

FIRST TIME GENERIC APPROVAL

Brand Name	BiDil®
Generic Name	isosorbide dinitrate and hydralazine hydrochloride
Drug Manufacturer	Wilshire Pharmaceuticals

New Drug Approval

TYPE OF CLINICAL UPDATE

First Time Generic

FDA APPROVAL DATE

January 13, 2021

LAUNCH DATE

April 14, 2022

REVIEW DESIGNATION

Standard

TYPE OF REVIEW

New Drug Application (NDA): 020727; Type 4 - New Combination

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION FOR USE

Isosorbide dinitrate and hydralazine hydrochloride tablets are a combination of isosorbide dinitrate, a nitrate vasodilator, and hydralazine hydrochloride, an arteriolar vasodilator, indicated for:

- The treatment of heart failure as an adjunct therapy to standard therapy in self-identified black patients to improve survival, prolong time to hospitalization for heart failure and to improve patient-reported functional status

MECHANISMS OF ACTION

The mechanism of action underlying the beneficial effects of isosorbide dinitrate and hydralazine hydrochloride tablets in the treatment of heart failure has not been established.

Isosorbide dinitrate is a vasodilator affecting both arteries and veins. Its dilator properties result from the release of nitric oxide and the subsequent activation of guanylyl cyclase, and ultimate relaxation of vascular smooth muscle.

Several well-controlled clinical trials have used exercise testing to assess the anti-anginal efficacy of chronically delivered nitrates. In the large majority of these trials, active agents were no more effective than placebo after 24 hours (or less) of continuous therapy. Attempts to overcome nitrate tolerance by dose escalation, even to doses

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far in excess of those used acutely, have consistently failed. Only after nitrates have been absent from the body for several hours is response to nitrates restored.

Hydralazine hydrochloride is a selective dilator of arterial smooth muscle. Animal data suggests that hydralazine may also mitigate tolerance to nitrates.

DOSE FORM AND STRENGTH

Tablets (scored): 20 mg isosorbide dinitrate and 37.5 mg hydralazine hydrochloride.

DOSE & ADMINISTRATION

One tablet three times a day titrated to a maximum tolerated dose up to two tablets three times a day, Dosage may be decreased to as little as one-half tablet three times a day if intolerable side effects occur.