BNSSG Shared Care Guidance
Please complete all sections

Section 1: Heading

Drug	Ivabradine (Procoralan®)
Amber ***three months***	
Indication	Symptomatic treatment of chronic stable angina in adults i) unable to tolerate/with a contraindication to beta blockers, OR ii) in combination with beta blockers in those inadequately controlled with an optimal dose. Treatment of chronic heart failure NHYA II to IV in adults who have been clinically stable for four weeks, with systolic dysfunction, sinus rhythm and heart rate ≥ 75 bpm i) in combination with standard therapy including a beta-blocker, ace-inhibitor, and aldosterone antagonist OR ii) when beta blockers are not tolerated/ contraindicated, for lowering heart rate. iii) with a left ventricular ejection fraction of 35% or less
Speciality / Department	Cardiology
Trust(s)	North Bristol NHS Trust
	University Hospitals Bristol NHS Trust
	WAHT

Section 2: Treatment Schedule

Usual dose and frequency of administration	Chronic stable angina: To start at a dose of 5mg twice a day, in patients aged below 75 years. This can be increased to 7.5mg twice a day if tolerated, after three to four weeks. (If receiving 2.5mg twice a day as an initial dose increase to 5mg twice a day).

	Maintenance dose should not exceed 7.5mg twice daily. Chronic Heart failure: To start at a dose of 5mg twice daily. This can be increased after two weeks to 7.5mg twice a day if resting heart rate is persistently above 60bpm, or decreased to 2.5mg twice daily if below 50bpm or if not tolerated.
Route and formulation	Oral, tablet
Duration of treatment	Maintenance treatment for as long as is tolerated/required.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate
No specific tests are required for monitoring. Resting heart rate should be monitored initially monthly and then every three months. Dose should be reduced, or treatment stopped if heart rate falls below 50 beats per minute.
Subsequent tests - where appropriate
1. N/A

Section 4: Side Effects

Please list the most common side effects and management. Please provide guidance on when the GP should refer back to the specialist.

Side effects and management	Potential side effects are: bradycardia, first degree heart block, ventricular extra-systoles, headache, dizziness, visual disturbance known as luminous phenomena (phosphenes) and blurred vision. Less commonly: nausea, constipation, diarrhoea, palpitations, supraventricular extrasystoles, dyspnoea, vertigo, muscle cramps, eosinophilia, hyperuricaemia, and raised plasma-creatinine concentration.
Referral back to specialist	Patients should be referred back to a specialist if there are significant side-effects, if there is no benefit of treatment or if symptoms deteriorate. If the patient goes into atrial fibrillation the drug is in-effective in controlling rate and the patient should be re-referred to a

	specialist. In angina, consider stopping if there is no or limited symptom improvement after 3 months.

Section 5: Drug Interactions

Please list clinically significant drug interactions (eMC link please click here)

Significant Drug Interactions	Avoid concommitant use of drugs that might prolong the QT interval. Ivabradine is metabolised by CYP3A4. Manufacturer advises reduce initial dose to 2.5mg twice daily with concurrent use of moderate CYP3A4 inhibitors e.g. antifungals, macrolide antibiotics, or avoid. (Except diltiazem, erythromycin and verapamil where concurrent use is contraindicated). Amiodarone increases risk of ventricular arrhythmias when given with ivabradine – avoid concomitant use. Amiodarone has a long half-life so there is the potential for an interaction to occur for several weeks (or even months) after treatment with it has been stopped. Plasma concentration of ivabradine possibly increased by clarithromycin, erythromycin, diltiazem, verapamil, itraconazole, ritonavir, nelfinavir, ketoconazole, and grapefruit juice - avoid concomitant use. Also fluconazole may increase plasma concentration - manufacturer advises reduce initial dose of ivabradine to 2.5mg twice daily. Increased risk of ventricular arrhythmias when ivabradine given with sotalol, disopyramide, pimozide, fluconazole, clarithromycin, and erythromycin – avoid concomitant use. (does not apply to small amounts of erythromycin used topically). Plasma concentration of ivabradine reduced by St John's wort- avoid concomitant use
Reminder to ask patient about specific problems	Ivabradine interacts with several medicines e.g. antibiotics, so ensure that your prescriber checks the suitability of any new medicines with your current treatment.

