BC's HEART FAILURE NETWORK
Quality care for quality life.

Cardiac Services BC
An agency of the Provincial Health Services Authority

Initiation, Titration and Monitoring Recommendations for Ivabradine (LANCORA™) Usage in British Columbia

Patient must meet all the British Columbia eligibility criteria prior to initiating ivabradine

Do NOT use ivabradine as a first line medication for heart failure. Ivabradine should be used in addition to maximally tolerated doses of guideline directed HF therapies, including ACE-I/ARB/ARNI, Beta Blocker and MRA
Ivabradine requires careful monitoring and titration.
Initiation of this medication should only be undertaken by physicians or nurse practitioners experienced in the treatment of HF

Prescribing tips

Patient MUST be in sinus rhythm to initiate ivabradine
Ivabradine is NOT to be used as a first line treatment for heart failure
Ivabradine is as an ***add on*** medication for patients already receiving maximally tolerated doses of guideline directed heart failure therapy for a minimum of three months, with:

- ✓ Heart rate ≥ 70 BPM identified by 12 lead ECG or 24 hour holter monitor
- ✓ NYHA II-III functional status
- ✓ LVEF ≤ 35% (preferably measured within the last year)

- The dose of ivabradine should be titrated to keep HR > 50 bpm (will add HR guidance narrative to inform the titration document)
- Start ivabradine at the lowest dose in patients ≥ 75years of age (e.g. 2.5mg po BID).
- Instruct patients they cannot drink grapefruit juice.
- If patient develops atrial fibrillation then ivabradine should be discontinued
- Patients starting on ivabradine should be cautioned to report any visual disturbances (luminous phosphenes)

Prescribing CAUTIONS:

- Should **not be** prescribed to patients:
  - With a heart rate < 70 BPM, or blood pressure less than 90/50 mmHg
  - In permanent or persistent atrial fibrillation/flutter
  - With severe hepatic or renal dysfunction (Child-Pugh Class C or eGFR < 15ml/min)
  - With recent MI (< 2 months) or stroke/ TIA (< 4 weeks)
  - With acute heart failure (cardiogenic shock)
  - Who are pacemaker dependent, have sick sinus syndrome or long QT interval
  - Who are taking medications that lengthen the QT interval
  - With sino-atrial or third degree atrioventricular heart block
  - Who are pregnant or breast feeding
  - Using medications that are **strong** CYP450 3A4 **inhibitors** (azole antifungals such as ketoconazole, macrolide antibiotics such as clarithromycin, azithromycin, HIV protease inhibitors such as nelfinavir, ritonavir and certain antidepressant medications such as nefazodone).
- Should be prescribed **with caution** to patients who are taking:
  - **Moderate** cytochrome P450 3A4 **inhibitors** (azole antifungals such as fluconazole, estrogen blockers such as tamoxifen, immunosuppressants such as cyclosporine etc.) – may consider starting at lowest dose of 2.5mg po BID with careful monitoring of heart rate.
  - QT prolonging agents eg. Antidepressants, antiarrhythmic, fluoroquinolones etc.
  - Cytochrome P450 3A4 **inducers** (e.g antidepressant medications such as St. John's Wort , antiepileptic medications such as phenytoin, barbiturates and antibiotic medications such as rifampin) - may require higher doses of ivabradine with appropriate HR monitoring.

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Ordering Ivabradine (Lancora™)

Ivabradine Dose **Must take with food**
2.5mg (1/2 of the 5mg tablet) orally TWICE daily
5mg ONE tab orally TWICE daily
7.5mg ONE tab orally TWICE daily

Titration Algorithm

Assess

- ☐ Eligibility Checklist Completed
- ☐ Patient on guideline directed triple therapy at optimally tolerated dose
  - if not, titrate to optimally tolerated dose and reassess eligibility for ivabradine in 3 months

Initiate

Initiate ivabradine: at 5mg twice a day if patient has stable HF and heart rate >or equal to 70 bpm (HR assessed by 12 lead ECG or 24 hr holter monitor)
Initiate ivabradine: at 2.5mg (1/2 of 5mg tab) twice a day if patient is on drugs inhibiting the moderate CYP3A4 enzyme, patients with arrhythmias or geriatric patients aged 75 years or above

Titrate

In 2 weeks after initiation adjust dose based on HR verified by 12 lead ECG
Titrate dose to HR- the maximum dose is 7.5 mg twice daily

Heart Rate	Dose adjustment
>60 bpm	Increase dose by 2.5mg twice daily (maximum dose 7.5mg twice daily)
50-60 bpm	Maintain dose
< 50 bpm or signs and symptoms of bradycardia (eg. dizziness, fatigue, hypotension)	Decrease dose by 2.5mg twice daily: if current dose is 2.5mg twice daily, discontinue therapy

Monitor

Blood Pressure & Heart Rate
2 weeks after initiation, after each dose increase and with each practitioner visit do a 12 lead ECG (to ensure patient is in sinus rhythm and to check QT interval)
Consider assessment of LV Function only if it will alter treatment or if otherwise clinically indicated
If change in rhythm is suspected confirm sinus rhythm with 12 lead ECG

Reassess

Consider decreasing or stopping ivabradine

- **Symptomatic** hypotension (< 95 mmHg)
- HR < 50 bpm **or symptomatic bradycardia**