Ivabradine (Procoralan®)

Please note: Ivabradine is to be initiated by a cardiology specialist/ cardiologist and communicated to either primary care or the community heart failure team.

Angina patients will be followed up by primary care within 4 weeks
Heart failure patients will be followed up by the community heart failure team within 2 weeks

Should a patient require referral back to a cardiologist, please refer back to initiating consultant.

Background Information	**Indication/Licensing information** • Symptomatic Treatment of Chronic Stable Angina Pectoris: Ivabradine is licensed for the symptomatic treatment of chronic stable angina pectoris in coronary artery disease adults with normal sinus rhythm and heart rate ≥ 70bpm. Ivabradine is indicated: - in adults unable to tolerate or with a contra-indication to the use of beta-blockers - or in combination with beta-blockers in patients inadequately controlled with an optimal beta-blocker dose. • Treatment of Chronic Heart Failure: Ivabradine is also licensed for use in patients with chronic heart failure (NYHA class II to IV) with systolic dysfunction, in patients in sinus rhythm and whose heart rate is ≥ 75 bpm, in combination with standard therapy (including beta-blockers) or when beta-blocker therapy is contraindicated or not tolerated. NICE have issued a positive technology appraisal for the use of ivabradine in heart failure. (TA267 available at: http://www.nice.org.uk/guidance/TA267) **Pharmacology** Ivabradine selectively and specifically blocks the (If) or funny ion channel which is found in sino-atrial node cells which results in a reduction in resting heart rate. **Dosage and administration** **Angina:** The starting dose of ivabradine should not exceed 5 mg twice daily in patients aged below 75 years. After three to four weeks of treatment, if the patient is still symptomatic, if the initial dose is well tolerated and if resting heart rate remains above 60 bpm, the dose may be increased to the next higher dose in patients receiving 2.5 mg twice daily or 5 mg twice daily. The maximum dose should not exceed 7.5 mg twice daily. *Angina in Elderly patients* Initially 2.5mg twice daily. Dose reduction or cessation should be considered if the heart rate drops below 50bpm. If there is no improvement in symptoms of angina within 3 months after start of treatment, treatment of ivabradine should be discontinued. In addition, discontinuation of treatment should be considered if there is only limited symptomatic response and when there is no clinically relevant reduction in resting heart rate within three months. • If, during treatment, heart rate decreases below 50 beats per minute (bpm) at rest or the patient experiences symptoms related to bradycardia such as dizziness, fatigue or hypotension, the dose must be titrated downward including the lowest

	dose of 2.5 mg twice daily (one half 5 mg tablet twice daily). • After dose reduction, heart rate should be monitored. Treatment must be discontinued if heart rate remains below 50 bpm or symptoms of bradycardia persist (despite dose reduction). **<u>Heart failure:</u>** Initially 5 mg twice daily, increased if necessary after 2 weeks to 7.5 mg twice daily (Dose should be reduced to 2.5mg twice daily if not tolerated) • If, during treatment, heart rate decreases persistently below 50 beats per minute (bpm) at rest or the patient experiences symptoms related to bradycardia, the dose must be titrated downward to the next lower dose in patients receiving 7.5 mg twice daily or 5 mg twice daily. • If heart rate increases persistently above 60 beats per minute at rest, the dose can be up titrated to the next upper dose in patients receiving 2.5 mg twice daily or 5 mg twice daily. Treatment must be discontinued if heart rate remains below 50 bpm or symptoms of bradycardia persist (see section 4.4 of the SPC).
BNF therapeutic class	2.6.3 Other antianginal drugs
Contraindications and Cautions	<u>Contraindications:</u> • Hypersensitivity to the active substance or to any of the excipients • Immediately after cerebrovascular accident • <u>If used for angina:</u> resting heart rate below 70 beats per minute prior to treatment • <u>If used for heart failure:</u> resting heart rate below 75 beats per minute • Cardiogenic shock, Acute myocardial infarction • Severe hypotension (< 90/50 mmHg) • Severe hepatic insufficiency • Sick sinus syndrome, Sino-atrial block, Unstable or acute heart failure • Pacemaker dependent (heart rate imposed exclusively by the pacemaker) • Unstable angina • AV-block of 3rd degree • Combination with strong cytochrome P450 3A4 inhibitors such as azole antifungals (ketoconazole, itraconazole), macrolide antibiotics (clarithromycin, erythromycin), HIV protease inhibitors and nefazodone • Combination with verapamil or diltiazem which are moderate CYP3A4 inhibitors with heart rate reducing properties • Pregnancy, lactation and women of child-bearing potential not using appropriate contraceptive measures • Congenital QT syndrome <u>Cautions:</u> • Mild heart failure • Monitor for Atrial fibrillation or other arrythmias • Intraventricular conduction defects • Hypotension • Retinitis pigmentosa • Elderly
Adverse Drug Reactions	Uncontrolled blood pressure. Bradycardia, AV first-degree heart block (ECG prolonged PQ interval), ventricular extrasystoles, atrial fibrillation, headache, dizziness, visual disturbances including phosphenes and blurred vision; *less commonly* nausea, constipation, diarrhoea, palpitations, supraventricular extrasystoles, dyspnoea,