Section 6: Contra-indications, Cautions and Special Recommendations

Please list

1. Ivabradine is contraindicated in patients with unstable angina, unstable or acute heart failure, hypersensitivity to the active substance or any of the excipients, in patients with cardiogenic shock, acute myocardial infarction, immediately after cerebrovascular accident, severe hepatic insufficiency, sick sinus syndrome, sinoatrial block, second and third degree heart block, and in pacemaker dependent patients.
2. Do not initiate for chronic heart failure if heart rate is below 75bpm; do not initiate for angina if heart rate is below 70bpm.
3. It is not effective in the treatment or prevention of cardiac arrhythmias and probably loses its

effectiveness when a tachyarrhythmia occurs. It is therefore not recommended in patients with AF or other cardiac arrhythmias that interfere with sinus node function.
4. If the heart rate is persistently below 50bpm or the patient experiences symptoms of bradycardia e.g. dizziness, then the dose should be titrated downwards or discontinued if this is not resolved.
5. It should not be used in patients with heart failure NYHA class III/IV and it should not be introduced to patients with decompensated heart failure.
6. Ivabradine is contraindicated in patients with BP<90/50mmHg. It should be used in caution in those with mild to moderate hypotension.
7. Non-urgent DC cardioversion is ideally performed 24 hours after the last dose of ivabradine.
8. It should be avoided in those with congenital QT syndrome or those treated with QT prolonging medicines.
9. It should be used in caution in patients with moderate hepatic insufficiency and patients with creatinine clearance <15ml/min, in the elderly (consider lower starting dose of 2.5mg twice daily), and in those with retinitis pigmentosa
10. It should not be used during pregnancy or lactation

Section 7: Advice to the patient

Advice for prescribing clinician to inform patient

1. Explain the expected benefits of treatment
2. Encourage patient to measure/record pulse on a frequent basis to detect potential bradycardia
3. Advise patient to report side effects due to symptomatic bradycardia: breathlessness, fatigue, syncope, dizziness
4. The most common side effect is transient areas of enhanced brightness (flashing lights) in the eyes/parts of the visual field, known as visual luminous phenomena. This most often occurs during changes in light intensity, and so should be taken into account when driving or using machines in situations when there may be sudden variatins in light intensity e.g. driving at night. This is most common during the first three months of treatment, and usually resolves on its own. There is no need to alter dosing unless vision is impaired.
5. Ivabradine interacts with several medicines e.g. antibiotics, so ensure that your prescriber checks the suitability of any new medicines with your current treatment.

Section 8: Responsibilities for Secondary Care

Core responsibilities

1. Initiating treatment and prescribing for the first three months
2. Undertaking the clinical assessment and monitoring for the first three months.
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of Ivabradine.
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see section 5.

Other specific to drug

1. N/A

Section 9: Responsibilities for Primary Care

Core responsibilities
2. Responsible for taking over prescribing after the first three months 3. Responsible for the clinical assessment and monitoring after the first three months 4. Review of any new concurrent medications for potential interactions. 5. Reporting adverse events to the MHRA. 6. Refer for advice to specialist where appropriate. 7. Reminder to ask patients about particular problems see section 5.
Other specific to drug
1. N/A

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Section 11: Document Details

Date prepared	Jan 2010. Updated March 2018.
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Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

1. UHB; Heart Failure Team
2. NBT; Robert Brown, Cardiac Pharmacist

Section 13: References

Please list references

1. BNF On-line, accessed March 2018
2. EMC On-line, Ivabradine 5mg/7.5mg tablets, accessed March 2018 https://www.medicines.org.uk/emc/product/9082/smpc
3. Ivabradine for treating Chronic Heart Failure, NICE TAG, Nov 2012 https://www.nice.org.uk/guidance/ta267
4. Tardif JC, Ford I, Tendera M, Bourassa MG, Fox K. Efficacy of ivabradine, a new selective If inhibitor, compared with atenolol in patients with chronic stable angina. Eur Heart J 2005;26(3):25292536.