroxaban in combination with ASA is greater than that of ASA alone. This is based on a positive effect on cardiovascular mortality, myocardial infarction and stroke, and on mortality irrespective of cause, as found in the COMPASS study. The observed advantages outweigh the increased risk of haemorrhage, as long as rivaroxaban is used on patients with a high risk of ischaemic events and who do not have a high risk of haemorrhage. It is possible that in Dutch clinical practice patients with a SMART risk score of ≥20% are classed as high risk for ischaemic events, or a similar score may be used.

Budget impact analysis
Taking into account the uncertainty regarding the prevalence of CAD, PAD or both, the number of high-risk patients and the estimated market penetration, extending the specific conditions for rivaroxaban (Xarelto®) for the prevention of atherothrombotic complications in adult patients with CAD or symptomatic PAD with a high risk of ischaemic events will be accompanied by added costs to the pharmacy budget amounting to €6.9 million and €16.3 million, with an estimated average of €11.6 million. When taking into account a patient adherence of 80%, the added costs to the pharmacy budget will be between €5.5 million and €13 million, with an estimated average of €9.3 million. Uncertainty exists about the size of the high-risk population and the degree of market penetration.

Outcome of the pharmacoeconomic analysis
The *Zorginstituut* concludes, with advice from the WAR, that the cost-effectiveness analysis of rivaroaban as treatment for the prevention of atherothrombotic complications in adult patients with CAD or symptomatic PAD with a high risk of ischaemic events is of sufficient methodological quality. The critical point in the analysis is that the patient population in the model probably has a lower risk of ischaemic events than the population for which reimbursement is being requested in the Netherlands.

Based on a reference value applicable to this disorder of €20,000 per quality-adjusted life-year gained (QALY), the chance that rivaroxaban + acetylsalicylic acid is cost-effective in comparison with acetysalicylic acid (ASA) as monotherapy is about 99.2%. The incremental cost-effectiveness ratio (ICER) is about €7,464 per QALY.

Advice
Rivaroxaban is already included on List 1A. According to the GVS system, this implies a therapeutic added value and a sufficiently substantiated cost-effectiveness analysis, and the *Zorginstituut* advises the Minister to extend rivaroxaban's List 2 conditions and stipulate the following condition. Extending with this specific condition will result in additional costs.

Condition
Only for an insured person aged eighteen or older:

5. who relies on this drug in combination with acetylsalicylic acid for the preventive treatment of atherothrombotic complications in patients with coronary artery disease (CAD) or symptomatic peripheral arterial disorder (PAD) with an increased risk of ischaemic events.

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The original text of this excerpt from advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of Zorginstituut Nederland's advice.
Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.