Rationale for Initiation, Continuation and Discontinuation (RICaD)

Ranolazine

Initiated as monotherapy or adjunct therapy in the treatment of stable angina in patients inadequately controlled or intolerant of first-line antianginal therapies

This document supports the use and transfer of an agent which is classified as **AMBER**.
It is intended for completion by specialist in order to give Primary Care prescribers a clear indication of the reason for recommending an **AMBER** medication together with suggested criteria for its subsequent continuation or discontinuation. This RICaD should be provided as a supplement to the specialist's clinical letter.

Patient details		**GP details**		**Specialist details**	
Name		**GP name**	**Dr**	**Specialist name**	
PID		**GP address**		**I confirm that this patient is eligible to receive ranolazine under the restrictions listed below**	
DOB				**Signature**	
Patient address				**Date**	
				Contact details	

Rationale for Choice

Relevant Diagnosis:	Stable angina
Agreed Indication(s) for inclusion in the BSSE APC Formulary:	For specialist initiation when (Please cross the relevant box):- As add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled ☐ or Patient intolerant to first-line antianginal therapies (such as beta-blockers and/or calcium antagonists). ☐
Reason why ranolazine has been chosen in preference to drugs without Formulary restrictions:	Following NICE CG 126 states ranolazine is an option • If the person cannot tolerate beta blockers and calcium-channel blockers or both are contraindicated, consider monotherapy with one of the following drugs: a long-acting nitrate or ivabradine or nicorandil or ranolazine. • For people on beta blocker or calcium-channel blocker monotherapy whose symptoms are not controlled and the other option (calcium-channel blocker or beta-blocker) is contraindicated or not tolerated, consider one of the following as an additional drug: a long-acting nitrate or ivabradine or nicorandil or ranolazine. Do not offer a third anti-anginal drug to people whose stable angina is controlled with two anti-anginal drugs. Consider adding a third anti-anginal drug only when: • the person's symptoms are not satisfactorily controlled with two anti-anginal drugs and • the person is waiting for revascularisation or revascularisation is not considered appropriate or acceptable Decide which drug to use based on comorbidities, contraindications, the person's preference and drug costs.

Rationale for Choice cont….

Special precautions	**Contraindications** • Hypersensitivity to the active substance or to any of the excipients listed • Severe renal impairment (eGFR < 30 ml/min/1.73m^2) • Moderate or severe hepatic impairment • Concomitant administration of potent CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, voriconazole, posaconazole, HIV protease inhibitors, clarithromycin, telithromycin) • Concomitant administration of Class Ia (e.g. quinidine) or Class III (e.g. dofetilide, sotalol) antiarrhythmics other than amiodarone. **Cautions** (As per BNF online May 15- for more information please see SmPC) Caution should be exercised when prescribing or uptitrating ranolazine to patients in whom an increased exposure is expected: • Moderate to severe congestive heart failure • QT interval prolongation • Elderly • Body-weight less than 60 kg • Concomitant administration of moderate CYP3A4 inhibitors (e.g. erythromycin, fluconazole, diltiazem) • Concomitant administration of P-gp inhibitors (e.g. ciclosporin, verapamil) • Mild hepatic impairment • Mild to moderate renal impairment (eGFR 30–80 ml/min/1.73m^2)
Drug Interaction (significant interaction as outlined in BNF, please see BNF and SPC for more detail)	**Ranolazine** has the following interaction information:

Atazanavir	plasma concentration of ranolazine possibly increased by atazanavir —manufacturer of ranolazine advises avoid concomitant use
Clarithromycin	plasma concentration of ranolazine possibly increased by clarithromycin —manufacturer of ranolazine advises avoid concomitant use
Darunavir	plasma concentration of ranolazine possibly increased by darunavir —manufacturer of ranolazine advises avoid concomitant use
Disopyramide	manufacturer of ranolazine advises avoid concomitant use with disopyramide
Fosamprenavir	plasma concentration of ranolazine possibly increased by fosamprenavir —manufacturer of ranolazine advises avoid concomitant use **Note:** Fosamprenavir is a prodrug of amprenavir
Grapefruit Juice	plasma concentration of ranolazine possibly increased by grapefruit juice —manufacturer of ranolazine advises avoid concomitant use
Indinavir	plasma concentration of ranolazine possibly increased by indinavir —manufacturer of ranolazine advises avoid concomitant use
Itraconazole	plasma concentration of ranolazine possibly increased by itraconazole —manufacturer of ranolazine advises avoid concomitant use
Ketoconazole	plasma concentration of ranolazine increased by ketoconazole —avoid concomitant use
Lopinavir	plasma concentration of ranolazine possibly increased by lopinavir —manufacturer of ranolazine advises avoid concomitant use**. Note:** In combination with ritonavir as *Kaletra*® (ritonavir is present to inhibit lopinavir metabolism and increase plasma-lopinavir concentration)
Posaconazole	plasma concentration of ranolazine possibly increased by posaconazole —manufacturer of ranolazine advises avoid concomitant use
Rifampicin	plasma concentration of ranolazine reduced by rifampicin —manufacturer of ranolazinea dvises avoid concomitant use
Ritonavir	plasma concentration of ranolazine possibly increased by ritonavir —manufacturer of ranolazine advises avoid concomitant use
Saquinavir	plasma concentration of ranolazine possibly increased by saquinavir —manufacturer of ranolazine advises avoid concomitant use
Simvastatin	ranolazine increases plasma concentration of simvastatin

	Sotalol	manufacturer of ranolazine advises avoid concomitant use with sotalol
	Tacrolimus	ranolazine increases plasma concentration of tacrolimus **Note:** Interactions do not generally apply to tacrolimus used topically; risk of facial flushing and skin irritation with topical tacrolimus on consumption of alcohol
	Telithromycin	plasma concentration of ranolazine possibly increased by telithromycin —manufacturer of ranolazine advises avoid concomitant use
	Tipranavir	plasma concentration of ranolazine possibly increased by tipranavir —manufacturer of ranolazine advises avoid concomitant use
	Voriconazole	plasma concentration of ranolazine possibly increased by voriconazole —manufacturer of ranolazine advises avoid concomitant use
Pre-treatment test results	Check renal and hepatic function	

Guidance on initiation

Initiation dose:	The recommended initial dose of ranolazine is 375 mg twice daily. After 2–4 weeks, the dose should be titrated to 500 mg twice daily and, according to the patient's response, further titrated to a recommended maximum dose of 750 mg twice daily See SmPC for further advice on dose titration in renal or hepatic impairment, in the elderly and those with low weight or heart failure
Additional info:	SmPC can be accessed at http://emc.medicines.org.uk for further information
Monitoring:	No specific/ mandatory monitoring required However, check renal function at regular intervals during treatment with ranolazine

Suggested Criteria for Continuation or Discontinuation (to be completed by the specialist)

Assessment of Efficacy	
Frequency	Around once a month initially (at GP surgery) until symptom control has been achieved.
Location	During admission and on review in OPD/ GP practice
Method (what tests are required)	Routine outpatient clinical review as already occurs.
Continuation Criteria	To continue as tolerated by the patient.
Discontinuation Criteria	Any side effects or intolerance to the medication. Main reported side effects include dizziness, nausea and constipation.
Follow up action	No specific monitoring required
Shared Care read code	In the patients notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement/RICaD

GP Prescribing System	Read Code	Description
EMIS and Vision	8BM5.00	Shared care prescribing
SystmOne	XaB58	Shared care