Local New Medicine Treatment Protocol for Ranolazine

1. **New medicine name:** Ranolazine 375mg, 500mg and 750mg M/R tablets

2. **Licensed indication(s):** As add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line antianginal therapies (such as beta-blockers and/or calcium antagonists).

3. **Scottish Medicines Consortium advice:** Not recommended for use within NHS Scotland. The submitting company did not present a sufficiently robust clinical and economic case to gain acceptance by the Independent Review Panel.

   **Medicines Advisory Group advice:** Can be prescribed under direction of Cardiology (amber traffic light) in patients who are inadequately controlled or intolerant of standard therapy as outlined below and in the Tayside flow chart for treatment of stable angina.

4.** Prescriber details:** Consultant cardiologists initially (first 4 weeks), then primary care under the direction of Cardiology.

5.** Criteria for patient selection:** To be used as an add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled or intolerant to first-line antianginal therapies and other second-line antianginal therapies, who remain unsuitable for surgical revascularisation procedures.

6. **Administration details:** Oral. Treatment will be commenced by consultant cardiologist (by hospital issued prescription for 6 weeks supply*) at 375mg M/R BD and may be increased to 500mg M/R BD on GP prescription following 4 week patient telephone review with Consultant Cardiologist, if appropriate. At 4 weeks, issue of prescriptions should be transferred to primary care. Further titration can be considered at 3 month consultant review, to maximum dose 750mg M/R BD.

   *6 weeks supply will ensure patient does not run out of ranolazine before a new prescription / supply has been organised by primary care after 4 week telephone consultation.

7. **Contra-indications:**
   - Hypersensitivity to the active substance or to any of the excipients.
   - Severe renal impairment (creatinine clearance < 30 ml/min).
   - Moderate or severe hepatic impairment.
   - Concomitant administration of potent CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, voriconazole, posaconazole, HIV protease inhibitors, clarithromycin, telithromycin, nefazodone).
   - Concomitant administration of Class Ia (e.g. quinidine) or Class III (e.g. dofetilide, sotalol) antiarrhythmics other than amiodarone.

8. **Side-effects/cautions:**
   Caution / careful dose titration should be under taken in the following situations:
   - Concomitant administration of moderate CYP3A4 inhibitors or P-gp inhibitors (e.g. diltiazem, fluconazole, erythromycin) or P-gp inhibitors (e.g. verapamil, ciclosporin).
   - Mild hepatic impairment.
• Mild to moderate renal impairment (creatinine clearance 30–80 ml/min.
• Elderly.
• Patients with low body weight <60kg.
• Patients with moderate to severe CHF (NYHA Class III–IV).
• Caution should be observed when treating patients with a history of congenital or a family history of long QT syndrome, in patients with known acquired QT interval prolongation, and in patients treated with drugs affecting the QTc interval.

In patients with a combination of these factors, additional exposure increases are expected and dose-dependent side effects are likely to occur.

Common side effects may be: Dizziness, headache, GI disturbance.

9.* Monitoring - response to treatment:
Cardiology: Treatment to be reviewed within 4 weeks by patient telephone consultation with consultant, to assess if dose can be titrated. If treatment is to continue beyond 4 weeks, then cardiologist should communicate treatment plan to patient’s GP, so that primary care can continue prescription.

Patient will be reviewed by consultant at 3 months to assess if benefit from treatment. If no benefit from treatment (i.e. no reduction in angina symptoms), then ranolazine should be stopped. Cardiologist should communicate ongoing treatment plan (i.e. if treatment to stop, to remain on the same dose, or dose increase) to patient’s GP at this point.

10.* Monitoring – treatment safety:
Secondary care: Baseline urea, creatinine, LFTs and body weight.
Primary care (note – yearly monitoring is advised for best practice, it is not a prescribing requirement and is to identify patient groups who may be more likely to experience side effects):
  1. Yearly creatinine – if eGFR falls <30mL/min, then stop ranolazine and inform prescribing consultant. If new mild-moderate renal impairment, inform prescribing consultant (as patient more likely to experience side effects).
  2. Yearly LFTs. If new moderate-severe hepatic impairment, then stop ranolazine and inform prescribing consultant. If LFTs increase to x3 ULN, inform prescribing consultant (as patient more likely to experience side effects).
  3. Yearly body weight. If patient weight falls <60kg, then please inform prescribing consultant (as patient more likely to experience side effects).

11.* Updated by: Joanne McGeoghie  
Approved by: Stuart Hutcheon

12.* Review date: March 2020

* essential fields