Nonformulary Criteria: Ranolazine (Ranexa®)
VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel

The following recommendations are based on current medical evidence. The content of the document is dynamic and will be revised as new clinical data become available. The purpose of this document is to assist practitioners in clinical decision making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The clinician should utilize this guidance and interpret it in the clinical context of the individual patient situation.

Ranolazine is an anti-anginal agent that was FDA approved in January 2006 for treatment of patients with chronic stable angina. Because ranolazine prolongs the QT interval, it should be reserved for patients who have NOT received an adequate response with other antianginal drugs. It should be used in combination with beta-blockers, nitrates and dihydropyridine (e.g. felodipine, amlodipine or long-acting forms of nifedipine) calcium channel blockers. (For details, refer to the monograph at www.pbm.va.gov or http://vaww.pbm.va.gov)

EXCLUSION CRITERIA (If one is selected, patient is not eligible)

- Pre-existing QT interval prolongation (Normal QTc < 440 milliseconds [ms])
- Mild, moderate or severe hepatic impairment [Child-Pugh Classes A (mild), B (moderate), or C (severe)].
- Receiving QT prolonging drugs (e.g. Class Ia [quinidine] or Class III [amiodarone, dofetilide, sotalol] antiarrhythmics, erythromycin and some antipsychotic agents [thioridazine, ziprasidone]) (list is not comprehensive).
- Receiving potent or moderately potent CYP 3A4 inhibiting products/agents, including azole antifungals, amiodarone, macrolide antibiotics, HIV protease inhibitors, grapefruit juice, diltiazem and verapamil (list is not comprehensive).

INCLUSION CRITERIA (Both must be selected to be eligible)

- Anginal episodes an average of 3 or more times per week despite maximal or maximally tolerated anti-anginal drug therapy (Defined as treatment with a beta-blocker, long-acting dihydropyridine calcium channel blocker and a long-acting nitrate).
- A VA healthcare provider is actively involved in the monitoring and management of ranolazine therapy and will re-assess ranolazine's therapeutic effectiveness and safety within 12 weeks after initiation of therapy.

PRECAUTIONS

- Ranolazine can prolong the QT interval in a dose-dependent manner. The mean increase (QTc) seen with 1000 mg twice daily was 6 milliseconds.
- Repeat dosing of ranolazine in patients with severe renal impairment (CrCl <30 ml/min, not on dialysis) was associated with an increase in diastolic BP of 15 mm Hg.
- Drug-Drug interactions: Carefully review medications for possible drug-drug interactions prior to initiating ranolazine (Ranolazine is both an inhibitor of and a substrate for CYP 3A4 and P-glycoprotein and to a lesser extent CYP 2D6). Dose adjustment of the object drug or avoidance of ranolazine may be recommended.

DOSAGE AND ADMINISTRATION

- 500 mg twice daily. Dose can be increased to a maximum of 1000 mg twice daily but dose escalation has not consistently been shown to improve symptoms. Adverse events with ranolazine are dose-related.

RECOMMENDED MONITORING

- Baseline and follow-up electrocardiograms (ECG) are recommended to examine the effect of ranolazine on the QT interval.

RENEWAL CRITERIA (Both must be selected for renewal)

Both the therapeutic effectiveness and the safety of ranolazine should be assessed within the first 12 weeks of ranolazine therapy:

- An improvement in anginal symptoms and/or a reduction in sublingual nitroglycerin consumption is documented in the medical record (while receiving ranolazine).
- QTc interval on follow up ECG (while receiving ranolazine) has not increased >30% above baseline and/or is not >500 ms.