Prescribing ivabradine as an adjunct for the management of on-going symptoms in patients with chronic stable angina

The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Ivabradine (Procoralan®) is a novel antianginal therapy licensed for use in patients with chronic stable angina in sinus rhythm, who have a contraindication or intolerance to beta-blockers or in combination with beta-blockers for patients inadequately controlled with an optimal beta-blocker dose and whose heart rate is > 60 bpm. It is a pure heart rate lowering agent and has been shown to be as effective as beta-blockers in anti-anginal and anti-ischaemic activity, but as yet is only supported by limited cardiovascular outcomes data. Ivabradine is listed by NICE as an option for the treatment of chronic stable angina.

Ivabradine is approved for use locally as an option in patients in sinus rhythm:

- **that have a contraindication to or cannot tolerate either beta-blockers or rate-limiting calcium channel blockers (diltiazem / verapamil)**
- **in combination with beta-blockers where there are on-going angina symptoms and a heart rate above 60 beats per minute despite optimised beta-blocker therapy.**

See also SLCSN algorithm 'Optimising Prescribing in Chronic Stable Angina' at:
www.slcsn.nhs.uk/prescribing

Pay careful attention to the contraindications and cautions listed below before initiating therapy.

Contra-indications	Cautions
– Sick sinus syndrome – Bradycardia (resting heart rate <60bpm) prior to initiation – Cardiogenic shock and acute MI – Within 4 weeks of CVA – Sino-atrial block & 3rd degree AV-block – Unstable or acute HF – Congenital QT syndrome and drugs which prolong the QT interval – Pacemaker dependent patients – Unstable angina – Pregnancy and lactation	– Pre-existing cardiac arrhythmias including atrial fibrillation – Concurrent HR lowering agents – 2nd degree AV block – Post-CVA – Retinis pigmentosa – Hypotension (avoid if BP<90/50mmHg) – Hepatic insufficiency (avoid if severe) – Severe renal insufficiency (CKD stage 5; eGFR<15ml/min)

Commonly Used Interacting Drugs (See BNF for a full list of drug interactions)

- Amiodarone or disopyramide – increased risk of ventricular arrhythmias
- Macrolide antibiotics, particularly clarithromycin and erythromycin – avoid concomitant use
- 'azole' anti-fungals, particularly ketoconazole and itraconzole – avoid concomitant use
- Nelfinavir and ritonavir – avoid concomitant use
- Sotalol – increased risk of ventricular arrhythmias
- Diltiazem and verapamil – avoid concomitant use
- Mefloquine – avoid concomitant use

Initiation and dose titration:

Obtain baseline BP and pulse rate before initiation and after each dose change.

- **Ivabradine is usually initiated at a dose of 5mg twice daily.**
- After 3 to 4 weeks the dose may be increased to 7.5mg twice daily if required for greater symptom control and heart rate remains > 60bpm.
- If the patient is elderly (>75 years) or 5mg twice daily is not tolerated, the dose can be reduced to 2.5mg twice daily.

Monitoring

If heart rate falls persistently below 50 beats per minute at rest and / or the patient experiences symptoms related to bradycardia such as dizziness, fatigue or hypotension - reduce the dose:

- from 7.5mg twice daily to 5mg twice daily; or
- from 5mg twice daily to 2.5mg twice daily (half a 5 mg tablet twice daily).

Discontinue treatment if heart rate falls below 50bpm or symptoms of bradycardia persist.

Ivabradine is not recommended in patients with atrial fibrillation (AF) or other cardiac arrhythmias that interfere with sinus node function; as it is unlikely to be effective in this circumstance. It is recommended that all patients prescribed ivabradine are regularly monitored for the occurrence of AF (sustained or paroxysmal).

Adverse effects (refer to SPC for full list of adverse effects)

- Visual symptoms are the most common adverse effect reported. Luminous phenomena were reported in 14.5% of patients and therefore new patients should be warned about this potential side effect. Phosphenes generally begin to occur within the first two months of treatment after which they may occur repeatedly. Phosphenes were generally reported to be of mild to moderate intensity. All phosphenes resolved during or after treatment. Blurred vision also occurs commonly.
- Other common side effects (occurring in between 1 in 10 and 1 in 100 patients) include headache and dizziness, bradycardia, 1st degree AV block and ventricular extrasystoles and uncontrolled blood pressure.

References

1. Summary of Product Characteristics, Procoralan. Amended 19/11/12. Accessed at: http://www.medicines.org.uk/EMC/medicine/17188/SPC/Procoralan/
2. NICE CG126: Management of chronic stable angina 2011