


**CALCIUM CHANNEL BLOCKER (CCB): Comparison Chart** <sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15</sup>

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Generic Pregnancy Rating TRADE Rating (Dosage & form) ↓	ONSET; & DURATION of effect	SA NODE AUTO- MATICITY	AV NODE CON- DUCTION	Periph. Vascular Resistance	HEART RATE	CONTRAC- TILITY	CARDIAC OUTPUT	APPROVED INDICATIONS	COMMENTS	INITIAL & (MAX Dose)	USUAL DOSE RANGE	\$COST/ MONTH 
<b>Amlodipine</b> [C] NORVASC 5 <sup>s</sup> & 10mg tab	~6 hr; 24 hr	↔	↔	↓↓↓	↔	↔/↑	↑	✓HTN (2.5-10mg od <sup>ALLHAT</sup> ) ✓Stable Angina (ALT systolic Dysfx <sup>CND 2003</sup> )	<b>DI</b> : grapefruit juice ↓dose in hepatic dysfx •??preferred CCB in non-ischemic HF	2.5-5mg OD (10mg OD)	2.5mg po OD 5mg po OD 10mg OD <sup>VALUE 16</sup>	30 53 75
<b>Felodipine</b> [C] RENEDIL,PLENDIL 2.5, 5 & 10mg tab ext. release	2-6 hr; 24 hr	↔	↔	↓↓↓	↔/↑	↔/↑	↑	✓HTN (ALT systolic Dysfx <sup>CND 2003</sup> )	<b>DI</b> : grapefruit juice (↑ absorption >2X) •do not chew or crush •safe in heart failure	2.5-5mg OD (20mg OD)	5mg po OD 10mg po OD <sup>HOT</sup> 15mg po OD	31 42 78
<b>Nifedipine</b> [C] ADALAT/GENERIC  REG 5, 10mg cap PA 10, 20mg tab XL 20, 30, 60mg tab	<20 min; 6 hr <60 min; 12 hr 2 hr; 24 hr	↔	↔	↓↓↓	↔/↑	↔/↓	↑↑	✓HTN (PA & XL forms) ✓Stable Angina (Reg. & XL) ✓Coronary Artery Spasm (Reg. caps) • (Reg. caps <b>NOT</b> recom- mended for acute BP reduction due to assoc. of ↑ MI & stroke)	<b>DI</b> : grapefruit juice <b>SE</b> : reflex tachycardia with short acting forms; more headache •avoid in CHD & HF (negative inotrope)	5mg TID 10mg PA BID 30mg XL OD (120mg/d)	10mg po TID 10mg PA po BID 20mg PA po BID 30mg XL po OD 60mg XL po OD 90mg XL po OD	27 24 35 42 62 112
<b>Diltiazem</b> [C] CARDIZEM/GENERIC  REG. 30, 60 <sup>s</sup> mg tab SR 60, 90, 120mg cap CD 120, 180, 240, 300mg cap TIAZAC 120,180,240, 300,360mg cap  Vial- 50mg/10ml *	<30min; 4-8 hr <60min; 12 hr <60min; 24 hr  <60min; 24hr  3-7min; 1-3hr	↓	↓	↓	↓	↓	↔/↑	✓HTN (SR & CD & Tiazac forms) ✓Stable Angina (All dosage forms; initial titration with reg. tabs recommended) ✓Coronary Artery Spasm (Reg. tabs)  •CD or Tiazac caps: can sprinkle contents but do not chew/crush -not interchangeable.	<b>DI</b> : ↑cyclosporine & carbamazepine levels; simvastatin(↑myopathy). <b>SE</b> : heart failure, AV block & headache • Tiazac: macrocap bead technology with similar cost as CD • AVOID in CHD & HF (negative inotrope)	30mg TID 60mg SR BID 120mg CD/TiazacOD (420- 540mg/d)	30mg po TID 60mg po TID 120mg SR po BID 120mg CD po OD 120mg CD po OD 240mg CD po OD 300mg CD po OD 120mg Tiazac OD 240mg Tiazac OD	25 38 59 36 58 70 36 58
<b>Verapamil</b> [C] ISOPTIN/GENERIC REG ISOPTIN SR tab REG 80, 120mg tab SR 120, 180 <sup>s</sup> , 240 <sup>s</sup> mg tablet CHRONOVERA (CV) (Controlled Onset Extended Release) 180, 240mg tablet  Vial 5mg/2ml *	<30min; ~8 hr <30min; 24 hr  4-5hr post ingestion;11 hr post ingestion  1-5min; 30min	↓↓	↓↓	↓↓	↓	↓↓	↓/↑	✓HTN (Reg. & SR) ✓Stable Angina & Coronary Artery Spasm (Reg Tabs) ✓Atrial Fib ✓SV arrhythmias ✓Cardiomyopathy: obstructive hypertrophic	<b>DI</b> amiodarone;↑ alcohol effect; ↑ digoxin <sup>-70%</sup> ; cyclosporin & carbamazepine levels; grapefruit juice; rifampin; simvastatin <sup>↑ myopathy</sup> & terazosin <b>SE</b> : heart failure, AV block, constipation •SR tabs may be halved •AVOID in CHD & HF (negative inotrope)	40-80mg TID 120mg SR OD (480mg/d)	80mg po TID 120mg po BID  120mg SR po OD 180mg SR po OD 240mg SR po OD  CV: 180mg po HS CV: 240mg po HS	31 37  32 30 31  36 39

☐=scored tablet ⚡=EDS status in Sask. ALT=alternate CD=controlled delivery CHD=coronary heart disease COST=markup & dispensing fee **DI**=drug interaction HF=heart failure HTN=hypertension **SE**=side effect SR=sustained release

\* IV diltiazem & IV verapamil indicated for atrial fibrillation/flutter & paroxysmal supraventricular tachycardia.

