Wyoming Drug Utilization Review

Calcium Channel Blockers

Written by Noah Paiz PharmD, 2025

Hypertension at first glance may not seem a serious concern for healthcare professionals. However, hypertension is commonly known as the silent killer and is a major contributing factor to the development of heart disease (1). The National Center for Health Statistics documents that hypertension occurs in almost one-half of adult citizens in the United States (1). During the 20th century, scientists discovered calcium as the second messenger for numerous cellular processes (2). The understanding of calcium's use in cellular processes resulted in pharmaceutical companies developing the first calcium channel blockers (CCBs) in the 1960s for blood pressure management (2).

CCBs work by inhibiting voltage-gated L-type calcium channels preventing the influx of extracellular calcium leading to a decrease of muscle contraction (3-5). A decrease in muscle contraction from CCBs results in vasodilation, decreased cardiac load, and reduced oxygen demand (3-5). Also, L-type calcium channels are found in cardiac cells and skeletal muscle cells (4).

Even though all CCBs inhibit calcium channels they are further divided into two main CCBs categories non-dihydropyridine (non-DHPs) and dihydropyridine (DHPs) (3-5). The divide between the two categories of CCBs stems from different affinities to blinding sites in the peripheral vasculature or cardiac tissue. Non-DHPs (e.g., verapamil and diltiazem) work primarily on the L-type calcium channels found in the intrinsic conduction system of the heart (3,5). While, DHPs (e.g., nifedipine and amlodipine) have a greater selectivity for smooth muscle tissue in the body's periphery (3,5).

Current data from the Medical Expenditure Panel Survey (MEPS) 2013-2022 shows that amlodipine is the fifth most popular medication on the market with over 17 million unique patients currently prescribed the medication (6). These numbers illustrate the point that CCBs are mainstream first-line therapy for the management of hypertension by the American College of Cardiology/American Heart Association (ACC/AHA) (7-8).Large meta-analysis of the current literature have shown CCBs are as effective as other blood pressure medications (9). CCBs can be used in monotherapy or combination therapy with other blood pressure medications as first-line pharmacological therapy (5,7-8). Commonly DHPs are prescribed for their vasodilatory effects for the management of hypertension, migraines, Raynaud's Phenomenon, and even treat premature labor/ delayed birth (5,7-8). Unlike the DHP, the non-DHPs play a role in combatting cardiac arrhythmias by lowering cardiac conductivity and contractility (7-8).

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CCBs' most common side effects are a result of their vasodilatory effects. Patients report experiencing orthostatic hypotension, peripheral edema, headache, dizziness, and a mild rash (5,9). The non-DHP can also cause bradycardia through the suppression of AV conduction (5,9). Patients with heart failure with reduced ejection fracture (HFrEF) should not be given non-DHP due to their effects on the heart (negative inotropic) (9). Verapamil has also been reported to cause more constipation than other CCBs (5).

All CCBs except clevidipine are metabolized extensively by CYP 3A4 enzymes (5,9). Therefore CYP 3A4 inhibitors and inducers can alter CCB concentrations (5,9). Consequently, non-DHPs like verapamil and diltiazem are also CYP-3A4 and p-glycoprotein inhibitors. Patients on simvastatin and immunosuppressants (tacrolimus and cyclosporine) should be monitored for increased concentrations and toxicity while also taking CCBs; dose adjustment may be necessary (5). Lastly, careful consideration should be given when using multiple hypotensive agents. Beta blockers have negative inotropic effects that can lead to bradycardia and other cardiac issues (5,9). For example, verapamil has been shown to increase propranolol concentration by up to 50% and decrease the clearance of digoxin and beta blockers (5,11).

Calcium channel blockers are first-line therapy for the management of hypertension and are used in multiple other conditions for their vasodilatory properties. Calcium channel blockers are divided into two main categories, non-dihydropyridine and dihydropyridine, that either work on peripheral smooth muscle tissue or cardiac tissue. Careful monitoring should be given with calcium channel blockers when other medications with anti-arrhythmic properties are co-administered and with medications that can alter CYP-3A4. Calcium channel blockers are well tolerated and as effective as other hypertension medications.

References

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The P&T Committee met for its quarterly business meeting on February 13, 2025.

Highlights of this meeting include:

The Omega-3 agents will no longer require prior authorization.

The Tryvio criteria was updated to require a patient to have been on three antihypertensive medications from different pharmacological classes for four weeks prior to initiation of Tryvio.

Zoryve will require a 21-day trial and failure of a medium to high potency corticosteroid or a mild potency steroid if using in intertriginous areas for treatment of plaque psoriasis and for seborrheic dermatitis. For atopic dermatitis, Zoryve will require a 21-day trial and failure of a medium to high potency corticosteroid and an immunomodulator (pimecrolimus or tacrolimus) prior toa approval for atopic dermatitis.

Voquezna will require a 30-day trial and failure of two proton pump inhibitors prescribed twice daily at maximum dose.

Nemluvio for atopic dermatitis and Hympavzi, were reviewed with no evidence of a difference in safety or efficacy versus the current products in their respective class. Both were limited to indication and referred to the Department of Health for cost analysis and PDL placement.

Atruby, Crenessity, Tryngolza, Alyftrek and Kebilidi were all limited to indication.

Zepbound is limited to indication for obstructive sleep apnea. At six months, the prior authorization will require a minimum loss of 5% of the patient's baseline body weight. At twelve months, prior authorization will require evidence of improvement in obstructive sleep apnea.

Spravato will not be covered for treatment-resistant depression in adults as monotherapy.

All prior authorization criteria are open for public comment. Comments should be sent by email to alewis13@uwyo.eduby April 15, 2025.

The next P&T Committee meeting will be held May 8, 2025 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

The P&T Committee is looking for a Family Physician to fill an open position on the Committee. If you are interested in participating, please email Aimee Lewis at alewis13@uwyo.edu for more information.

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