

Guidelines for the Prescribing of Ranolazine

1. BACKGROUND

Ranolazine is an anti-anginal drug in the treatment of stable angina in patients inadequately controlled or intolerant of first-line anti-anginal therapies

2. INDICATION

Within Hull and East Riding, ranolazine will be prescribed for patients with stable angina in line with [NICE CG 126](#) which states:

- Beta blockers and calcium channel blockers are first line treatment either alone, or in combination where necessary
- Other anti-anginal treatments including long-acting nitrates, nicorandil, ivabradine or ranolazine should be offered where first line treatments are contraindicated or not tolerated and where symptoms are not controlled.

Choice of agent should be based on patient's co-morbidities, contraindications, patient's preferences and drug costs

- Treatment with more than two anti-anginal drugs is recommended only when symptoms are not controlled AND patient is waiting for revascularisation or revascularisation is not an option

3. DOSE

Initial dose: 375mg twice daily for 2 – 4 weeks

If tolerated then increase to 500mg twice daily

Dose may be further increased to 750mg twice daily if tolerated, where symptoms are on-going. If patients experience treatment related side effects, down titration to 500mg bd or 375mg bd may be required.

4. DRUG INTERACTIONS

Drug interactions where concomitant use of ranolazine is contraindicated:

- Azole antifungals: ketoconazole, itraconazole, posaconazole, voriconazole, (*caution with fluconazole – see below*)
- Macrolide antibiotics: clarithromycin, telithromycin (*caution with erythromycin – see below*)
- HIV protease inhibitors – e.g. *azatanavir, ritonavir* . Check BNF for details
- Other CYP3A4 inhibitors - Grapefruit juice
- CYP3A4 inducers - rifampicin, phenytoin, phenobarbital, carbamazepine, St. John's Wort
- Antiarrhythmics – *Avoid class Ia and III antiarrhythmics including disopyramide, sotalol, quinidine. Amiodarone can be used in combination.*

- *Nefazodone*

Drug interactions where caution, additional monitoring or dose adjustment may be required:

- Antiarrhythmics / cardiac drugs - digoxin, diltiazem, flecainide, metoprolol, verapamil, propafenone
- Antidepressants – paroxetine, tricyclic antidepressants
- antipsychotics
- antihistamines which prolong QTc interval – mizolastine, rupatadine
- bupropion
- ciclosporin, tacrolimus, sirolimus, everolimus
- cyclophosphamide
- efavirenz
- erythromycin
- fluconazole and miconazole oral gel
- simvastatin – limit dose to 20mg
- Ranolazine may increase metformin levels
- Any other drugs with the potential to prolong QTc interval

5. CONTRAINDICATIONS AND CAUTIONS

Ranolazine is contraindicated in patients with severe renal impairment (creatinine clearance < 30 ml/min), moderate or severe hepatic impairment, and in pregnant and breast-feeding women.

There are a number of clinically significant drug interactions listed with ranolazine – see details above.

Further caution is recommended in use and during dose titration for patients with mild to moderate renal impairment (creatinine clearance 30-80ml/min), mild hepatic impairment, moderate to severe congestive heart failure (*NYHA class III or IV*), QT interval prolongation, in elderly patients and patients weighing under 60 kg.

In patients with a combination of these factors, dose- dependent side effects are more likely to occur. Monitoring of adverse events should be frequent, the dose reduced, and treatment discontinued, if needed.

6. ADVERSE EFFECTS

Most commonly reported side effects ($\geq 1/100$ to $< 1/10$): dizziness, headache, constipation, nausea, vomiting, asthenia. Side effects are more common in the first two weeks of treatment

For further information including full details of contraindications, cautions, drug interactions and adverse effects always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).

7. INFORMATION TO PATIENT

Patients should be advised of benefits and risks of treatment, including common side effects which may affect ability to drive or performed skilled tasks, and need to inform health care staff that they are taking ranolazine before any new medicines are prescribed (because of number of drug interactions).

APPROVAL PROCESS

Written by:	Marie Miller, Interface Pharmacist updated Jane Morgan, Acting Interface Pharmacist and Yvonne Holloway, Senior Pharmacist June 17; Updated by Jane Morgan May 2020
Consultation process:	Sally Griffiths, Specialist Pharmacist-Cardiology Cardiology Consultants, HEY
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