Ivabradine ▼ AMBER 0

For the symptomatic treatment of chronic stable angina or chronic heart failure
Information for prescribers - to be read in conjunction with the SPC

Background

Heart rate is regulated normally by spontaneous activity in pacemaker cells in the sinoatrial (SA) node. Early in diastole the negative membrane potential of SA node cells activates a cation channel giving rise to an inward current, the I_f current, which contributes to depolarisation of SA node cells which in turn leads to action potential firing. Ivabradine selectively blocks the I_f channel thus slowing the diastolic depolarisation of the SA node resulting in a reduction in heart rate both at rest and during exercise. Myocardial contractility and atrioventricular (AV) conduction are not affected.

Angina

Ivabradine is recommended for the symptomatic treatment of chronic stable angina pectoris in patients with normal sinus rhythm:

- who have a resting heart rate of at least 70 beats per minute (bpm) and a contra-indication or intolerance to beta blockers or rate limiting calcium channel blockers **or**
- in combination with beta-blockers where symptoms are not controlled with an optimal beta-blocker dose and heart rate is at least 70bpm (if rate limiting calcium channel blocker not tolerated/contra-indicated) **or**
- **in combination with a dihydropyridine calcium channel blocker (e.g. slow release nifedipine, amlodipine or felodipine) where symptoms are not controlled and beta blockers are not tolerated/contra-indicated. (concomitant use of ivabradine with rate limiting calcium channel blockers e.g. verapamil and diltiazem is contraindicated).**
- **Prescribers should consider stopping ivabradine if there is no or only limited symptom improvement after 3 months.**

Heart Failure

- Ivabradine is recommended within its marketing authorisation for people:
  - with New York Heart Association (NYHA) class II to IV chronic heart failure with systolic dysfunction **AND**
  - who are in sinus rhythm with a heart rate of **75 bpm or more AND**
  - when given in combination with standard therapy including: **maximum tolerated dose** of a beta-blocker, ACE inhibitors and aldosterone antagonists, or when beta-blocker therapy is contraindicated or there is **true intolerance** (symptomatic low BP or unstable asthma).
- ***Ivabradine should only be initiated after a stabilisation period of 4 weeks on optimal standard therapy with angiotensin-converting enzyme (ACE) inhibitors, beta-blockers and aldosterone antagonists as outlined in NICE Technology Appraisal 267.***
- Ivabradine should be initiated by a heart failure specialist with access to a multidisciplinary heart failure team
- Following initiation, dose titration and monitoring should be carried out by a heart failure specialist, or in primary care by either a GP with a special interest in heart failure or a heart failure specialist nurse.

Dosage and Administration

- Patients should be advised to take the tablets during meals to avoid variation in bioavailability.
- **Down titrate the dose to 2.5mg twice daily if the heart rate drops below 50 bpm or the patient experiences symptoms of bradycardia that persist. If despite a dose reduction the resting heart rate remains below 50 bpm or symptoms of bradycardia persist, stop treatment.**

Chronic Stable Angina

- The recommended starting dose is 5mg twice daily.
- After three to four weeks the dose may be increased to a maximum of 7.5mg twice daily if the initial dose is well tolerated, resting heart rate remains above 60 bpm and the patient is still symptomatic.
- In patients aged over 75years a starting dose of 2.5mg twice daily (one half 5 mg scored tablet twice daily) should be considered (before up titration if necessary).

Chronic Stable Heart Failure

- The recommended starting dose is 5 mg twice daily.

Version 2.1
Date: May 2018
Review Date: May 2021

- After two weeks, the dose can be increased to 7.5 mg twice daily if resting heart rate is persistently above 60 bpm or decreased to 2.5 mg twice daily (one half 5 mg tablet twice daily) if resting heart rate is persistently below 50 bpm or if there are symptoms of bradycardia.
- If the heart rate is between 50 and 60 bpm, the dose of 5 mg twice daily should be maintained.
- If heart rate increases persistently above 60 bpm 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.

Monitoring

It is recommended to regularly monitor heart rate (including monitoring for bradycardia and its symptoms) and assess for the occurrence of atrial fibrillation (sustained or paroxysmal) including ECG monitoring if clinically indicated.

Contraindications

Ivabradine is contraindicated in:

- hypersensitivity to the active substance or any excipients
- patients with a pre-treatment resting heart rate below 70bpm
- severe hypotension (<90/50 mmHg)
- unstable angina
- sick sinus syndrome or congenital QT syndrome
- severe hepatic insufficiency
- unstable or acute heart failure
- acute MI myocardial infarction / cardiogenic shock / immediately post CVA
- sino-atrial block / 2nd or 3rd degree AV-block / pacemaker dependent patients.
- pregnancy or lactation and women of child-bearing potential not using contraceptive measures
- patients on potent CYP3A4 inducers / inhibitors (macrolide antibiotics, HIV protease inhibitors, ketoconazole, itraconazole, grapefruit juice and St John's Wort) / rate limiting calcium channel blockers (verapamil or diltiazem) / QT prolonging medicinal products

Cautions for Use

- Ivabradine is not effective in the treatment or prevention of cardiac arrhythmias and should not be used in patients with AF or other cardiac arrhythmias that interfere with sinus node function.
- Ivabradine should be used with caution in patients with NYHA functional class IV due to the limited amount of data in this population.
- Chronic heart failure patients with intraventricular conduction defects (bundle branch block left, bundle branch block right) and ventricular dyssynchrony should be monitored closely.
- AF is more common in patients using amiodarone or potent class I anti-arrhythmic concomitantly.
- Potassium-depleting diuretics: hypokalaemia increases the risk of arrhythmia. Ivabradine may cause bradycardia, the combination of hypokalaemia and bradycardia is a predisposing factor to the onset of severe arrhythmias. Concomitant use with caution.

Side Effects

In clinical trials the most frequently reported adverse events were visual symptoms and bradycardia.

Luminous phenomena (phosphenes) described as a transient enhanced brightness in a limited area of the visual field, were reported by 14.5% of patients. These are usually triggered by sudden variations in light intensity. Patients should be warned of this effect, particularly with regard to driving at night. Cessation of treatment should be considered if any unexpected deterioration in visual function occurs
Other possible side effects are AV 1st degree block (ECG prolonged PQ interval), ventricular extra systoles, headache, dizziness and uncontrolled BP.

This is not an exhaustive list of side effects, cautions, contra-indications or interactions please refer to the BNF or Summary of Product Characteristics for more information.

Midlands and Lancashire Commissioning Support Unit,
Jubilee House, Lancashire Business Park, Leyland, PR26 6TR
Tel: 01772 644 400 | www.midlandsandlancashirecsu.nhs.uk

Version 2.1
Date: May 2018
Review Date: May 2021