

# PHARMCON

## freeCE Monograph

Overview of Dextromethorphan

0.25 HOUR CE



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I have seen three cases of serotonin syndrome. Pharmacists need to be cognizant of the potential interactions between “good old Dextromethorphan” and antidepressants that can lead to increased serotonin levels.

Back in 2007, one of my patients came into the pharmacy with her husband. She was a thin and frail woman of about 40 years and weighed around 100 pounds. She presented with clonic jerking of her arms. I asked her husband what was going on, and he said, “she had a drug interaction between her Prozac-40 and Robitussin DM cough syrup.”

We had a patient at the primary care practice I staffed who was “chugging Nyquil” for a bad cough. She ended up being flown via helicopter to a Pittsburgh hospital due to excess dextromethorphan ingestion while taking Citalopram 40 mg once daily.

On Monday, while I was working on the bench, a patient called. She was taking Fluoxetine 40 mg and Quetiapine 100 mg twice daily. Her doctor just added Trazodone 50 mg at bedtime to help her sleep. The patient said that she had developed a tremor in both hands. I told the patient to call the prescriber and to consider stopping the trazodone due to possible serotonin syndrome. The prescriber called and asked me if I thought the trazodone was really the culprit since it was a low dose of 50 mg. I told the nurse practitioner that there is a lot of patient variability with this condition and, since the tremors presented after starting trazodone, it would be prudent to start there. The NP thanked me for my advice and took my recommendation.

**Figure 1.** States Prohibiting DXM Sales to Minors

- **Maryland** effective October 2007
- **New York** effective March 26, 2014
- **Virginia** effective January 1, 2015
- **Arizona** effective July 24, 2014
- **Kentucky** effective March 2015
- **New Jersey** effective February 2016
- **Delaware** effective June 2016
- **Nevada** effective June 2017
- **Colorado** effective August 2018
- **Texas** effective September 2019
- **Ohio** effective September 2021
- **California** effective January 1, 2012
- **Rhode Island** effective 2014
- **Washington** effective July 1, 2015
- **Louisiana** effective August 1, 2014
- **Tennessee** effective January 1, 2016
- **Alaska** effective May 2016
- **Florida** effective January 2017
- **Oregon** effective January 2018
- **Wisconsin** effective January 2019
- **Michigan** effective July 2020

## Dextromethorphan (DXM)

### History

The FDA approved DXM in 1958 and, during the 1960s and 1970s, dextromethorphan became available in an over-the-counter tablet form by the brand name Romilar®. In 1973, Romilar® was taken off the shelves because of frequent misuse and was replaced by cough syrup to cut down on abuse. Manufacturers began introducing refined DXM products (Robitussin-DM®, Vicks-44®) that were designed to limit recreational use by creating an unpleasant taste if consumed in large quantities.<sup>1</sup> It wasn't long ago that drug companies started marketing a higher concentration and more pleasant-tasting preparation (Delsym®). Keep in mind, when the recommended dose is taken, DXM has few adverse side effects, and has a long history of safety and efficacy.

### Pharmacology

Dextromethorphan is the d-isomer of the codeine analog of levorphanol.<sup>1</sup> Older “seasoned” pharmacists remember dispensing levorphanol under the brand name of Levo-

Dromoran, a Schedule II narcotic made by Roche and FDA approved in 1953. It is still available as a generic for almost \$40.00 per PILL!<sup>2</sup> Dextromethorphan is a codeine-like drug that binds and acts as antagonist to the NMDA glutamatergic receptor. It is an agonist to the opioid Sigma-1 and Sigma-2 receptors, it is an alpha-3 beta-4 nicotinic receptor antagonist, and it targets the serotonin reuptake pump. The net effect is that DM decreases the sensitivity of cough receptors and interrupts cough impulse transmission by depressing the medullary cough center in the brain.<sup>3</sup>

- Rapid GI absorption
- Half-life = 1.5-2.2 hours
- Substrate of CYP450: 3A4, 2D6, so watch for drug interactions<sup>3</sup>
- First pass through the hepatic portal vein results in some of the drug being metabolized into an active metabolite of dextromethorphan, dextrophan, the 3-hydroxy derivative of dextromethorphan
- Easily crosses the blood-brain barrier

## Pediatric Dosing:

- Children under than 4 years: Not for OTC use<sup>4</sup>
- Children 4-6 years (syrup):
  - Oral: 2.5-7.5 mg every 4-8 hours
  - Extended-release (Delsym) is 15 mg twice daily (maximum: 30 mg/24 hours)<sup>3</sup>
- Children 6-12 years:
  - 5-10 mg every 4 hours or 15 mg every 6-8 hours;
  - Extended-release is 30 mg twice daily (maximum: 60 mg/24 hours)
- Over age 12: use the adult dose<sup>3</sup>

## Warnings

Serotonin syndrome occurs when drugs that increase serotonin levels are combined with other drugs that increase serotonin levels.

