ISOSORBIDE DINITRATE TABLETS, USP
Revised: 11/21/2021

DESCRIPTION
Isosorbide dinitrate, an organic nitrate (or nitro compound), acts by relaxing smooth muscle and consequent dilatation of peripheral arteries and veins, especially the coronary arteries. The principal pharmacological action of isosorbide dinitrate is relaxation of vascular smooth muscle and consequent dilatation of peripheral arteries and veins, especially the coronary arteries. The principal pharmacological action of isosorbide dinitrate is relaxation of vascular smooth muscle and consequent dilatation of peripheral arteries and veins, especially the coronary arteries. The principal pharmacological action of isosorbide dinitrate is relaxation of vascular smooth muscle and consequent dilatation of peripheral arteries and veins, especially the coronary arteries. The principal pharmacological action of isosorbide dinitrate is relaxation of vascular smooth muscle and consequent dilatation of peripheral arteries and veins, especially the coronary arteries.

Isosorbide dinitrate is a white, crystalline, odorless compound which is stable in air and in solution, has a melting point of 70°C and has an optical rotation of +13.6° (α1.0, 20°C). Isosorbide dinitrate is freely soluble in organic solvents such as acetone, alcohol, ether, but is only sparingly soluble in water. Isosorbide dinitrate is freely soluble in organic solvents such as acetone, alcohol, ether, but is only sparingly soluble in water. Isosorbide dinitrate is freely soluble in organic solvents such as acetone, alcohol, ether, but is only sparingly soluble in water. Isosorbide dinitrate is freely soluble in organic solvents such as acetone, alcohol, ether, but is only sparingly soluble in water.

Pharmacokinetics
Absorption of isosorbide dinitrate after oral dosing is nearly complete, but bioavailability is highly variable (10% to 90%), with extensive first-pass metabolism in the liver. Serum levels reach their maxima about an hour after ingestion. The average bioavailability of isosorbide dinitrate is about 25%; most studies have observed progressive increases in bioavailability with long-term dosing. Only after nitrates have been absent from the body for several hours has their anti-anginal efficacy been restored. Pharmacokinetics
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Drug Interactions
The vasodilating effects of isosorbide dinitrate may be additive with those of other vaso-
dilators. Alcohol, in particular, has been found to exhibit additive effects of this variety. Concurrent use of isosorbide dinitrate with phosphodiesterase inhibitors in any form is contraindicated (see CONTRAINDICATIONS).

Concomitant use of isosorbide dinitrate with nicotine, a soluble guanylate cyclase stimula-
tor, is contraindicated (see CONTRAINDICATIONS).

Carcinogenesis, Mutagenesis, Impairment of Fertility
No long-term studies in animals have been performed to evaluate the carcinogenic potential of isosorbide dinitrate. In a modified two-tumor reproduction study, there was no remarkable gross pathology and no altered fertility or gestation among rats fed isosorbide dinitrate at 25 or 100 mg/kg/day.

Pregnancy Category C
At total doses 15 and 100 times the maximum recommended human daily dose, isosorbide dinitrate has been shown to cause a dose-related increase in embryonic/fetal mortality (increase in mummified pups) in rabbits. There are no adequate, well-controlled studies in pregnant women. Isosorbide dinitrate should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether isosorbide dinitrate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when isosorbide dinitrate is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
Clinical studies of isosorbide dinitrate did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of other concomitant disease or other drug therapy. ADVERSE REACTIONS

Adverse reactions to isosorbide dinitrate are generally dose-related, and almost all of these reactions are the result of isosorbide dinitrate’s activity as a vasodilator. Headache, which may be severe, is the most commonly reported side effect. Headache may be recurrent with each daily dose, especially at higher doses. Tremendous episodes of light-headedness, dizziness, and faintness may occur, especially when arising from a recumbent position. These effects may be more frequent and more intense in patients with a history of convulsions, cerebrovascular accidents, and congestive heart failure or who are hydropic; or patients with renal disease or congestive heart failure. Therapy with isosorbide dinitrate must provide a daily dose-free interval to minimize the development of this tolerance. With immediate-release isosorbide dinitrate, it appears that one daily dose-free interval must be at least 14 hours long. As also noted under CLINICAL PHARMACOLOGY, the effects of the second and later doses have been smaller and shorter-lasting than the effects of the first.

Large controlled studies with other nitrates suggest that no dosing regimen with isosorbide dinitrate tablets should be expected to provide more than about 12 hours of continuous anti-anginal efficacy per day.

DOSAGE AND ADMINISTRATION
Biological half-life of isosorbide dinitrate is about 4 hours. When isosorbide dinitrate per hour), the average methemoglobin level measured was 0.2%; this equated, in total administered dose of nitrate ions, to 4.8 to 6.9 mg of bioavailable isosorbide dinitrate per hour). The average methemoglobin level measured was 0.2%; this equated, in total administered dose of nitrate ions, to 4.8 to 6.9 mg of bioavailable isosorbide dinitrate per hour). The average methemoglobin level measured was 0.2%; this equated, in total administered dose of nitrate ions, to 4.8 to 6.9 mg of bioavailable isosorbide dinitrate per hour). The average methemoglobin level measured was 0.2%; this equated, in total administered dose of nitrate ions, to 4.8 to 6.9 mg of bioavailable isosorbide dinitrate per hour).

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