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

Cardiac Services BC
An agency of the Provincial Health Services Authority

IVABRADINE (LANCORA ™) for Heart Failure
Summary & Practical Tips

Ivabradine belongs to a class of medication called hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers.

Mechanism of action:
Ivabradine acts on the I_f or funny channel current, which is located in the sinoatrial (SA) node. It inhibits the pacemaker I_f current, in a dose-dependent manner by blocking the cardiac pacemaker channel activity, slowing the heart rate but without loss of contractility.

SHIFT Trial:

In this trial ivabradine reduced the risk of cardiovascular death by 18% and hospital admission by 26% among patients with chronic heart failure (HF), NYHA Class II-IV symptoms, left ventricular ejection fraction of ≤ 35% and heart rate 70 BPM or greater , despite maximally tolerated guideline directed HF therapies. The effects were mainly driven by decreased hospital admissions for worsening heart failure compared to placebo.

N**umber needed to treat (NNT) with ivabradine** to prevent cardiovascular death or HF hospitalization was 26 patients over an average of 22 months**.**

The relative risk reduction (RRR) for cardiovascular death or heart failure hospitalization was 18% with an absolute risk reduction (ARR) of 4.2% when a patient was treated for an average of 22 months.

Cost- $2.50 per day= $75 per month- not currently covered by Fair PharmaCare BC (need to confirm cost as it varies depending on dose)

Indications for Usage

Canadian Cardiovascular Society HF 2014 Guidelines companion document - https://www.ccs.ca/images/Guidelines/Companion_Resources/CCS_Guidelines_eng.pdf

GPAC- Guidelines – http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/heart-failure-chronic

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
- 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 QTc 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).

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- 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.