Dextromethorphan can precipitate a serotonin syndrome event. Symptoms include agitation, confusion, hallucinations, hyper-reflexia, muscle twitch/jerk, shivering, and tachycardia. Serotonin syndrome may occur with drugs such as:<sup>3</sup>

- SSRI/SNRI (antidepressants like fluoxetine, paroxetine, venlafaxine, duloxetine, etc.)

**Table 1.** DXM Intoxication Doses<sup>1,3</sup>

Plateau	Dose (mg)	Behavior Effects	Robitussin DM®	Delsym®	Coricidin HPB®
1 <sup>st</sup>	100-200	Mild stimulation	50-100mL	17-34mL	3-7 tabs
2 <sup>nd</sup>	200-400	Euphoria, hallucinations	100-200mL	34-68mL	7-14 tabs
3 <sup>rd</sup>	300-600	Distorted visual perception, Loss of coordination	150-300mL	50-100mL	10-20 tabs
4 <sup>th</sup>	500-1500	Dissociative sedation	250-750mL	83-250mL	17-50 tabs

- Monoamine oxidase inhibitors MAOI (for Parkinson's and depression)
- Tramadol, especially at high doses
- Trazodone (over 150 mg)
- Linezolid (Zyvox), which has some MAO inhibition effect

## Novel Use for Dextromethorphan That Illustrates the Mental Effects of This Drug

Nuedexta® Rx (dextromethorphan/quinidine) is a new drug designed to treat pseudobulbar affect (PBA), which is caused by neurologic conditions like Alzheimer's disease, stroke, traumatic brain injury (TBI), Parkinson's disease, multiple sclerosis (MS), and Lou Gehrig's disease (ALS).

Symptoms of PBA include outbursts of crying or laughing that are often sudden and exaggerated or do not match what the person is feeling inside. This drug contains 20 mg DM and 10 mg quinidine. It works by using quinidine to block the metabolism of DM for a prolonged effect in treatment of PBA<sup>5</sup>.

## DXM Abuse

- Most abused: Coricidin® HBP (DM-30 mg + Chlorpheniramine 4 mg), often referred to as "CC" or "triple C" or "Skittles". Robitussin products can be used, called "Robo-tripping" or "Robo-shakes". May lead to elevated body temperature and death.
- The effects seen with dextromethorphan abuse are like those seen after phencyclidine (PCP) use, another agent which blocks NMDA receptors. DXM is sometimes referred to as "Poor man's PCP".

## Effects of Excessive DXM Intake:<sup>1</sup>

- Increased perceptual awareness
- Altered time perception
- Feelings of "floating" or dissociation of the body
- Visual disturbances
- Tactile, auditory, or visual hallucination
- Paranoia
- Disorientation and lack of coordination
- Slurred speech
- Impaired judgment and mental performance

**Table 1** is a chart I prepared to illustrate the doses needed to cause all the levels of DXM intoxication. As you can see, just one bottle of Delsym® (89 mL) can cause an abuser to experience dissociative sedation. I am much more concerned about the Delsym® and the Coricidin® products, because, as we all know, excess guaifenesin causes nausea and, most likely, vomiting.

*-Have a great day on the bench!!*

# References

1. Rosenbaum MD. *Dextromethorphan abuse and poisoning: Clinical features and diagnosis*. Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc. <https://www.uptodate.com> (Accessed on May 26, 2023.)
2. Levorphanol. In: *Lexi-Drugs*. Lexi-Comp, Inc. Updated May 17, 2023. Accessed May 26, 2023
3. Dextromethorphan. In: *Lexi-Drugs*. Lexi-Comp, Inc. Updated May 24, 2023. Accessed May 26, 2023
4. *Should you give kids medicine for coughs and colds?* FDA. January 5, 2023. Accessed May 26, 2023
5. *Nuedexta [package insert]*. Aliso Viejo, CA: Avanir Pharmaceuticals, Inc.; 2010.

## Test Questions Pharmacist, Pharmacy Technician

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1. **When dextromethorphan is taken with drugs like antidepressants it can lead to an increase of serotonin in the brain. This is called:**
  - a. Drug abuse
  - b. Drug-induced euphoria
  - c. Serotonin syndrome
  - d. Synergistic medication use
2. **What are the dangers of a patient accidentally ingesting 50 mL of Delsym® instead of 5 mL?**
  - a. Euphoria, hallucinations, and mild stimulation
  - b. Tachycardia and hypertension
  - c. Bradycardia and hypotension
  - d. None of the above, Delsym® is an exceptionally safe drug.

## PHARMACIST LEARNING OBJECTIVES

1. Recognize the potential dangers and interactions of the common over the counter drug dextromethorphan

## PHARMACY TECHNICIAN LEARNING OBJECTIVES

1. Recognize the potential dangers and interactions of the common over the counter drug dextromethorphan
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## OVERVIEW

Micro-learning opportunities were created in response to evidence that learning is maximized when delivered in short and focused. In this session, dextromethorphan, its warnings, and its drug interactions will be discussed.

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Pharmacist, Pharmacy Technician

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