

Wyoming Drug Utilization Review

Effects of Concurrent Use of Cyclobenzaprine and TCAs

Justine Frantz, PharmD

Is there an added risk of QT prolongation with the use of cyclobenzaprine (Flexeril) and tricyclic antidepressants (TCAs) concurrently?

Cyclobenzaprine is closely related to the tricyclic antidepressants (TCAs), structurally differing from amitriptyline by only one double bond. Cyclobenzaprine,

a skeletal muscle relaxant, has a major side effect of CNS depression. TCAs through their mechanism of action can also produce CNS depression and sedation. It is important to realize that effects of CNS depression can include ataxia, confusion, drowsiness, respiratory depression and weakness. If both cyclobenzaprine and TCAs are taken together, this effect could be intensified. This interaction is rated as moderate in severity. Another side effect of using cyclobenzaprine along with TCAs stems from both drugs acting as serotonin modulators. There is a chance of toxicity through central serotonergic overstimulation from using 2 or more of these agents. The interaction is rated as major, due to the seriousness of “serotonin syndrome” which affects autonomic, neuromuscular and cognitive function. Both drugs when used

together can enhance the amount of anticholinergic activity that is exhibited as well. These effects may include dry mouth, dry eyes, blurred vision, urinary retention and constipation. This interaction is rated as moderate in severity. Please refer to the diagram and table on page 2.

In a case study published in 2011, cyclobenzaprine overdoses were not reported to show a widened QRS, despite the structural similarities with TCAs. Furthermore, dysrhythmia or seizures were not found in cyclobenzaprine overdose either. The main issues seen were sedation, tachycardia and mild hypertension, associated with anticholinergic activity. Tricyclic like effects, such as QT prolongation was seen more often in amitriptyline overdoses. Anticholinergic effects were exhibited in cyclobenzaprine overdoses, so this could be magnified with the use of a TCA.

In conclusion, when taken concurrently, cyclobenzaprine and TCAs can increase the risk of CNS depression, serotonin syndrome, and anticholinergic effects. They have not been shown to exaggerate QT prolongation when used in combination. The two drugs do have similar pharmacology, so considering an alternative agent for a skeletal muscle relaxant would be a good choice in patients who are well controlled on TCAs. Providers should be knowledgeable of these major side effects when prescribing these drug therapies concurrently. The main issue is to ensure that the patient understands the risks and what side effects to take note of when being prescribed any new medications.

References

1. Bebarta, V. S., Maddry, J., Borys, D. J., & Morgan, D. L. (2011). Incidence of tricyclic antidepressant-like complications after cyclobenzaprine overdose. *The American journal of emergency medicine*, 29(6), 645-649.
2. “Drug Interaction Report.” Cyclobenzaprine, TCAs, Clinical Pharmacology, 2019, www-clinicalkey-com.libproxy.uwyo.edu/pharmacology/reports/interactions?gpcid=1598&dt=true&type=p.
3. “LexiComp Drug Interactions.” *LexiComp Online*, 2019, www-uptodate-com.libproxy.uwyo.edu/drug-interactions/?source=responsive_home#di-document.

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P&T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on May 8, 2019.

Highlights of this meeting include:

The Adult ADHD PA form will be updated to include a check box for developmentally/intellectually disabled and a free form area for history of symptoms in other environments.

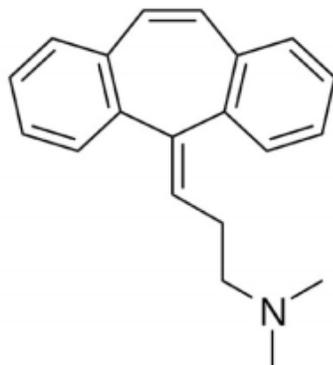
The time for antidepressant cross tapering will be increased to 90 days.

Savella will be limited to a maximum of 200 mg per day.

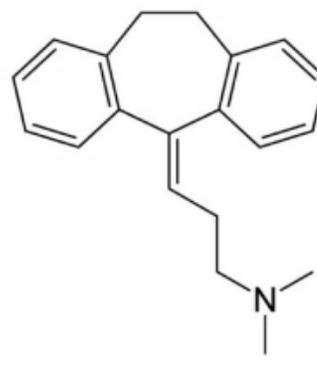
Bijuva will be limited to indication. Motegrity and Apadaz will be referred to the Department of Health for cost analysis and PDL placement.

The proposed prior authorization criteria will be posted for public comment at www.uwyo.edu/DUR. Comments may be sent by email to alewis13@uwyo.edu or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to July 31, 2019.

The next P&T Committee meeting will be held August 15, 2019 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.



Cyclobenzaprine



Amitriptyline

Drug	QT prolongation	CNS depression	Serotonin modulator	Anticholinergic activity
Cyclobenzaprine (Flexeril)		X	X	X
Amitriptyline (Elavil)	X	X	X	X
Amoxapine	X	X	X	X
Desipramine (Norpramin)	X	X	X	X
Doxepin	X	X	X	X
Imipramine (Tofranil)	X	X	X	X
Nortriptyline (Pamelor)	X	X	X	X
Protriptyline (Vivactil)	X	X	X	X
Trimipramine (Surmontil)	X	X	X	X

Naloxone Survey of Wyoming Pharmacies

In order to better understand the dispensing of naloxone by Wyoming pharmacies and to assist Wyoming residents in locating pharmacies that dispense naloxone, the Wyoming Rx Abuse Stakeholders (RAS) is conducting a survey specific to naloxone dispensing in the state. We ask that you take a few minutes to complete and return the survey to RAS Advisor, Antoinette Brown, RPh at: abrown13@uwyo.edu or by fax at: 307-766-2953. Please submit your survey responses by July 31, 2019.

With your permission, the RAS will highlight your pharmacy on their website (wyrxabusestakeholders.com) as a naloxone dispenser. This will assist patients, healthcare providers and the public at large in locating a pharmacy who is trained in and capable of dispensing naloxone.

How many pharmacists in your pharmacy have completed naloxone education training? _____

What training was used?

Is anyone in your pharmacy aware of the Wyoming Pharmacy Association / WyoCourses training?

<https://wind.catalog.instructure.com/courses/naloxone>

How many pharmacists in your pharmacy have prescribed naloxone? _____

What are the barriers, if any, to prescribing naloxone in your pharmacy? _____

Name of pharmacy: _____

Pharmacy address: _____

Person filling out survey: _____

Do you give the Wyoming Rx Abuse Stakeholders (RAS) permission to place your pharmacy on their website (wyrxabusestakeholders.com) as a naloxone dispenser? YES / NO

We encourage all pharmacists in the state to obtain the required training necessary to dispense this life saving medication. Information on the Emergency Administration of Opiate Antagonist Act which allows a pharmacist to prescribe and dispense an opiate antagonist (naloxone) is located on our website at: <http://pharmacyboard.wyo.gov/latest-news>. An informational brochure may be downloaded from the site, as well as a sample prescription, and a summary of the rules for a pharmacist who prescribes naloxone. Please refer to the Wyoming Pharmacy Act Rules Chapter 18 under the “laws” tab for additional information.

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www.uwyo.edu/DUR/newsletters.