



November 2022 ~ Resource #381108

Comparison of Calcium Channel Blockers

Calcium channel blockers (CCBs) are divided into two classes: the non-dihydropyridines (diltiazem [e.g., *Cardizem*] and verapamil [e.g., *Calan*]) and the dihydropyridines (all CCBs except verapamil and diltiazem). The terminology used, especially for long-acting products (e.g., ER, CD, CR, XL), is not standardized and can create confusion when trying to determine which products can be substituted for one another. In the US, pharmacists can consult to FDA's Orange Book for help identifying therapeutic equivalence.

Drug	Indication and ADULT Dose ^b	Comments/Clinical Pearls ^b		
DIHYDROPYRIDINES : Mechanism of action involves coronary and peripheral arteriolar vasodilation. ¹ This can lead to reflex tachycardia, headache, flushing, and peripheral edema. ¹ The dihydropyridines can impair myocardial contractility to varying degreess. ¹ Dihydropyridines are				
CYP3A4 substrates. ²				
Once-a-day (24 hour) Dihydropyridines				
Amlodipine (<i>Norvasc</i> , generics); also see footnote a	HTN, CAD: initial 5 mg QD (2.5 mg QD for small, frail, elderly [US], or liver impairment); max 10 mg QD.	 Longest-acting CCB.¹ Causes less tachycardia.³ Has the most HTN outcomes data.³ Safe choice if a CCB is needed in a patient with HFrEF.¹ Oral suspension (<i>Katerzia</i> [US]) and oral solution (<i>Norliqva</i> [US]; pdp-amlodipine [Canada]) available. 		
Levamlodipine (Conjupri) (US)	• HTN: initial 2.5 mg QD (1.25 mg QD for small, frail, elderly, or liver impairment); max 5 mg QD.	• Levamlodipine is the active isomer of amlodipine.		
Felodipine ER (<i>Plendil</i> [brand discontinued in US], generics)	HTN: initial 5 mg QD (Canada: 2.5 mg QD for elderly or liver impairment); max 10 mg QD.	 Swallow whole. Do not crush or chew. Give on an empty stomach or with a light meal. Safe choice if a CCB is needed in a patient with HFrEF.¹ 		
Nifedipine ER (Adalat XL [Canada], Adalat CC [US; brand discontinued], generics [US Orange Book code AB1])	 HTN: initial 30 mg QD (Canada: 20 to 30 mg QD); doses >90 mg NOT recommended. Chronic stable angina (Canada): initial 30 mg QD; doses >90 mg not recommended. 	 Take on an empty stomach (US). Swallow whole. Do no crush or chew. Empty nonabsorbable shell may appear in stool (Canada). Acceptable safety profile in pregnancy.⁴ 		

Drug	Indication and ADULT Doseb	Comments/Clinical Pearls ^b		
Once-a-Day (24 hour) Dihydro	pyridines, continued			
Nifedipine ER (<i>Procardia XL</i> [US], generics [US orange Book code AB2])	HTN, vasospastic or chronic stable angina: initial 30 to 60 mg QD; max 120 mg QD. Limited experience with >90 mg for angina.	 Swallow whole. Do not crush or chew. Active drug release from nonabsorbable shell (osmotic release). Patients may notice "ghost" tab in their stool. Acceptable safety profile in pregnancy.⁴ 		
Nisoldipine ER (Sular [US], generics)	HTN: initial 17 mg QD; max 34 mg QD.			
Twice Daily Dihydropyridines				
Isradipine (<i>DynaCirc</i> [US; brand discontinued], generics)	HTN: initial 2.5 mg BID; max daily dose 20 mg (given in divided doses).	Patients may have more side effects with no additional benefit with >10 mg daily.		
Three Times Daily Dihydropyr	idines			
Nicardipine (<i>Cardene</i> [US; brand discontinued], generics)	• HTN, chronic stable angina: initial 20 mg TID; usual 20 to 40 mg TID.	• Start with 20 mg BID in liver insufficiency.		
Nifedipine IR (<i>Procardia</i> [US], <i>Adalat</i> [Canada; brand discontinued], generics)	Vasospastic or chronic stable angina: initial 10 mg TID; usual 10 to 20 mg TID; max 60 mg TID (Canada: max 120 mg/day, divided).	Not to be used to treat acute BP elevation or HTN. Not to be administered within one to two weeks after an MI. Avoid during ACS.		
NON-DIHYDROPYRIDINES: Compared to dihydropyridines, non-dihydropyridines provide relatively less peripheral and coronary arteriolar vasodilation. ¹ They have significant negative inotropic and chronotropic effects, with verapamil having the most pronounced effect. ³ Use with beta-blockers should be avoided. ² Verapamil and diltiazem are among the first-line options for rate control in A-fib. ⁵ Diltiazem and verapamil are CYP3A4 substrates and inhibitors. ² Constipation is common with verapamil. ¹				
Once-a-Day Non-Dihydropyridines				
Diltiazem ER (Cardizem CD [US; brand discontinued in Canada], generics [US Orange Book code AB3])	 HTN: initial 180 to 240 mg QD; usual 240 to 360 mg QD; max 480 mg QD (Canada: max 360 mg QD). Vasospastic or chronic stable angina: initial 120 to 180 mg QD; max 480 mg QD (Canada: max 360 mg QD). 	 Cartia XT (US) is a generic for Cardizem CD. Some patients may respond to a lower dose. 		

