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 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 > 75 years 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.
Ordering Ivabradine (Lancora™)

<table>
<thead>
<tr>
<th>Ivabradine Dose</th>
<th>Must take with food</th>
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<tbody>
<tr>
<td>2.5mg (1/2 of the 5mg tablet)</td>
<td>orally TWICE daily</td>
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<tr>
<td>5mg ONE tab</td>
<td>orally TWICE daily</td>
</tr>
<tr>
<td>7.5mg ONE tab</td>
<td>orally TWICE daily</td>
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</tbody>
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**Titration Algorithm**

- 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** 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

In 2 weeks after initiation adjust dose based on HR verified by 12 lead ECG

**Tritrate dose to HR** - the maximum dose is 7.5 mg twice daily

<table>
<thead>
<tr>
<th>Heart Rate</th>
<th>Dose adjustment</th>
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<tbody>
<tr>
<td>&gt;60 bpm</td>
<td>Increase dose by 2.5mg twice daily (maximum dose 7.5mg twice daily)</td>
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<tr>
<td>50-60 bpm</td>
<td>Maintain dose</td>
</tr>
<tr>
<td>&lt; 50 bpm or signs and symptoms of bradycardia (eg. dizziness, fatigue, hypotension)</td>
<td>Decrease dose by 2.5mg twice daily: if current dose is 2.5mg twice daily, discontinue therapy</td>
</tr>
</tbody>
</table>

**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

Consider decreasing or stopping ivabradine

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