Indiana Medicaid Therapeutics Committee
Therapeutic Class Review Summary

Therapeutic class:
Beta-blockers

Overview:
In general, all non-selective beta-blockers compete with catecholamines for binding at $beta_1$- and $beta_2$-receptor sites. However, selective beta-blockers bind to $beta_1$-receptor sites at normal doses, but only bind to $beta_2$-receptor sites at high doses. Blockage of $beta_1$-receptors results in decreased heart rate, cardiac output, and systolic and diastolic blood pressure. Alternatively, blockage of $beta_2$-receptors may induce bronchospasms. Other concerns associated with beta-receptor blockage include hypotension, bradycardia, masking of hypoglycemic effects, and thyrotoxicosis. Penbutalol is the only beta-blocker included in this review that is not available as a generic.

All beta-blockers are indicated for hypertension. Some are also indicated for angina, myocardial infarction, treatment of left ventricular dysfunction following myocardial infarction, migraines, and cardiac arrhythmias. Recent studies, such as Packer et al., evaluated carvedilol versus placebo in heart failure patients. The results showed that carvedilol, a nonselective alpha-beta blocker with antioxidant properties, reduced the rate of death in heart failure patients. Another study, MERIT-HF showed that metoprolol succinate (Toprol XL), a cardioselective beta-blocker, was beneficial for heart failure patients over placebo. The majority of the current data is limited to the comparison of carvedilol or metoprolol succinate with placebo. Until recently, the head-to-head studies comparing carvedilol and metoprolol were small-scale and yielded inconclusive results to determine a superior agent. However, at the recent European Society of Cardiology's Heart Failure 2003 meeting, results of the Carvedilol or Metoprolol European Trial (COMET) were released. COMET was a double-blind, randomized, parallel group study design that compared the effects of carvedilol or metoprolol tartrate (metoprolol tartrate does not have an indication for CHF) on the risk of death or hospitalizations in patients with congestive heart failure. COMET is the largest and longest study in CHF and the first head-to-head survival study comparing two beta-blocker agents. Results showed that patients with CHF treated with the non-selective alpha-beta blocker, carvedilol, had a significant survival benefit ($p = 0.0017$) as compared to those treated with metoprolol, a $beta_1$-selective agent.

Generic Name	Brand Name	Manufacturer	Generic
Carteolol	Cartrol® (PRODUCT DISCONTINUED)	Abbott Laboratories	N
Carvedilol	Coreg®, Coreg CR™	GlaxoSmithKline	Y
Labetalol	Trandate® (BRAND PRODUCT NORMODYNE DISCONTINUED)	Schering Corp., Promethius	Y
Nadolol	Corgard®	Monarch Pharm Inc.	Y
Penbutolol	Levatol®	Schwarz Pharma Inc.	N
Pindolol	Visken®	Novartis	Y
Propranolol	Inderal®, Inderal® LA InnoPran XL™	Wyeth, Reliant Pharmaceuticals	Y
Sotalol	Betapace®, Betapace AF®	Berlex	Y
Timolol	Blocadren® (BRAND PRODUCT DISCONTINUED)	Merck and Co	Y
Acebutolol	Sectral®	ESP Pharma	Y
Atenolol	Tenormin®	AstraZeneca	Y
Betaxolol	Kerlone®	Sanofi-Synthelabo	Y
Bisoprolol	Zebeta®	Duramed	Y

fumarate			
Metoprolol tartrate	Lopressor®	Novartis	Y
Metoprolol succinate	Toprol XL®	AstraZeneca	Y

Summary:
Overall, the beta-blockers appear to have similar efficacy in the treatment of hypertension. Some agents are also indicated for angina (propranolol, nadolol, atenolol, and metoprolol), arrhythmias (propranolol, sotalol and acebutolol), myocardial infarction (propranolol, timolol, atenolol, and metoprolol), treatment of left ventricular dysfunction following a myocardial infarction (carvedilol) and migraine (propranolol and timolol). The preferred drug list should be based upon FDA indications and generic availability.

*Note: Esmolol, injectables and ophthalmic preparations were not discussed in this review.