

Diltiazem Shortages

In light of the recent diltiazem shortages, many patients' regimens will require modification. One can consider switching diltiazem formulations; patients can be changed to modified-release formulations at the same total daily dose as the regular formulation.¹ In some patients, the dosage of the modified-release formulation may require adjustment.¹ Therefore, when switching to any other diltiazem formulation, the starting point should be the same daily dose with adjustments made as required.

Diltiazem products on the Saskatchewan Drug Plan formulary:²

Diltiazem CD (various manufacturers) 120 mg, 180 mg, 240 mg, 300 mg
Diltiazem ER capsule = Tiazac 120 mg, 180 mg, 240 mg, 300 mg, 360 mg
Diltiazem ER tablet = Tiazac XC 120 mg, 180 mg, 240 mg, 300 mg, 360 mg
Diltiazem immediate release tablet – 30, 60 (**Not** indicated for hypertension)

Alternative CCBs According to Indication:

Other CCBs indicated for **hypertension** include verapamil, amlodipine, felodipine and nifedipine XL Dosing.^{1,3}

Diltiazem (for reference)

CD: Initial 120-240 mg once daily; Usual 240-360 mg once daily; Max 420 mg daily*
Tiazac: Initial 120-240 mg once daily; Usual 120-360 mg once daily; Max 420 mg daily*
Tiazac XC: Initial 120-240 mg HS; Usual 240 – 360 mg HS; Max 420 mg daily*

*360 mg maximum daily dose recommended by manufacturers; doses up to 540 mg daily have been used in some trials, though 420 mg is recommended by JNC 7 as the usual maximum dose.⁴

Verapamil:

IR: Initial 40-80 mg TID; Usual 80 -120 mg TID; Max 480 mg / day, though additional benefit with daily doses > 360 mg has not been established.⁵
SR: Initial 120 - 180 mg/day; Usual 180-360 mg daily; Max 480 mg/ day. Administer doses in two divided dose if daily dose ≥ 360 mg

Amlodipine:

Initial 2.5 - 5 mg once daily; Usual 5-10 mg once daily; Max 10 mg once daily

Felodipine:

Initial 2.5 – 5 mg once daily; Usual 5-10 mg once daily; Max 20 mg once daily*

*Manufacturer recommends 10 mg daily as maximum dose; JNC 7 suggests dose can be increased to 20 mg daily if required and tolerated.⁴

Nifedipine XL:

Initial 30 mg once daily; Usual 30- 60 mg once daily; Max 90 mg once daily*

*Manufacturer recommends 90 mg daily as maximum; JNC 7 suggests 60 mg daily be considered maximum daily dose and if greater antihypertensive effect is required, add a different agent because of reduced tolerance to higher nifedipine XL doses.⁴

For **stable angina**, amlodipine, nifedipine, and verapamil IR are indicated. IR diltiazem and IR nifedipine not recommended for monotherapy. Doses:

Diltiazem:¹

CD: Initial 120-180 mg once daily; Usual 240 – 360 mg once daily; Max 360 mg once daily

Tiazac: Initial 120-180 mg daily; Max 360 mg daily

Tiazac XC: Initial 180 mg daily; Max 360 mg daily

IR: (in combination therapy): Initial 30 mg QID; Usual 240 mg/day in 3-4 divided doses; Max 360 mg/day in 3-4 equally divided doses

Verapamil:¹

IR: Initial 80 mg TID-QID; Usual 120 mg TID–QID; Max 480 mg/day, divided
(Isoptin SR does not have indication for stable angina)

Amlodipine:¹

Initial 2.5 - 5 mg once daily; Usual 5-10 mg once daily; Max: 10 mg once daily

Nifedipine:^{1,3}

Initial 30 mg/day Max: 90 mg/ day (dosed once daily)

For **coronary artery spasm**, only IR formulations of diltiazem, nifedipine and verapamil are indicated.³
Doses same as for stable angina.⁴

For **control of heart rate in patients with supraventricular tachycardia**, diltiazem is an alternative.
Doses:⁵

Verapamil (IR or SR)

Initial 120 mg / day; Max 480 mg/ day (either as IR divided TID-QID or SR divided OD or BID)

Diltiazem (CD, Tiazac, Tiazac XC)

180- 540 mg once daily

Notes:

This would be a good time to assess if other agents may serve the hypertensive patient better (any new comorbidities since starting diltiazem treatment?).

Verapamil and diltiazem lower heart rate and reduce blood pressure, whereas the dihydropyridine CCBs (nifedipine, felodipine, amlodipine) exert their effects primarily by arteriolar dilatation.⁶

In stable angina, titrate the dose of diltiazem and verapamil to achieve a resting heart rate between 50 and 60 beats per minute (BPM) and an exercise heart rate that does not exceed 100 to 110 BPM. IR CCBs are not recommended as monotherapy for stable angina. The dose of dihydropyridines (e.g. amlodipine, nifedipine) should be titrated to achieve maximum symptom relief with minimal adverse effects.⁶

When switching products, BP should be monitored and nitrates should be on hand if the indication is stable angina.

Keep in mind diltiazem and verapamil are inhibitors of 3A4. All CCBs are substrates of 3A4. Additionally, verapamil is also a substrate of CYP1A2, 2C9, and 2C19.⁷

References:

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Prepared October 21, 2009
Updated December 7, 2010