PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
REF: PS103 FINAL
FIRST APC BOARD DATE: 29 APR 2015
LAST APC BOARD DATE: 24 MAY 2017

NHS Pan Mersey Area Prescribing Committee

# RIVAROXABAN 2.5mg tablets (Xarelto®▼) for Acute Coronary Syndrome

**AMBER**

**The Pan Mersey Area Prescribing Committee recommends the prescribing of Rivaroxaban 2.5mg tablets (Xarelto®▼) following specialist initiation for preventing adverse outcomes after acute management of acute coronary syndrome in accordance with NICE TA335**

**FOLLOWING SPECIALIST INITIATION**

Rivaroxaban is recommended as an option within its marketing authorisation[1], in combination with aspirin plus clopidogrel or aspirin alone, for preventing atherothrombotic events in people who have had an acute coronary syndrome with elevated cardiac biomarkers. See NICE TA335.[2]

Clinicians should carefully assess the person's risk of bleeding before treatment with rivaroxaban is started. The decision to start treatment should be made after an informed discussion between the clinician and the patient about the benefits and risks of rivaroxaban in combination with aspirin plus clopidogrel or with aspirin alone, compared with aspirin plus clopidogrel or aspirin alone.

Following admission to hospital, suitable patients will be commenced on rivaroxaban for a period to be determined by the hospital physician. Clear diagnosis and duration of treatment information will be relayed to GPs upon discharge.

**Note**: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

# Rivaroxaban 2.5mg tablets (Xarelto®▼) for Acute Coronary Syndrome

## EFFECTIVENESS

Rivaroxaban is a highly selective direct factor Xa inhibitor, inhibiting both thrombin formation and development of thrombi. No effects on platelets have been demonstrated.

In the pivotal double-blind, placebo-controlled trial[3] 15,526 patients with a recent acute coronary syndrome received twice-daily doses of either 2.5 mg or 5 mg of rivaroxaban or placebo for a mean of 13 months and up to 31 months. Rivaroxaban significantly reduced the primary composite endpoint of CV death, MI or stroke compared with placebo (hazard ratio in the rivaroxaban group, 0.84; 95% confidence interval [CI], 0.74 to 0.96; P=0.008). The twice-daily 2.5-mg dose of rivaroxaban reduced the rates of death from cardiovascular causes (2.7% vs. 4.1%, P=0.002) and from any cause (2.9% vs. 4.5%, P=0.002) compared to placebo. The overall benefit was driven by a reduction in CV death and MI and appeared early with a constant treatment effect over the entire treatment period.

## SAFETY

Bleeding risk is the most important safety consideration of anticoagulant therapy.

In the pivotal trial, compared with placebo, rivaroxaban increased the rates of major bleeding not related to coronary-artery bypass grafting (2.1% vs. 0.6%, P<0.001) and intracranial haemorrhage (0.6% vs. 0.2%, P=0.009), without a significant increase in fatal bleeding (0.3% vs. 0.2%, P=0.66) or other adverse events.

Contraindications:

-Concomitant treatment of ACS with antiplatelet therapy in patients with a prior stroke or a transient ischaemic attack (TIA)
-Hypersensitivity to the active substance or to any of the excipients
-Active clinically significant bleeding
-Concomitant treatment with any other anticoagulants
-Hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C
-Pregnancy and breast feeding
-Concomitant systemic treatment with azole-antimycotics (such as ketoconazole, itraconazole, voriconazole and posaconazole) or HIV protease inhibitors (e.g. ritonavir).

Consult the Summary of Product Characteristics for a full list of adverse drug reactions, potential drug-drug interactions and contraindications at: **www.medicines.org.uk**

## COST (ex VAT) [4]

Rivaroxaban 2.5mg bd £657 (1 year)
Aspirin dispersible 75mg od £9.13 (1 year)
Clopidogrel 75mg od £17.34 (1 year)

Based on the NICE costing template developed for TA 335[5], estimated demand would be up to 149 patients per 100,000 population, at an estimated annual cost of £14,000.

## PATIENT FACTORS

Rivaroxaban use in renal impairment:
CrCl <15ml/min - not recommended
CrCl 15-29ml/min - use with caution
CrCl >30ml/min - no dose adjustment needed

## PRESCRIBING INFORMATION AND IMPLEMENTATION NOTES

The recommended dose is 2.5 mg twice daily.
Rivaroxaban is not licensed for use with concurrent ticagrelor or prasugrel.
For patients who are unable to swallow whole tablets, Xarelto tablet may be crushed and mixed with water immediately prior to use and administered orally or via gastric tube.
Treatment should be regularly evaluated in the individual patient weighing the risk for ischaemic events against the bleeding risks. Extension of treatment beyond 12 months should be done on an individual patient basis as experience up to 24 months is limited.

## REFERENCES

1. SPC for Xarelto 2.5mg tablets (last updated: 07/07/15) [online]. Accessed 23/02/17 at: http://www.medicines.org.uk/emc
2. NICE TA335, March 2015. Available at: http://www.nice.org.uk/guidance/ta335
3. Mega JL, Braunwald E, Wiviott SD, et al. Rivaroxaban in patients with a recent acute coronary syndrome. *N Engl J Med* 2011; DOI: 10.1056/NEJMoa1112277. Available at: http://www.nejm.org
4. NHS Electronic Drug Tariff. Available at: http://www.ppa.org.uk/ppa/edt_intro.htm. Accessed 23/02/17.
5. NICE Costing Statement: Implementing the NICE guidance on Rivaroxaban for preventing adverse outcomes after acute management of acute coronary syndrome in accordance with NICE TA335, March 2015