February 2020
Issue 42

ToxUpdate

Regional Poison Control Center, Birmingham, AL
www.childrensal.org/rpcc 1-800-222-1222

Conjupri®: New Calcium Channel Blocker

By Mallory Mullins, Samford University PharmD Candidate

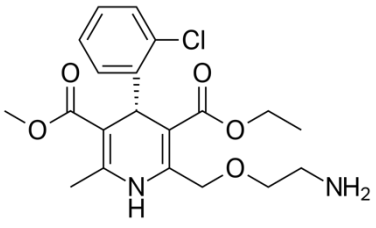
Amlodipine is composed of a 1:1 mixture of levamlodipine and dextroamlodipine, with levamlodipine as the active, antihypertensive isomer. Conjupri, or levamlodipine, is a new calcium channel blocker that was approved on December 19, 2019. Conjupri appears to have less adverse effects than amlodipine and is available in 1.25 mg, 2.5 mg, and 5 mg tablets. Conjupri is not approved for patients less than 6 years old. It can be used alone or in combination with other antihypertensive medications. Following oral administration of therapeutic doses of levamlodipine, peak plasma concentrations occur between 6 and 12 hours and the duration is 24 hours.

The most common adverse reactions include edema and dizziness. Abdominal pain, nausea, somnolence, and fatigue have been seen with the use of Conjupri but are less common. Peripheral vasodilation with significant hypotension is expected after an overdose. Early mild to moderate exposure presents as reflex tachycardia and hypotension. However, hypotension may not develop for several hours. Drowsiness, nausea and vomiting may also occur. Severe toxicity may cause acute renal failure, metabolic acidosis, respiratory failure and/or hypoxemia.

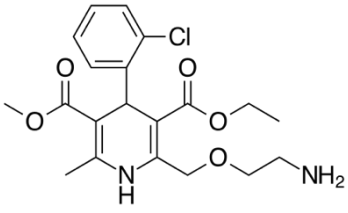
References

1. Levamlodipine. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com/ (Accessed January 22, 2020).
2. FDA Approves Conjupri (levamlodipine maleate) for the Treatment of Hypertension. https://www.drugs.com/newdrugs/fda-approves-conjupri-levamlodipine-maleate-hypertension-5128.html (Accessed January 22, 2020).
3. Conjupri Highlights of Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212895s000lbl.pdf (Accessed January 22, 2020).
4. Levamlodipine. Lexicomp (electronic version). Wolters Kluwer Clinical Drug Information, Alphen aan den Rijn, South Holland, Netherlands. https://online-lexi-com.ezproxy.samford.edu/lco/action/doc/retrieve/docid/patch_f/6883924?cesid=1K0eRFXW6ls&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dlevamlodipine%26t%3Dname%26va%3Dlevamlodipine#pha (Accessed January 22, 2020).

Levamlodipine



Amlodipine



POISON Help® 1-800-222-1222

Special Interest Articles

- Conjupri
- Cholinesterase Inhibitors
- Influenza Drugs

Did you know?

A study was published in the *Journal of the American Pharmacists Association showing that there is an increase in older adults taking more* psychoactive medication than they did in years past. Anticonvulsant use has increased 450%, SSRI use has increased by 300%, opioid use has increased by 140%, and benzodiazepine use has increased 50% from 1996 to 2013.

Cholinesterase Inhibitor Drugs for Alzheimer's

By Taylor Moore, Samford University PharmD Candidate

"Alzheimer's is the leading cause of dementia and each year more and more Americans are being diagnosed."

Alzheimer's Association reports that one in ten people aged 65 years and older have been diagnosed with Alzheimer's disease (AD). Alzheimer's is the leading cause of dementia and each year more and more Americans are being diagnosed. The U.S. Food and Drug Administration has approved the following acetylcholinesterase inhibitor drugs for the treatment of AD: Donepezil (Aricept®), Galantamine (Razadyne®), Rivastigmine (Exelon®), and Donepezil/Memantine (Namzaric®). The most common signs of toxicity for acetylcholinesterase inhibitors include muscarinic effects. A mnemonic device used to remember muscarinic effects from acetylcholinesterase inhibitors is SLUDGE (salivation, lacrimation, urination, diaphoresis, gastrointestinal upset, emesis). Nicotinic effects such as respiratory depression may also be present, along with signs of involuntary movement such as muscle fibrillation, fasciculations, and even paralysis.

