Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: Beta-Blockers
-August 2014-

Background:
The National Pharmacy and Therapeutics Committee (NPTC) reviewed the beta-blocker class to provide guidance in helping determine when beta blockers are indicated for a multitude of disease states. The disease states reviewed include chronic stable angina, HTN, congestive heart failure (CHF), recent myocardial infarction, atrial arrhythmias, migraine headaches, bleeding esophageal varices. Of particular note, consensus among current hypertensive guidelines advocate for the second-line use of beta-blockers in hypertension (HTN).

Discussion:
-**Hypertension (HTN)**:
Beta blockers were one of the primary agents first used to treat HTN. In 2003, the JNC 7 recommended beta blockers as a first line agent to treat elevated HTN. The 2006 British National Institute for Health and Clinical Excellence (NICE) was the first to report that beta blockers should not be recommended as initial therapy and utilized only in younger individuals, patients with increased adrenergic participation, women of childbearing potential and patients unable to take ACE inhibitors. A 2007 Cochrane Review found that initiating treatment of HTN with beta blockers lead to modest reductions in cardiovascular disease and no significant effects on mortality. The review also showed the effects of beta blockers are inferior to other antihypertensive drugs. Currently, the JNC 8 recommends beta blockers be used as second-line treatment of HTN, citing beta blockers resulted in a higher rate of cardiovascular death, myocardial infarction or stroke compared to use of an ARB.

***-**Chronic Stable Angina (CSA):*
Numerous beta blockers have an FDA indication for CSA. National guidelines recommend beta blockers may be considered as chronic therapy for all other patients with coronary or other vascular disease (recommendation: Class IIB; level of evidence: C). Head to head studies with other beta blockers showed no difference in attack frequency or exercise tolerance. Beta blockers have been standard of care for patients with coronary artery disease and post myocardial infarction however studies are old and advances in reperfusion have led clinicians to question how long beta blockers should be continued once patients are stable.

-Congestive Heart Failure (CHF):
Beta blockers have long been recommended as first line agents in the treat of patients with left ventricular dysfunction or CHF with reduced ejection fraction. Their use is proven to provide patients with reductions in mortality, sudden death, cardiovascular deaths and death due to CHF. The majority of studies showing benefits are in patients with reduced ejection fraction or post myocardial infarction. The American College of Cardiology/American Heart Association (ACC/AHA) 2013 Heart Failure Guidelines recommend beta blockers (bisoprolol, carvedilol, and metoprolol succinate) for all patients with current or prior symptoms of CHF with reduced ejection fraction, unless contraindicated, to reduce morbidity and mortality.

-Recent Myocardial Infarction (MI):
Beta blockers have been proven to reduce total mortality, sudden death and reinfarction in patients with acute MI. Metoprolol, carvedilol, timolol, and propranolol have shown evidence for utilization during and after patients have suffered a MI. The ACC/AHA Guideline for the Management of ST-Elevation Myocardial Infarction (STEMI) recommends beta blockers be initiated within the first 24 hours, during, and continued after the STEMI admission. In addition, the ACC/AHA recommends patients who have an initial contraindication for a beta blocker by re-evaluated to determine eligibility for a beta blocker. The reduction in total mortality, sudden death and reinfarction were observed in patients studied up to three years.

-Atrial arrhythmia:
Beta blockers reduce incidence of and relapse of atrial arrhythmias/fibrillation as well as reduce heart rate in patients with atrial arrhythmias. In one study, metoprolol succinate was effective in preventing relapse into atrial fibrillation or atrial flutter after patients were cardioverted. A systematic review evaluating beta blockers in prevention of atrial fibrillation (AF) onset in CHF patients showed that beta blockers significantly reduced the incidence of AF onset from 39 to 28 per 1000 patient years. The 2014 ACC/AHA/Heart Rhythm Society Guideline

for the management of AF recommends beta blockers (Class I recommendation) for patients with paroxysmal, persistent or permanent AF.

-Migraine headache:
Beta blockers are utilized to reduce migraine attack frequency and severity. Older head-to-head studies showed no difference in the reduction of attack, frequency or severity between beta blockers however they did show positive outcomes when compared to placebo. The 2012 American Headache Society/American Academy of Neurology Guidelines for Prevention of Episodic Migraine recommends atenolol, propranolol, or timolol for migraine prevention.

-Bleeding esophageal varices:
Currently, no beta blockers have an FDA indication for treatment of esophageal varices. The Portal Hypertension Collaborative Report studied how effective beta blockers (timolol vs. placebo) were at preventing gastroesophageal varices in patients with cirrhosis. No significant differences in the rates of ascites, encephalopathy, liver transplantation or death were seen and there were increased adverse effects with timolol. This study showed that nonselective beta-blockers are ineffective in preventing varices in patients with cirrhosis and portal hypertension. Practice Guidelines from the American Association for the Study of Liver Disease recommend the prevention and management of gastroesophageal varices and variceal hemorrhage in patients with cirrhosis. In patients with cirrhosis who do not have varices, nonselective beta blockers cannot be recommended to prevent their development. In patients with medium/large varices that have not bled but have a high risk of hemorrhage, beta blockers are recommended. In patients with cirrhosis and small varices that have not bled, long-term benefit has not been established.

Findings:
Beta blockers can be an effective medication when used appropriately. Given the number of conditions and current indications for beta blocker use, paralleled with current IHS usage data which indicated wide utilization (particularly propranolol), the NPTC voted to add propranolol to the National Core Formulary. The following recommendations are based upon the above findings and articles cited in the reference section.

1. **Hypertension:**
    a. **No longer recommended as first-line treatment in guidelines.**
2. Chronic stable angina:
    a. May be considered in certain patients.
3. Heart Failure:
    a. Utilize one of the three beta blockers (carvedilol, metoprolol succinate or bisoprolol) in patients with left ventricular dysfunction.
4. Atrial arrhythmias:
    a. Utilize in select patients and use agents recommended by national guidelines (metoprolol tartrate, metoprolol succinate).
5. Migraine headache:
    a. Utilize one of the recommended agents for prevention of migraines (metoprolol tartrate, propranolol, timolol).
6. Bleeding esophageal varices
    a. Consider in certain patients.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

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