

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:	<p>For specialist initiation when (Please cross the relevant box):-</p> <p>As add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled <input type="checkbox"/></p> <p>or</p> <p>Patient intolerant to first-line antianginal therapies (such as beta-blockers and/or calcium antagonists). <input type="checkbox"/></p>
Reason why ranolazine has been chosen in preference to drugs without Formulary restrictions:	<p>Following NICE CG 126 states ranolazine is an option</p> <ul style="list-style-type: none"> 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. <p>Do not offer a third anti-anginal drug to people whose stable angina is controlled with two anti-anginal drugs.</p> <p>Consider adding a third anti-anginal drug only when:</p> <ul style="list-style-type: none"> 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 <p>Decide which drug to use based on comorbidities, contraindications, the person's preference and drug costs.</p>

Rationale for Choice cont....

<p>Special precautions</p>	<p>Contraindications</p> <ul style="list-style-type: none"> • Hypersensitivity to the active substance or to any of the excipients listed • Severe renal impairment (eGFR < 30 ml/min/1.73m²) • 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. <p>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:</p> <ul style="list-style-type: none"> • 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/1.73m²) 																														
<p>Drug Interaction (significant interaction as outlined in BNF, please see BNF and SPC for more detail)</p>	<p>Ranolazine has the following interaction information:</p> <table border="1" data-bbox="352 786 1465 2004"> <tr> <td>Atazanavir</td> <td>plasma concentration of ranolazine possibly increased by atazanavir —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Clarithromycin</td> <td>plasma concentration of ranolazine possibly increased by clarithromycin —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Darunavir</td> <td>plasma concentration of ranolazine possibly increased by darunavir —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Disopyramide</td> <td>manufacturer of ranolazine advises avoid concomitant use with disopyramide</td> </tr> <tr> <td>Fosamprenavir</td> <td>plasma concentration of ranolazine possibly increased by fosamprenavir —manufacturer of ranolazine advises avoid concomitant use Note: Fosamprenavir is a prodrug of amprenavir</td> </tr> <tr> <td>Grapefruit Juice</td> <td>plasma concentration of ranolazine possibly increased by grapefruit juice —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Indinavir</td> <td>plasma concentration of ranolazine possibly increased by indinavir —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Itraconazole</td> <td>plasma concentration of ranolazine possibly increased by itraconazole —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Ketoconazole</td> <td>plasma concentration of ranolazine increased by ketoconazole —avoid concomitant use</td> </tr> <tr> <td>Lopinavir</td> <td>plasma concentration of ranolazine possibly increased by lopinavir —manufacturer of ranolazine advises avoid concomitant use. Note: In combination with ritonavir as <i>Kaletra</i>[®] (ritonavir is present to inhibit lopinavir metabolism and increase plasma-lopinavir concentration)</td> </tr> <tr> <td>Posaconazole</td> <td>plasma concentration of ranolazine possibly increased by posaconazole —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Rifampicin</td> <td>plasma concentration of ranolazine reduced by rifampicin —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Ritonavir</td> <td>plasma concentration of ranolazine possibly increased by ritonavir —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Saquinavir</td> <td>plasma concentration of ranolazine possibly increased by saquinavir —manufacturer of ranolazine advises avoid concomitant use</td> </tr> <tr> <td>Simvastatin</td> <td>ranolazine increases plasma concentration of simvastatin</td> </tr> </table>	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 <i>Kaletra</i> [®] (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 ranolazine advises 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
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	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
	SystemOne	XaB58	Shared care