

## Verapamil Shortages

Slow-release (SR) verapamil tablets in all strengths have been shorted. One can consider switching from the SR product to the immediate release (IR) tablets at the same total daily dose (or closest possible).<sup>1</sup> Depending on the indication of the verapamil, choosing another calcium channel blocker (CCB) may be preferred to avoid multiple daily doses. In all cases, patients will need to be monitored and doses adjusted as required.

Should the verapamil 240 mg SR tablet become available, the modified release properties will still be maintained if it is cut in half.<sup>2</sup>

Verapamil products on the Saskatchewan Drug Plan Formulary:<sup>3</sup>

Verapamil SR tablet (various manufacturers): 120 mg, 180 mg, 240 mg

Verapamil IR tablet (various manufacturers): 80 mg, 120 mg

### **Alternative CCBs According to Indication:**

Other CCBs indicated for **hypertension** include amlodipine, diltiazem (CD, Tiazac reg, Tiazac XC), felodipine, nifedipine (XL). Dosing:<sup>1,4,5</sup>

#### Verapamil (for reference):

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.<sup>5</sup>

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

#### Diltiazem

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.<sup>5</sup>

#### 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.<sup>5</sup>

#### 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.<sup>5</sup>

For **stable angina**, amlodipine, diltiazem and nifedipine XL are indicated. IR diltiazem and IR nifedipine not recommended for monotherapy. Note: Isoptin SR does not have indication for stable angina. Doses:

Verapamil:<sup>1</sup>

IR: Initial 80 mg TID-QID; Usual 120 mg TID-QID; Max 480 mg/day, divided

Amlodipine:<sup>1</sup>

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

Diltiazem:<sup>1</sup>

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

Nifedipine:<sup>1,4</sup>

XL: Initial 30 mg once daily; Usual 30-60 mg once daily; Max: 90 mg once daily

IR (in combination therapy): Initial 5-10 mg TID; Usual 10-20 mg TID; Max 120 mg / day

For **coronary artery spasm**, only IR formulations of diltiazem, nifedipine and verapamil are indicated.<sup>4</sup> Doses same as for stable angina.<sup>5</sup>

For **control of heart rate in patients with supraventricular tachycardia**, diltiazem is an alternative. Doses:<sup>6</sup>

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.<sup>7</sup>

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.<sup>7</sup>

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.<sup>8</sup>

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