



Isosorbide Mononitrate (ISMN) Shortage

Suppliers of isosorbide mononitrate (ISMN) extended-release tablets in Canada^{1,2}

DIN	Brand Name	Manufacturer
02272830	APO-ISMN 60 mg	APX
02301288	pms-ISMN 60 mg	PMS
02126559	Imdur® 60 mg (Discontinued July 2024)	JNO

Indication for ISMN extended-release tablets³

- Prevention of anginal attacks in patients with chronic stable angina pectoris associated with coronary artery disease. ISMN is not intended for the immediate relief of acute attacks of angina pectoris.

Note: when switching drug treatment for stable ischemic heart disease (angina pectoris), *ensure that patients have rescue nitroglycerin (sublingual spray or sublingual tablets) with them at all times.* The agents discussed below are NOT indicated or appropriate for the treatment of immediate relief of acute symptoms of angina.

Alternatives for ISMN

Long-acting nitrates, beta blockers, and calcium channel blockers (CCBs) can all be considered for angina prophylaxis in uncomplicated patients as monotherapy or combinations.^{4,5} Consider using a beta blocker or CCB instead of a nitrate product to avoid risk of tolerance. If symptoms are not controlled after switching nitrate products, consider adding a beta blocker or CCB.

Nitrates

- Nitrates improve symptoms of angina by improving oxygen supply via vasodilation.⁵
 - All nitrates are equally effective at symptom relief⁴; they do not prevent cardiovascular events.⁵
- Fast-acting nitrates (sublingual nitroglycerin spray or tablets) are used to relieve anginal attacks, whereas long-acting nitrates (ISMN, ISDN, nitroglycerin transdermal patch) are used to prevent anginal attacks.⁶
- Headache, flushing, and hypotension are common adverse effects.^{4,7}
- Nitrate-free periods of 10 to 12 hours per day are necessary to prevent tolerance/tachyphylaxis.^{4,6,8}

Isosorbide dinitrate (ISDN) Tablets

- The active metabolite of ISDN is ISMN.⁸
- ISMN is formulated as an extended-release (ER) tablet whereas ISDN is an immediate-release oral tablet and pharmacokinetics differ:
 - Onset: 30 minutes (ISDN) vs. <4 hours (ISMN ER)⁴
 - Duration of action: 5 hours (ISDN) vs. 12 hours (ISMN ER)⁴
- Usual maintenance doses^{4,6}:
 - ISDN: 10-40 mg TID
 - ISMN ER: 60-240 mg once daily in the morning
- Little information is available regarding direct switches from ISMN to ISDN. Note that bioavailability of ISDN is variable (10-90%)⁹ compared to 100% for ISMN.^{10,11} Consider starting ISDN at the same daily dose in three divided doses.
 - Titrate dose of ISDN as needed according to angina symptoms or adverse effects.
 - Administer ISDN tablets three times daily, including a nitrate-free period of 10-14 hours (e.g., doses at 8 a.m., 12 p.m., and 5 p.m.).⁴

Nitroglycerin Transdermal Patches

- Initial dose is 0.2 mg/hr.^{4,6,12}
- Usual maintenance dose is 0.2 mg/hr to 0.8 mg/hr.^{4,6,12}
- Each day, apply a patch for 12 to 14 hours during the time when symptoms are more frequent (usually the day). Remove the patch to maintain a 10- to 12-hour nitrate-free period.^{4,6}

Non-Nitrate Therapies

- Both dihydropyridine (DHP) CCBs (amlodipine, felodipine, long-acting nifedipine) and non-DHP CCBs (diltiazem, verapamil) can be considered; however, patients with low heart rate, taking beta blockers, and/or with heart failure should use DHP CCBs.⁴
- Ensure close monitoring of heart rate and blood pressure if combinations are used.
- See [RxFiles Angina](#)⁴ and [CPS Stable Angina](#)¹² for details about these agents.

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