Drug	Indication and ADULT Doseb	Comments/Clinical Pearls ^b
Once-a-Day Non-Dihydropyrid	ines, continued	
Diltiazem ER (Cardizem LA [US], generic)	 HTN: initial 180 to 240 mg QD; max 540 mg QD Chronic stable angina: initial 180 mg QD; max 360 mg QD. 	 Matzim LA is the generic for Cardizem LA. Some patients may respond to a lower dose. When switching to Cardizem LA from another diltiazem product, choose the nearest equivalent total daily dose.
Diltiazem ER (<i>Dilacor XR</i> [US; brand discontinued], generics [Orange Book code AB2])	 HTN: initial 180 to 240 mg QD; usual 180 to 480 mg QD; max 540 mg QD. Chronic stable angina: initial 120 mg QD; max 480 mg QD. 	HTN: Patients ≥60 years may respond to lower dose of 120 mg.
Diltiazem ER (<i>Tiazac</i> , generics [US Orange Book code AB4])	 HTN: initial 120 to 240 mg QD (Canada: 180 to 240 mg, some patients may respond to 120 mg QD); max 540 mg QD (Canada: max 360 mg QD). Chronic stable angina: initial 120 to 180 mg QD; max 540 mg QD (Canada: max 360 mg QD). 	 Taztia XT (US) is a generic for Tiazac. US: may administer capsule contents sprinkled on a spoonful of applesauce, followed by a glass of cool water; do not chew.
Diltiazem ER (<i>Tiazac XC</i> [Canada])	 HTN: initial 180 to 240 mg QD; max 360 mg QD. Angina: initial 180 mg QD; max 360 mg QD. 	 Taken at bedtime, peak diltiazem plasma concentrations occur in the early morning hours. Take consistently with or without food. Swallow whole. Do not crush or chew.
Verapamil ER (Verelan [US], generic available)	HTN: 240 mg QD (120 mg QD for small or elderly patients); max 480 mg QD.	May administer capsule contents sprinkled on a spoonful of applesauce, followed by a glass of cool water; do not chew.
Verapamil ER (Verelan PM [US])	HTN: 200 mg HS (100 mg HS for small or elderly patients, or those with kidney or liver impairment); max 400 mg HS.	May administer capsule contents sprinkled on a spoonful of applesauce, followed by a glass of cool water; do not chew. Taken HS, peak effect occurs in morning & early afternoon.
Verapamil ER/Trandolapril (<i>Tarka</i> [US; brand discontinued]; generic	HTN: use as a replacement for individual agents at equivalent doses.	Not for initial therapy.