In acetylcholinesterase inhibitor overdose, atropine works to reduce the effects of excessive acetylcholine. In treating rivastigmine overdose, pralidoxime may also be considered for treatment. Atropine reduces the binding of acetylcholine to muscarinic receptors and pralidoxime reverses the binding of cholinesterase inhibitors to acetylcholinesterase. In addition to those treatments, benzodiazepines should be used for seizures.

References

1. McCament-Mann LA. Donepezil Can Be Toxic if Too Much Is Taken. Poison Control expert help online or by phone. https://www.poison.org/articles/donepezil-can-be-toxic-if-too-much-is-taken-or-child-swallows-174. Published July 31, 2019. (Accessed January 24, 2020).
2. Medications for Memory. Alzheimer's Disease and Dementia. https://www.alz.org/alzheimers-dementia/treatments/medications-for-memory. (Accessed January 24, 2020).
3. Singh R, Sadiq NM. Cholinesterase Inhibitors. [Updated 2019 Jul 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan- . Available from: https://www.ncbi.nlm.nih.gov/books/NBK544336/

Samford pharmacy students, Taylor Moore and Mallory Mullins visited Odenville Senior Citizen Center to teach them about medication safety on January 23, 2020.

Approved Antiviral Drugs for Influenza

By Laura Read, RPh, CSPI, Regional Poison Control Center, Children's of AL

According to the Center for Disease Control and Prevention (CDC), there have been 22 million influenza (flu) illnesses, 210,000 hospitalizations and 12,000 deaths from the flu so far this season. There are four United States Food and Drug Administration (FDA)-approved antiviral drugs recommended by CDC to treat flu this season.

- **Oseltamivir phosphate** (Tamiflu®)- oral suspension and capsules, 13 years and older, 75 mg twice daily for 5 days
- **Zanamivir** (Relenza®)- inhalation powder, for oral inhalation, 7 years and older, 10 mg inhalation twice daily (12 hours apart) for 5 days
- **Peramivir** (Rapivab®)- intravenous infusion over 15-30 minutes in one dose
- **Baloxavir marboxil** (Xofluza®)- oral tablets – 20- 40 mg tablets taken in one dose

Oseltamivir, zanamivir, and peramivir are neuraminidase inhibitors and are selective inhibitors of influenza A and B neuraminidase (sialidase). The chemical structure of peramivir allows it to bind to the influenza neuraminidase with much higher affinity than oseltamivir. Baloxavir has a different mechanism of action from the neuraminidaste inhibitors. Baloxavir marboxil is a prodrug that is converted by hydrolysis to baloxavir. Baloxavir inhibits the endonuclease activity of the polymerase acidic (PA) protein which is a flu virus-specific enzyme in the viral RNA polymerase complex required for viral gene transcription. This results in inhibition of flu virus replication.

For the neuraminidase inhibitors, there are usually minimal effects in an overdose or therapeutic error. Sometimes it is hard to distinguish symptoms from normal effects of the flu. Commonly seen symptoms might include nausea, vomiting, diarrhea and abdominal pain. Neuropsychiatric symptoms have been reported mostly among pediatric patients taking oseltamivir. This is seen with high-dose therapy for critically ill patients with influenza and whether the cause is directly due to oseltamivir toxicity or the flu virus, remains unclear.

Baloxavir marboxil's safety profile includes data from three placebo-controlled trials. Adverse effects seen in at least 1% of the subjects included diarrhea, bronchitis, nausea, sinusitis, and headache. The package insert includes a warning of risk of bacterial infection with baloxavir marboxil. This may co-exist with or occur as a complication of the flu. Baloxavir should not be taken with laxatives, antacids, calcium, iron, magnesium, selenium, or zinc due to decreased absorption and possible reduction in baloxavir's effectiveness.

References

1. Fluview Weekly U.S. Influenza Surveillance Report. Centers for Disease Control and Prevention. April 22, 2019. https://www.cdc.gov/flu/weekly/index.htm. (Accessed February 12, 2020).
2. What You Should Know About Flu Antiviral Drugs. Centers for Disease Control and Prevention. April 22, 2019. https://www.cdc.gov/flu/treatment/whatyoushould.htm. (Accessed February 5, 2020).
3. Wester, A., Shetty, A.K. Peramivir injection in the treatment of acute influenza: a review of the literature. *Infect Drug Resist*. 2016; 9:201–214.
4. Tamiflu. Micromedex® 2.0, (electronic version). Truven Health analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com. (Accessed February 4, 2020).
5. Xofluza [package insert]. San Francisco, CA: Genentech USA Inc; 2019.