Prescribing ivabradine for patients with chronic heart failure due to left ventricular dysfunction

South London Cardiovascular and Stroke Network

This 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 is a pure heart-rate lowering agent. Data from the SHIFT study has demonstrated that heart rate reduction using ivabradine in selected patients with chronic heart failure can significantly reduce hospitalisations due to worsening heart failure and prevent heart failure and CV-related death.

Selection of Patients

Ivabradine should ONLY be considered for patients that meet all the following criteria:

- Left ventricular systolic dysfunction with an ejection fraction of ≤35% and NYHA class II-IV
- On maximum tolerated dose of both ACE inhibitor (or ARB) and beta-blocker (unless contraindicated); and an aldosterone antagonist
- In sinus rhythm, with a resting heart rate ≥ 75 beats per minute (bpm)

Ivabradine should only be initiated after a stabilisation period of 4 weeks on optimised standard therapy with ACE inhibitors, beta-blockers and aldosterone antagonists.

- **Ivabradine should be initiated by a heart failure specialist with access to a multidisciplinary team. Dose titration and monitoring should be carried out by a heart failure specialist in primary or secondary care, such as a GP with a special interest in heart failure or a heart failure specialist nurse**

- **Responsibility for the prescribing of ivabradine may be transferred to the GP when the dose of ivabradine is optimised (i.e. heart rate controlled to between 50-60bpm or on maximum ivabradine dose) and the patient is considered stable**

Contra-indications	Cautions
– Sick sinus syndrome – Bradycardia prior to initiation (resting heart rate <60bpm) – Pacemaker dependent patients* (ie where heart rate is maintained exclusively by the pacemaker) – Cardiogenic shock and acute MI – Within 4 weeks of CVA – Sino-atrial block & 3rd degree AV-block – Congenital QT syndrome – Unstable angina – Pregnancy and lactation	– Pre-existing cardiac arrhythmias – Concurrent HR lowering agents – Post-CVA – Retinitis pigmentosa – Hypotension (avoid if BP < 90/50mmHg) – Hepatic impairment (avoid if severe) – Severe renal impairment (CrCl<15ml/min; eGFR<15ml/min)

**Ivabradine is suitable for use in patients with specialist pacing devices under cardiology supervision.*

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
- Imidazole anti-fungals, particularly ketoconazole and itraconazole – avoid concomitant use
- Nelfinavir and ritonavir – avoid concomitant use
- Sotalol – increased risk of ventricular arrhythmias
- Calcium channel blockers, specifically diltiazem and verapamil – avoid concomitant use
- Mefloquine – avoid concomitant use

Initiation and Dose Titration

- **Ivabradine should be initiated at a dose of 5mg twice daily.** If the patient is elderly or 5mg twice daily is not tolerated, the dose can be reduced to 2.5mg twice daily.
- Obtain baseline BP and pulse before initiation and after each change in dose.
- **Once initiated the dose of Ivabradine should be adjusted to achieve a heart rate ≤ 60bpm.**

- Review within two to four weeks of initiation:
  - If heart rate remains ≥ 60bpm, consider increasing dose to 7.5mg twice daily taking into account the heart rate response to the initial dosage.
  - If heart rate is < 50bpm consider dose reduction or cessation of therapy.

Adverse Effects

Asymptomatic bradycardia is the most common adverse effect when using Ivabradine in chronic heart failure; although a small proportion of patients will experience symptomatic bradycardia, for which dose reduction or cessation of therapy should be considered.

Other side effects reported commonly include headache, especially during the first week of therapy. Visual symptoms were also reported, such as blurred vision and luminous phenomena (phosphenes), described as a transient enhanced brightness in a limited area of the visual field.

As a black triangle drug for this indication all adverse effects should be reported to the CSM using the yellow card system, even if well documented, in addition to any local reporting arrangements

References

1. Summary of Product Characteristics, Procoralan® Updated 02/2012 Ivabradine (Procoralan®).
2. Swedberg K, Komajda M, Böhm M et al, on behalf of the SHIFT Investigators. Lancet 2010; 376:875-85
3. NICE TA 267: Ivabradine for treating Chronic Heart failure. 2012. http://publications.nice.org.uk/ivabradine-for-treating-chronic-heart-failure-ta267