Pregnancy [C] rating =possible fetal risk

**Drug Class:** **Dihydropyridine** - amlodipine, felodipine, nicardipine, nifedipine, nimodipine (relatively: **more peripheral vasodilation**, less effect on heart). **Benzothiazepine** - diltiazem. **Phenylalkylamine** - verapamil (relatively: **more negative chronotropic** effect on heart, less on peripheral vasodilation).

**Dosage adjustments:** every 2-4 weeks in HTN (HTN dose often higher than anti-anginal dose.) **Combination** with ACE inhibitors & diuretics reasonable; Dihydropyridines (e.g. nifedipine) may be given with a beta blocker to prevent reflex tachycardia; however use PRECAUTION as possible negative inotropic effects. Generally neutral effect on lipids & glucose tolerance.

**Side Effects (General):** dizziness, headache, edema, flushing, rash, gingival hyperplasia; constipation esp. with verapamil; dyspnea & pulmonary edema in pts. with LV dysfunction, may worsen HF.

**Grapefruit juice** can inhibit metabolism via the cytochrome-P-450 system (CYP 3A4) resulting in significant increases in drug levels, especially with **felodipine**.

**ROLE:** 1<sup>ST</sup> LINE: Long acting dihydropyridines for **Uncomplicated HTN, Isolated Systolic HTN & Left Ventricular Hypertrophy.**

Long acting Calcium Channel Blockers: **Preferred** in vasospastic angina pt's; **Alternate** in diabetics & angina. Non-dihydropyridines (diltiazem & verapamil) useful for atrial fibrillation & SVT's.

**Other Uses:** blacks, esophageal disorders, ↓ migraines (flunarizine **SIBELIUM**), ↓ panic attacks, **Raynaud's phenomenon** (dihydropyridines), thyrotoxicosis, tardive dyskinesia & Tourette's Sx.

**Contraindications:** severe hypotension (SBP<90), recent MI with pulmonary edema, sick sinus syndrome or 2<sup>nd</sup> or 3<sup>rd</sup> degree AV block ; & if Systolic dysfx or CHF **avoid** diltiazem & verapamil.

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- <sup>1</sup> Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (**ALLHAT**). The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. JAMA. 2002;288:2981-2997.
- <sup>2</sup> 2001 Canadian Hypertension Recommendations: What's New & What's Not so New but is Still Important. CJHP 2002;55:4651.
- <sup>3</sup> FA McAlister, M Levine, KB Zarnke, et al. The 2000 recommendations for the management of hypertension. Can J Cardiol 2001; 17(5):543-559.
- <sup>4</sup> 1999 Canadian recommendations for the management of hypertension. CMAJ 1999;161(Suppl):S1-S16.
- <sup>5</sup> **1999 World Health Organization**—International Society of Hypertension Guidelines:Management of Hypertension. J Hypertens 1999;17:151-183.
- <sup>6</sup> 6<sup>th</sup> Report-Joint National Committee on Prevention, Detection, Evaluation & Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413-46.
- <sup>7</sup> Drugs for hypertension. Med Lett Drugs Ther 2001;43:17-22.
- <sup>8</sup> Drugs in Pregnancy & Lactation, 6<sup>th</sup> Ed. Briggs GE, et al. Wilkins; Baltimore, MD.
- <sup>9</sup> Micromedex 2004 →/hcs.micromedex.com.
- <sup>10</sup> Hansten & Horn's Drug Interactions: Analysis & Management-Facts & Comparisons 2004.
- <sup>11</sup> **Treatment Guidelines: Drugs for Hypertension** from The Medical Letter Feb **2003**.
- <sup>12</sup> The **2004 Canadian** Hypertension Education Program **Recommendations** [www.chs.md](http://www.chs.md)
- <sup>13</sup> ALLHAT Working Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (**ALLHAT**). JAMA 2000;283:1967-75.
- <sup>14</sup> The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (The **JNC 7**); JAMA. **2003** May;289(19):2560-72.
- <sup>15</sup> Black HR, Elliott WJ, Grandits G, Grambsch P, Lucente T, White WB, Neaton JD, Grimm RH Jr, Hansson L, Lacourciere Y, Muller J, Sleight P, Weber MA, Williams G, Wittes J, Zanchetti A, Anders RJ. Principal results of the Controlled Onset Verapamil Investigation of Cardiovascular End Points (**CONVINCE**) trial. JAMA. 2003 Apr 23-30;289(16):2073-82.
- <sup>16</sup> Julius S, Kjeldsen SE, Weber M, Brunner HR, Ekman S, Hansson L, Hua T, Laragh J, McInnes GT, Mitchell L, Plat F, Schork A, Smith B, Zanchetti A; VALUE trial group. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the **VALUE** randomised trial. Lancet. 2004 Jun 19;363(9426):2022-31.