	angioedema, vertigo, muscle cramps, eosinophilia, hyperuricaemia, raised plasma-creatinine concentration, rash; *very rarely* AV second- and third-degree heart block, sick sinus syndrome
Monitoring	Given that the heart rate may fluctuate considerably over time, serial heart rate measurements, ECG or ambulatory 24-hour monitoring should be considered when determining resting heart rate before initiation of ivabradine treatment and in patients on treatment with ivabradine when titration is considered. This also applies to patients with a low heart rate, in particular when heart rate decreases below 50 bpm, or after dose reduction. Resting heart rate. If heart rate decreases persistently below 50 beats per minute (bpm) at rest in angina patients (75 bpm for heart failure patients) or the patient experiences symptoms related to bradycardia such as dizziness, fatigue or hypotension, the dose must be titrated downward (see above). Treatment must be discontinued if heart rate falls below 50 bpm (75bpm in heart failure patients) or symptoms of bradycardia persists Atrial fibrillation and/or other arrythmias
Interactions	Anti-arrythmics Cytochrome P450 inhibitors (Macrolides, Azole antifungals, HIV protease inhibitors, nefazadone) Moderate CYP3A4 inhibitors with heart rate reducing properties (Verapamil or diltiazem) Beta blockers Calcium channel blockers Grapefruit

***Amber with Guidance**= To be initiated and titrated to a stable dose in secondary care with follow up prescribing and monitoring by primary care where deemed appropriate.*

Contact names and details

Contact Details	Telephone number	Email
Dr Naeem Tahir Consultant Cardiologist	01226 730000	**naeem.tahir@nhs.net**
Dr Abdul Qadeer Neghaban Consultant Cardiologist	01226 730000	**a.negahban@nhs.net**
Dr Zamvar Deoraj Consultant Cardiologist	01226 730000	**deoraj.zamvar@nhs.net**
Gillian Turrell Lead Pharmacist - Cardiology & Medicines Information	01226 432857	**gilliansmith2@nhs.net**
BHNFT Heart Failure Clinic	01226 434981	
Community Heart Failure Team	01226 209881	

References

- BNF February 2017. Available at: www.medicinescomplete.com
- SPC. Procolaran®, Servier Laboratories Limited. Available at: https://www.medicines.org.uk/emc/medicine/17188/SPC/Procoralan/#:~:text=Ivabradine%20is%20indicated%20for%20the%20symptomatic%20treatment%20of,sinus%20rhythm%20and%20heart%20rate%20%E2%89%A5%2070%20bpm. Last Accessed: October 2020
- https://www.nice.org.uk/guidance/ta267

Development Process

This Guideline was originally produced in 2007 By Chris Lawson following consultation with specialists at Barnsley Hospital. The Guideline was subsequently updated by Caron Applebee (Prescribing Support Pharmacist) with input from Gillian Smith (Medicines Information Pharmacist BHNFT) and the Cardiologists (Dr Tahir, Dr Etorki and Dr Yousaf).The guideline was further updated by Gillian Smith in December 2014 to include the use of Ivabradine in the management of mild to severe heart failure.
Review and update competed by Faraaz Hussain in May 2017.
This Guideline was last reviewed and further updated by Faraaz Hussain in October 2017.
This Guideline was last reviewed and further updated by Lauren Clarke in October 2020.

This guideline has been subject to consultation and endorsement by the Area Prescribing Committee on 11th November 2020.