This policy statement is approved by Halton, Knowsley, Liverpool, South Sefton, Southport and Formby, St Helens, Warrington, West Lancashire, and Wirral CCGs

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PAN MERSEY APC

PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
REF: PS142 FINAL
ORIGINAL APC BOARD DATE: 12 MAR 2013
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NHS Pan Mersey Area Prescribing Committee

IVABRADINE (Procoralan®) for the treatment of chronic heart failure

AMBER

Ivabradine has been approved by NICE (TA 267)[1] as an option for treating chronic heart failure following specialist initiation in patients with chronic, stable heart failure (NYHA class II-IV), left ventricular systolic dysfunction (LVEF 35% or less) and who are in sinus rhythm with a heart rate of 75 beats per minute or more.

FOLLOWING SPECIALIST INITIATION

The Pan Mersey Area Prescribing Committee recommends the prescribing of ivabradine, following specialist initiation, for the treatment of chronic, stable heart failure (NYHA class II-IV) with LV systolic dysfunction (LVEF 35% or less) in patients who are in sinus rhythm with a heart rate of 75 beats per minute or more, in combination with standard therapy (including beta-blockers, angiotensin-converting enzyme (ACE) inhibitors and aldosterone antagonists) or when a beta-blocker is contraindicated or not tolerated, in accordance with NICE TA 267[1].

Ivabradine should be initiated by a heart failure specialist, which includes consultant cardiologist and specialist heart failure nurse prescriber with access to a multidisciplinary heart failure team. Dose titration and monitoring should be carried out by a heart failure specialist (or a competent designated member of the heart failure team), or in primary care by a GP with a special interest in heart failure or a heart failure specialist nurse.

Ivabradine should only be initiated after a stabilisation period of 4 weeks on optimised (target dose or maximum tolerated dose) standard therapy with ACE inhibitors, beta-blockers and aldosterone antagonists.

Ivabradine is also recommended as a Green drug for the management of patients with chronic stable angina in the Pan Mersey Formulary.

Note: Patients who are not eligible for treatment under this policy may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. If appropriate an exceptional funding request may be required following the usual locally defined process.

SUPPORTING INFORMATION

IVABRADINE (Procoralan®) for the treatment of chronic heart failure

Effectiveness

Ivabradine blocks the I_f channel in the SA node resulting in a reduction in heart rate.

6558 patients (SHIFT study[2]) with symptomatic heart failure and LVEF ≤ 35%, in sinus rhythm with a heart rate of ≥70bpm, on stable background treatment (including beta-blockers if tolerated) were randomised to either ivabradine or placebo. Median follow up was for 22.9 months. The primary endpoint (a composite of CV death or hospitalisation due to worsening HF) occurred in 24% of those taking ivabradine and 29% of those taking placebo (HR 0.82 95% CI 0.75-0.90 p<0.0001). The effect was mainly driven by a reduction in hospitalisation (HR 0.74 95% CI 0.66-0.83 p<0.0001). There was no significant reduction in CV death but death due to HF (a pre-defined secondary endpoint) was significantly reduced (HR 0.74 95% CI 0.58-0.94 p=0.014). In a pre-defined sub-group analysis of baseline heart rate, there was a significant reduction in the primary endpoint in patients with a baseline heart rate of ≥77 bpm (HR 0.75 95% CI 0.67-0.85 p=0.029) but not in patients with a baseline heart rate < 77 bpm. The difference in primary endpoint was maintained irrespective of co-administration of a beta-blocker. The study authors reported a NNT of 26 patients treated for 1 year to prevent 1 CV death or 1 hospital admission.

Safety[3]

In the SHIFT study[2], ivabradine resulted in significantly more symptomatic bradycardia (5% vs 1% p<0.0001), asymptomatic bradycardia (6% vs 1% p<0.0001) and phosphenes (3% vs 1% p<0.0001) (phosphenes are a transient enhanced brightness in a restricted area of the visual field).

Other commonly reported side effects (incidence ≥ 1/100 to < 1/10) include headache (especially in the first month of treatment) and blurred vision.

The safety and efficacy of ivabradine in the treatment of chronic heart failure in children aged below 18 years has not been established.

Ivabradine is contraindicated in combination with strong cytochrome p450 3A4 enzyme inhibitors such as azole antifungals (ketoconazole and itraconazole), macrolide antibiotics (clarithromycin and erythromycin), HIV protease inhibitors (nelfinavir and ritanovir) and nefazodone; severe hepatic insufficiency, unstable or acute HF and unstable angina.

Consult SPC for more details http://www.medicines.org.uk/

Cost per patient per year[4]

Ivabradine 2.5mg-7.5mg bd	£262-£524
Bisoprolol 1.25mg-10mg od	£8.86-£11.73
Carvedilol 3.125mg-50mg bd	£19.03-£52.14
Ramipril 1.25mg-10mg od	£13.03-£17.34
Spironolactone 25mg-50mg od	£14.34-£57.09
Eplerenone 25mg-50mg od	£58.79-£76.65

The estimated local need for ivabradine treatment is likely to be around 10 per 100,000 of the population.

Patient Factors[3]

Side effects, especially bradycardia, are more common in elderly patients (over 75 years). A lower starting dose (2.5mg bd) should be considered in elderly patients.

Caution is required when combining ivabradine with drugs known to prolong QT interval (e.g. amiodarone, sotalol, citalopram), since QT prolongation may be exacerbated by a reduction in heart rate, and in severe renal impairment (CrCl<15ml/min).

PRESCRIBING[3] AND IMPLEMENTATION INFORMATION

The recommended starting dose of ivabradine for the treatment of chronic HF is 5mg bd. After 2 weeks of treatment, the dose can be increased to 7.5mg bd if the resting heart rate is persistently above 60 bpm or decreased to 2.5mg bd if the resting heart rate is persistently below 50 bpm or if symptoms related to bradycardia occur (dizziness, fatigue or hypotension). If the heart rate is 50-60 bpm the dose of 5mg bd should be maintained.

If during treatment the heart rate is persistently below 50 bpm or there are symptoms of bradycardia, the dose should be titrated downwards to the next lowest dose (in patients taking 7.5mg or 5mg bd). Ivabradine should be discontinued if bradycardia or symptoms persist. If the heart rate is persistently above 60 bpm the dose can be titrated upwards to the next upper dose in patients receiving 2.5mg or 5mg bd.

Ivabradine should be initiated by a heart failure specialist with access to a multidisciplinary heart failure team. Locally it has been agreed that initiation could be by a consultant cardiologist or a heart failure specialist nurse prescriber who is supported by a consultant cardiologist. Dose titration and monitoring should be carried out by a heart failure specialist (or a competent designated member of the heart failure team), or in primary care by a GP with a special interest in heart failure or a heart failure specialist nurse.

Ivabradine should only be initiated after a stabilisation period of 4 weeks on optimised (target dose or maximum tolerated dose) standard therapy with ACE inhibitors, beta-blockers and aldosterone antagonists.

REFERENCES

1. NICE TA 267. Ivabradine for treating chronic heart failure. November 2012
2. Swedberg K, Komajda M, Bohm M et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. Lancet 2010; 376: 875-85
3. Summary of Product Characteristics (SPC) for ivabradine (Procoralan®). www.medicines.org.uk. Accessed 09.01.18
4. NHS Electronic Drug Tariff Jan 2018. Available at http://www.ppa.org.uk/ppa/edt_intro.htm. Accessed 09.01.18