



Therapeutic Class ReviewSM

Cardiovascular Agents: isosorbide dinitrate / hydralazine (BiDil[®])

November 2005

New Product for Review:

isosorbide dinitrate / hydralazine (BiDil[®]) [NitroMed, Inc.]

Dossier Provided by Manufacturer: Yes

Quality of Dossier: 2

- 1 – Low quality (dossier w/ missing component)
- 2 – Medium quality (all components, except pharmacoeconomic model)
- 3 – High quality (all components, well done)

Executive Summary

- There is possibly useful evidence that addition of isosorbide dinitrate/hydralazine (BiDil) to standard treatment in self-identified black patients with heart failure may increase survival and decrease time to first hospitalization.
- There is not sufficient evidence to conclude isosorbide dinitrate / hydralazine (BiDil) provides superior health outcomes in comparison to currently available forms of isosorbide dinitrate and hydralazine on the Regence preferred medication list/formulary.
- The cost of BiDil is significantly greater than the combined cost of its two generically available components.

Decision

Maintain non-preferred/non-formulary status for isosorbide dinitrate/hydralazine (BiDil) because there is no evidence that BiDil provides superior health outcomes in comparison to the two generically available components.

Products ^[1, 2]

Drug Product	Date of FDA Approval	FDA Approved Indication(s)	Oral Dose	Potential Off-Label Use(s)
isosorbide dinitrate/ hydralazine (BiDil [®])	6/2005	Adjunct to standard therapy in self-identified black patients to improve survival, to prolong time to hospitalization for heart failure, and to improve patient-reported functional status.	Two possible dosing regimens: 1 tablet TID → 2 tablets TID →	
hydralazine (Apresoline [®])	1/1982	Essential hypertension, alone or in combination with other agents.	Two possible dosing regimens: 1 tablet (50mg) TID → 2 tablets (100mg) TID →	Afterload reduction in the treatment of congestive heart failure (CHF), severe aortic insufficiency, and after valve replacement.
isosorbide dinitrate (Isordil [®])	7/1988	Prophylaxis and long-term management of recurrent angina prior to events likely to provoke an attack.	Two possible dosing regimens: 1 tablet TID → 2 tablets TID →	Reduce cardiac workload in patients with acute MI and in CHF.

References

1. BiDil[®] (isosorbide dinitrate 20mg/hydralazine HCL 37.5mg) Product Information. Lexington, MA: NitroMed, Inc., 2005.
2. Thomson Micromedex © 1974-2005. Micromedex Healthcare Series, Vol 120.
3. National Institute for Clinical Excellence (NICE) Chronic heart failure: Management of chronic heart failure in adults in primary and secondary care. Clinical Guideline 5 July 2003. Available at: <http://www.nice.org.uk/pdf/CG5NICEguideline.pdf>. Accessed on August 17, 2005.
4. American College of Cardiology and the American Heart Association Task Force on Practice Guidelines 2001: Guidelines for the evaluation and management of chronic heart failure in the adult; Stages of heart failure and recommended therapy http://www.acc.org/clinical/guidelines/failure/hr_index.htm. Accessed on August 17, 2005.
5. Taylor AL, Ziesche S, Yancy C, Carson P, D'Agostin R, Ferdinand K, et al. Combination of Isosorbide Dinitrate and Hydralazine in Blacks with Heart Failure. NEJM. 2004 Nov;351(20):2049-2057.