



Oral Diltiazem Shortages

Diltiazem products on the Saskatchewan Drug Plan formulary¹

Diltiazem CD capsule 120 mg, 180 mg, 240 mg, 300 mg

Reference product = **Cardizem CD**, various generics (*often* denoted as diltiazem CD)

Release mechanism: encapsulated beads²

Diltiazem ER capsule 120 mg, 180 mg, 240 mg, 300 mg, 360 mg

Reference product = **Tiazac**, various generics (*often* denoted as diltiazem T)

Release mechanism: "drug-paste" is converted into small immediate release beads, which are then coated with a rate-controlling polymer.³

Diltiazem ER tablet 120 mg, 180 mg, 240 mg, 300 mg, 360 mg

Reference product = **Tiazac XC**, currently no generics

Release mechanism: diltiazem beads encased in wax.⁴

Diltiazem immediate release tablet – 30 mg, 60 mg (**Not** indicated for hypertension)

Switching between products

One can consider switching between diltiazem formulations; patients can be changed to modified-release formulations at the same total daily dose as the previous formulation.⁵ In some patients, the dosage of the new formulation may require adjustment.⁵ Therefore, when switching to any diltiazem formulation, the starting point should be the same daily dose with adjustments made as required. The products are not interchangeable;¹ therefore, either authorization from the prescriber or pharmacist prescribing as "Increasing Suitability of Drug Prescribed by a practitioner" is required to switch to a different formula.

Administration Notes

Cardizem CD and Tiazac (and their respective interchangeable generics) can be opened and sprinkled on food.⁶

Tiazac XC is an unscored tablet in which beads are encased in wax. While there is no data on administration of half tablets, splitting the tablet is not expected to damage the integrity of the release mechanism.⁴ The manufacturer suggests tablets only be split for easier administration and not to provide a smaller dose.⁴ Should the tablet be split as a means of providing half the dose, the tablets should only be split one at a time with both halves taken on consecutive days before the next tablet is taken.⁶

Tiazac XC is formulated to provide peak concentration approximately 14 hours after administration and is intended to be administered at bedtime. When switching from Cardizem CD or Tiazac capsules to Tiazac XC, the first dose of Tiazac XC can be taken the same evening of the last morning dose of Cardizem CD or Tiazac (because of its delayed onset).⁷

In the event all diltiazem modified release products are unavailable, therapeutic switching will be required.

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Alternative CCBs According to Indication:

Hypertension

- Other CCBs indicated include verapamil (IR and SR), amlodipine, felodipine, and nifedipine XL.^{5,8}

Dosing^{5,8}

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.⁹

Verapamil:

IR: Initial 40-80 mg TID; Usual 80 -120 mg TID; Max 480 mg/day

SR: Initial 120 - 180 mg/day; Usual 180-360 mg daily; Max 480 mg/day. Administer doses in two divided dose if daily dose \geq 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.⁹

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.⁹

Stable Angina

- Amlodipine, nifedipine (IR and XL), and verapamil (IR) are alternative CCBs indicated.^{5,8} IR diltiazem and IR nifedipine are not recommended for monotherapy.⁵

Dosing:

Diltiazem:⁵

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:⁵

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)

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Amlodipine:⁵

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

Nifedipine:^{5,8}

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

Control of heart rate in patients with supraventricular tachycardia,

- verapamil is an alternative⁵

Dosing:¹⁰

Diltiazem (CD, Tiazac, Tiazac XC)

180- 540 mg once daily

Verapamil (IR or SR)

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

Coronary artery spasm,

- Only IR formulations of diltiazem, nifedipine and verapamil are indicated.⁵
- Doses same as for stable angina.⁹

General 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.¹¹

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.¹¹

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 2C19.¹²

References:

1. Saskatchewan Formulary. Drug Plan and Extended Benefits Branch [homepage on the Internet]. Government of Saskatchewan; [cited 2014 Jul 22]. Available from <http://formulary.drugplan.health.gov.sk.ca/>
2. e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2014 [updated 2011 Feb 2; cited 2014 Jul 22]. Cardizem CD [product monograph]. Available from: <http://www.e-cps.ca>. Also available in paper copy from the publisher.

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3. Written communication. Kozmenko M. Tiazac® (diltiazem HCl) – Improved clinical efficacy vs. diltiazem CD. Biovail Pharmaceuticals Canada. 2005 Feb 15.
4. Written communication. Marino JP. Tiazac® XC (diltiazem HCl) – Splitting of extended-release tablets. Biovail Pharmaceuticals Canada. 2006 Apr 19.
5. e-CPS [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2014 [updated 2011 Sep; cited 2014 Jul 22]. Calcium Channel Blockers [CPhA monograph]. Available from: <http://www.e-cps.ca>. Also available in paper copy from the publisher.
6. PL Detail-Document, Meds That Should Not Be Crushed. Pharmacist's Letter/Prescriber's Letter. July 2012.
7. Written communication. Marino JP. Tiazac® XC (diltiazem HCl) – Dose equivalence with Cardizem® CD. Biovail Pharmaceuticals Canada. 2006 Apr 3.
8. Regier L, Jensen B. Calcium Channel Blocker (CCB): Comparison Chart. RxFiles drug comparison charts. 9th ed. Saskatoon, SK: Saskatoon Health Region; 2013. p. 5. Available from: www.RxFiles.ca. Accessed 2014 Jul 22.
9. AHFS Drug Information BOOK ONLINE. Jackson, WY, Teton Data Systems, 2014: Based on: McEvoy GK, editor. AHFS Drug Information®. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2014. Accessed 2014 Jul 22
10. Birnie D, Nery P. Supraventricular Tachycardia. In: Gray Jean, editor. e-Therapeutics+ [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2010 [updated Nov 2010; cited 2010 Dec 7]. Available from: <http://www.e-therapeutics.ca>. Also available in paper copy from the publisher.
11. Devereaux PJ. Stable Angina In: Gray Jean, editor. e-Therapeutics+ [Internet]. Ottawa (ON): Canadian Pharmacists Association; c2010 [updated Jan 2009; cited 2010 Dec 7]. Available from: <http://www.e-therapeutics.ca>. Also available in paper copy from the publisher.
12. Comparison of calcium channel blockers. Pharmacist's Letter/Prescriber's Letter 2009;25(5):250525.

Prepared October 21, 2009
Last Partial Update September 16, 2014