Drug	Indication and ADULT Doseb	Comments/Clinical Pearls ^b	
Once to Twice-a-Day (12 hour)	Non-Dihydropyridines		
Diltiazem ER (Cardizem SR [US; brand discontinued], generics [Orange Book code AB1])	HTN: initial 60 to 120 mg BID; usual daily dose 240 to 360 mg (divided twice daily).		
Verapamil ER (Calan SR [US], Isoptin SR [Canada], generics)	• HTN: initial 180 mg QD (Canada: 180 to 240 mg QD). Consider 120 mg in small (US) or elderly (Canada: age ≥65 years) patients; max 240 mg Q12 hours.	 Take with food. Do not crush or chew. The scored tablets (Canada: 240 mg only) may be cut in half. 	
Three and Four Times Daily No	on-Dihydropyridines		
Diltiazem IR (<i>Cardizem</i> [brand discontinued in Canada], generics)	Angina (including vasospastic): initial 30 mg QID; max 360 mg (divided TID or QID).	Take before meals and at bedtime. Swallow whole, do not split, crush, or chew.	
Verapamil IR (<i>Isoptin</i> [brand discontinued], generics)	 HTN: initial 80 mg TID; max 160 mg TID. US: no evidence of additional benefit beyond 360 mg. Angina: usual dose 80 to 120 mg TID; max 480 mg/day, divided (US); Canada: initial 80 mg TID to QID; max 120 mg QID. SVT (non-digitalized): 240 to 480 mg/day, divided TID to QID (US); Canada: as for angina. A-fib or A flutter: US: 240 to 320 mg/day, divided TID to QID (with digoxin); Canada: same as for angina, but digoxin dose reduction may be needed. Obstructive hypertrophic cardiomyopathy (Canada): 80 mg to 120 mg TID to QID. Some patients may need 600 to 720 mg/day, divided. 	 Take with food (Canada). For HTN and angina: consider 40 mg TID in patients that are elderly, small, or have hepatic impairment (US). Consider a lower dose in patients ≥65 years of age (Canada). Do not use in severe liver impairment (Canada). 	
Acute Care Calcium Channel Blockers			
Clevidipine (Cleviprex [US])	BP reduction: initial 1 to 2 mg/hour; usual 4 to 6 mg/hour. Usual max dose 16 mg/hour. There is limited short-term experience with doses up to 32 mg/hour.		

Drug	Indication and ADULT Doseb	Comments/Clinical Pearls ^b	
Acute Care Calcium Channel E	Acute Care Calcium Channel Blockers, continued		
Diltiazem injection (Cardizem [brand discontinued], generics)	 A-fib or A flutter: 0.25 mg/kg (20 mg for average size patient) over two min; after 15 min, if needed, give 0.35 mg/kg (25 mg for average size patient); if needed give additional boluses or start continuous infusion of 10 mg/hour (range 5 to 15 mg/hour) for up to 24 hours. SVT: 0.25 mg/kg (20 mg for average size patient) over two min; after 15 min, if needed, give 0.35 mg/kg (25 mg for average size patient); subsequent doses per patient need. 	 Some patients may respond to bolus doses of 0.15 mg/kg, but duration of action may be shorter. Diltiazem exhibits dose-dependent, nonlinear kinetics, and may accumulate with infusion for more than 24 hours. 	
Nicardipine injection (Cardene [US], generics)	HTN: initial 5 mg/hour, max 15 mg/hour. Decrease to 3 mg/hour when goal reached.	• As a substitute for oral nicardipine: 20 mg Q8 hours = 0.5 mg/hour. 30 mg Q8 hours = 1.2 mg/hour. 40 mg Q8 hours = 2.2 mg/hour.	
Nimodipine (<i>Nimotop</i> [brand discontinued in US], generics)	 Subarachnoid hemorrhage: 60 mg Q4 hours for 21 days, starting within 96 hours after the event. Canada: up to 90 mg Q4 hours has been used, but safety is not established. For patients with cirrhosis (Canada: liver impairment), reduce dose to 30 mg Q4 hours. 	 Give at least one hour before or two hours after meals, if possible (US). US: can puncture capsule on both ends, withdraw contents with 18-gauge needle, and administer through NG tube followed by 30 mL of water. Label syringe "Not for IV use." 	
Nimodipine (Nymalize [US])	 Subarachnoid hemorrhage: 60 mg Q4 hours for 21 days, starting within 96 hours after the event. For patients with cirrhosis, reduce dose to 30 mg Q4 hours. 	 Give at least one hour before or two hours after meals. If given via gastric or NG tube, after administration fill oral syringe with 20 mL of normal saline and flush tube. 	
Verapamil injection	• SVT, A-fib, A flutter: initial 5 to 10 mg (0.075 to 0.15 mg/kg) over two min; if needed, after 30 min., give 10 mg (0.15 mg/kg); optimal interval for subsequent doses not determined.	Infuse over at least three minutes in elderly patients.	

