East Lancashire Health Economy Medicines Management Board
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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.**

Treatment of angina in patients in normal sinus rhythm

Adult 18–74 years

Initially 2.5–5 mg twice daily for 3–4 weeks, then increased if necessary up to 7.5 mg twice daily, dose to be increased gradually; reduced if not tolerated to 2.5–5 mg twice daily, heart rate at rest should not be allowed to fall below 50 beats per minute, discontinue treatment if no improvement in symptoms within 3 months.

Adult 75 years and over

Initially 2.5 mg twice daily for 3–4 weeks, then increased if necessary up to 7.5 mg twice daily, dose to be increased gradually; reduced if not tolerated to 2.5–5 mg twice daily, heart rate at rest should not be allowed to fall below 50 beats per minute, discontinue treatment if no improvement in symptoms within 3 months.

Mild to severe chronic heart failure

Adult 18–74 years

Initially 5 mg twice daily for 2 weeks, then increased if necessary to 7.5 mg twice daily; reduced if not tolerated to 2.5–5 mg twice daily, heart rate at rest should not be allowed to fall below 50 beats per minute.

Adult 75 years and over

Initially 2.5 mg twice daily for 2 weeks, then increased if necessary up to 7.5 mg twice daily, dose to be increased gradually; reduced if not tolerated to 2.5–5 mg twice daily, heart rate at rest should not be allowed to fall below 50 beats per minute.

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

Acute myocardial infarction; cardiogenic shock; congenital QT syndrome; do not initiate for angina if heart rate below 70 beats per minute; do not initiate for chronic heart failure if heart rate below 75 beats per minute; immediately after cerebrovascular accident; patients dependent on pacemaker; second- and third-degree heart block; severe hypotension; sick-sinus syndrome; sino-atrial block; unstable angina; unstable or acute heart failure.

Cautions for Use

Atrial fibrillation or other arrhythmias (treatment ineffective); elderly; in angina, consider stopping if there is no or limited symptom improvement after 3 months; intraventricular conduction defects; mild to moderate hypotension (avoid if severe); retinitis pigmentosa.

Side Effects

Common or very common:
Arrhythmias; atrioventricular block; dizziness; headache; hypertension; vision disorders

Uncommon:
Abdominal pain; angioedema; constipation; diarrhoea; eosinophilia; hyperuricaemia; hypotension; muscle cramps; nausea; QT interval prolongation; skin reactions; syncope; vertigo

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.

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