




ATC codes: C07AB07

Indication	Cardiac arrhythmia <span style="background-color: #00a651; color: white; padding: 2px;">ICD11 code: BC8Z</span>
INN	Bisoprolol
Medicine type	Chemical agent
List type	Core
Formulations	Oral > Solid: 1.25 mg ; 5 mg
EML status history	First added in 2011 (TRS 965)
Sex	All
Age	Adolescents and adults
Therapeutic alternatives	metoprolol (ATC codes: C07AB02) carvedilol (ATC codes: C07AG02)
Patent information	Patents have expired in most jurisdictions Read more <a href="#">about patents.</a> 
Wikipedia	<a href="#">Bisoprolol</a> 
DrugBank	<a href="#">Bisoprolol</a> 

### Summary of evidence and Expert Committee recommendations

An application was prepared by Pharmacy Students: Sandeep Kishore, Maryam Shafae, Mathew Price, and Rajesh Vedanthan, and Marcus Reidenberg, Professor of Pharmacology, Medicine and Public Health, New York, for the addition of bisoprolol with a square box to the Model List, replacing atenolol as the representative medicine of the class in Sections 12.1 to 12.3, and the inclusion of beta-blockers as a therapeutic class in Section 14.4 (Medicines used in heart failure). Listing is requested as a representative of its therapeutic class. The Committee noted that heart failure is an important global health issue and its prevalence is increasing worldwide due to both communicable and noncommunicable causes. Recent guidelines from the National Institute of Clinical Excellence (NICE), United Kingdom, and Heart Failure Society of America (HSFA) recommend beta-blockers for the treatment of heart failure and specifically cite metoprolol, bisoprolol, and carvedilol (1, 2). The Committee considered evidence from 3 RCTs (3-5) to support the efficacy and safety of the beta-blockers bisoprolol, metoprolol, and carvedilol in the treatment of heart failure, as well as 3 meta-analyses that found a reduction of 29% to 34% in the composite end-point of mortality or hospital admission with beta-blocker therapy in patients with heart failure (6-8). Mortality benefits have been shown in diverse patient groups, including the elderly (9), patients with diabetes (5) and without (10), patients with an ejection fraction above or below 25% (11) and patients not receiving rennin-angiotensin inhibitors (12); additionally bisoprolol can be used in patients with chronic obstructive pulmonary disease (13). The Committee noted that there is no high-quality evidence to support the use of atenolol for the treatment of heart failure. The Committee noted that there is evidence from clinical trials to support the efficacy and safety of bisoprolol for the treatment of angina (14, 15) arrhythmias (3, 16-18), and hypertension (19-21). The Committee also took into consideration a meta-analysis (22) (5 studies, n=17671, follow-up 4.6 years) that suggested older hypertensive patients treated with atenolol have a significantly higher mortality when compared to patients treated with other classes of cardiovascular medicines. Cardiovascular mortality was also higher in the atenolol treated group than with other antihypertensive treatment, and strokes were more frequent with atenolol treatment. The Committee noted that on a cost per dose basis bisoprolol was cheaper than metoprolol and carvedilol. The Committee concluded that there was sufficient evidence of efficacy and safety compared to atenolol to support the request for bisoprolol to become the representative beta-blocker in sections 12.1 to 12.3 and also recommended,

based on evidence of efficacy, safety, and cost-effectiveness, that bisoprolol should be added to the Model List for the treatment of heart failure. Due to the similarities between bisoprolol and metoprolol in terms of efficacy, the Committee decided to add bisoprolol with a square box for this indication. It was noted that country programmes could choose between bisoprolol, metoprolol, or carvedilol, but that there were increasingly reasons not to select atenolol as the sole beta-blocker provided. References: 1. Chronic heart failure: management of chronic heart failure in adults in primary and secondary care. Full guidelines. London, National Institute for Health and Clinical Excellence, 2010 (<http://www.nice.org.uk/CG108>, accessed 21 September 2011). 2. HFSA. Heart Failure Society of America 2010 comprehensive heart failure practice guideline. *Journal of Cardiac Failure*, 2010, 16(6):e1-194. 3. CIBIS II investigators and committees. The cardiac insufficiency bisoprolol study II (CIBIS II): a randomised trial. *The Lancet*, 1999, 353:9-13. 4. MERIT-HF Study Group. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL randomised intervention trial in congestive heart failure (MERIT-HF). *The Lancet*, 1999, 353:2001-2009. 5. Eichhorn EJ, Bristow MR. Commentary: the carvedilol prospective randomized cumulative survival (COPERNICUS) trial. *Current Controlled Trials in Cardiovascular Medicine*, 2001, 2:20-23. 6. Funck-Brentano C. Beta-blockade in CHF: from contraindication to indication. *European Heart Journal Supplements*, 2006, 8(Suppl. C):C19-C27. 7. Bangalore S et al. Cardiovascular protecting using beta-blockers: a critical review of the evidence. *Journal of the American College of Cardiology*, 2007, 50:563-572. 8. Shibata MC et al. Systematic review of the impact of beta-blockers on mortality and hospital admissions in heart failure. *European Journal of Heart Failure*, 2001, 3(3):351-357. 9. Dulin BR et al. Do elderly systolic heart failure patients benefit from beta-blockers to the same extent as the non-elderly? Meta-analysis of 12,000 patients in large-scale clinical trials. *American Journal of Cardiology*, 2005, 95:896-898. 10. Haas SJ et al. Are beta-blockers as efficacious in patients with diabetes mellitus as in patients without diabetes mellitus who have chronic heart failure? A meta-analysis of large-scale clinical trials. *American Heart Journal*, 2003, 146:848-853. 11. Bouzamondo A et al. Beta-blocker benefit according to severity of heart failure. *European Journal of Heart Failure*, 2003, 5:281-289. 12. Krum H et al. Prognostic benefit of beta-blockers in patients not receiving ACE-inhibitors. *European Heart Journal*, 2005, 26:2154-2158. 13. Salpeter SS et al. Cardioselective beta-blockers for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*, 2005, (4):CD003566. 14. Gibbons RJ et al. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina. *Journal of the American College of Cardiology*, 2003, 41:159-168. 15. Weber F et al. Prognostic implications of autonomic function assessed by analyses of catecholamines and heart rate variability in stable angina pectoris. *European Heart Journal*, 1999, 20:38-50. 16. Konishi M et al. Comparative effects of carvedilol vs bisoprolol for severe congestive heart failure. *Circulation Journal*, 2010, 74(6):1127-1134. 17. Ishiguro H et al. Antiarrhythmic effect of bisoprolol, a highly selective  $\beta_1$ -blocker in patients with paroxysmal atrial fibrillation. *International Heart Journal*, 2008, 49(3):281-293. 18. Plewan A et al. Maintenance of sinus rhythm after electrical cardioversion of persistent atrial fibrillation: sotalol vs bisoprolol. *European Heart Journal*, 2001, 22(16):1504-1510. 19. Hiltunen TP et al. Predictors of antihypertensive drug responses: initial data from a placebo-controlled, randomized, cross-over study with four antihypertensive drugs (The GENRES Study). *American Journal of Hypertension*, 2007, 20(3):311-318. 20. Neutel JM et al. Application of ambulatory blood pressure monitoring in differentiating between antihypertensive agents. *American Journal of Medicine*, 1993, 94:181-187. 21. Deary AJ et al. Double blind, placebo controlled crossover comparison of five classes of antihypertensive drugs. *Journal of Hypertension*, 2002, 20:771-777. 22. Carlberg B et al. Atenolol in hypertension: is it a wise choice? *The Lancet*, 2004, 364(9446): 1684-1689.