- a. **Amlodipine combination products**: *Azor* (US; amlodipine/olmesartan; generics), *Caduet* (amlodipine/atorvastatin; generics), *Exforge* (US; amlodipine/valsartan; generics), *Exforge HCT* (US; amlodipine/valsartan/hydrochlorothiazide; generics), *Lotrel* (US; amlodipine/benazepril; generics), *Prestalia* (US; amlodipine/perindopril), *Tribenzor* (US; amlodipine/olmesartan/hydrochlorothiazide; generics), *Twynsta* (amlodipine/telmisartan [brand discontinued in US]; generics), *Viacoram* (Canada; atorvastatin/perindopril; generics)
- b. From US and Canadian product labeling unless otherwise noted.
 - US prescribing information used in the creation of this chart: *Norvasc* (January 2019); *Conjupri* (December 2019); felodipine ER (Torrent, July 2022); nifedipine extended-release (Aurobindo, June 2021); *Procardia XL* (May 2021); *Sular* (July2017); isradipine capsules (Epic, March 2021); nicardipine capsules (ANI, June 2021); *Procardia* (July 2016); *Cardizem CD* (April 2020); *Cardizem LA* (May 2019); diltiazem extended-release capsule (Apotex, July 2012); *Tiazac* (October 2020); *Verelan* (October 2019); *Verelan PM* (October 2019); verapamil ER/trandolapril (Glenmark, September 2019); diltiazem ER capsules (Mylan, November 2020); *Calan SR* (January 2022); *Cardizem* (June 2020); verapamil (Heritage, October 2021); *Cleviprex* (September 2022); Diltiazem injection (Hospira, December 2017); *Cardene* injection (March 2022); Nimodipine capsules (Bionpharma, November 2017); *Nymalize* (December 2019); verapamil injection (Exela, September 2021).
 - Canadian product monographs used in the creation of this chart: Norvasc (May 2020); Plendil (January 2015); Adalat XL (July 2016); Nifedipine IR capsule (AA Pharma Inc., June 2010); diltiazem CD (Sanis Health, January 2022); Tiazac (June 2021); Tiazac XC (June 2021); Isoptin SR (December 2021); Apo-diltiaz (April 2020); Apo-verap (May 2022); diltiazem injection (Omega Laboratories, March 2021); Nimotop (November 2011), verapamil hydrochloride injection (Sandoz Canada, July 2022).

Abbreviations: ACS = acute coronary syndrome; A-fib = atrial fibrillation; A flutter = atrial flutter; BID = twice daily; BP = blood pressure; CAD = coronary artery disease; CYP = cytochrome P450; ER = extended release; HFrEF = heart failure with reduced ejection fraction; HS = at bedtime; HTN = hypertension; IR = immediate release; MI = myocardial infarction; min = minutes; NG = nasogastric; QD = once daily; Q12 = every twelve; Q4 = every four; Q8 = every eight; QID = four times daily; SVT = supraventricular tachycardia; TID = three times daily.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

References

- Cheng JW. Essential hypertension. In: Zeind CS, Carvalho MG, Eds. Applied Therapeutics: the Clinical Use of Drugs. 11th ed. Philadelphia, PA: Wolters Kluwer Health, 2018: 132-61.
- Clinical Pharmacology powered by Clinical Key. Tampa, FL: Elsevier; 2022. http://www.clinicalkey.com. (Accessed October 4, 2022).
- 3. Elliott WJ, Ram CV. Calcium channel blockers. J Clin Hypertens (Greenwich). 2011 Sep;13(9):687-9.
- Briggs GG, Towers CV, Forinash AB. Drugs in Pregnancy and Lactation. 12th ed. Philadelphia, PA: Wolters Kluwer, 2021 (online version accessed October 12, 2022).
- January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation. 2014 Dec 2;130(23):e199-267. Erratum in: Circulation. 2014 Dec 2;130(23):e272-4.

Cite this document as follows: Clinical Resource, Comparison of Calcium Channel Blockers. Pharmacist's Letter/Prescriber's Letter. November 2022. [381108]

-To access hundreds more clinical resources like this one, visit trchealthcare.com to log in or subscribe-