Medication Prescribing Information

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Clinical Standards of Practice: Stimulant Dosages

TL;DR:

American Academy of Sleep Medicine (formerly American Sleep Disorders Association), Standards of Practice Committee, 1994, 2000, 2007, 2021:

- Patients have a wide variation in response to stimulants … therefore, full therapeutic response in adult patients with narcolepsy can usually be obtained with daily medication doses below the recommended maximal doses of: … **dextroamphetamine sulfate, 100 mg**

"Understanding Unapproved Use of Approved Drugs "Off Label", **United States Federal Drug Administration**, 02/05/2018

> The approved drug labeling for healthcare providers gives key information about the drug that includes:

- How to use the drug to treat those specific diseases and conditions.

From the **FDA perspective**, once the FDA approves a drug, healthcare providers generally may **prescribe the drug for an unapproved use when they judge that it is medically appropriate for their patient**.

Unapproved use of an approved drug is often called "off-label" use. This term can mean that the drug is:

- **Given in a different dose**, such as when a **drug is approved at a dose** of one tablet every day, **but a patient is told by their healthcare provider** to take two tablets every day.

References

Standards of Practice Committee of the American Sleep Disorders Association, Practice Parameters for the Use of Stimulants in the Treatment of Narcolepsy, Sleep, Volume 17, Issue 4, June 1994, Pages 348–351, https://doi.org/10.1093/sleep/17.4.348 (Highlighted: https://hyp.is/go?url=https%3A%2F%2Fdocdrop.org%2Fdownload_annotation_doc%2Fsleep-17-4-348-2acmm.pdf&group=__world__)

This report provides the first clinical guidelines on the appropriate use of stimulants in the treatment of narcolepsy.

The American Sleep Disorders Association (ASDA) expects these guidelines to have an impact on professional behavior

Treatment aims are to improve daytime alertness with stimulant medication

2. Treatment objectives and indications

(a) The objective of treatment with stimulants should be to alleviate daytime sleepiness, thereby allowing the fullest possible return of normal function for patients at work, at school and at home [1.0].

(b) Stimulants are most effective at producing improvement in fatigue and sleepiness in boring and in-active situations;

4. Dosage

Patients have a wide variation in response to stimulants and in the incidence of side effects; therefore, full therapeutic response in adult patients with narcolepsy can usually be obtained with daily medication doses below the recommended maximal doses of: pemoline, 150 mg; methylphenidate hydrochloride, 100 mg; dextroamphetamine sulfate, 100 mg

6. Abuse

(a) Patients with narcolepsy are no more likely to become drug abusers or to use stimulant medications illicitly than any other group of patients treated with stimulants [5.5]

7. Side effects

Most patients with narcolepsy can be effectively treated with stimulants without developing significant side effects.

Little evidence suggests that stimulants in therapeutic doses cause a significant increase in blood pressure in normo-or hypertensive patients

11. Follow-up

(a) A patient stabilized on stimulant medication should be seen by a physician at least once per year, and preferably once every 6 months, to assess the development of medication side effects

Littner M, Johnson SF, McCall WV, Anderson WM, Davila D, Hartse SK, Kushida CA, Wise MS, Hirshkowitz M, Woodson BT; **Standards of Practice Committee. Practice parameters for the treatment of narcolepsy: an update for 2000**. Sleep. 2001 Jun 15;24(4):451-66. PMID: 11403530. https://hyp.is/go?url=https%3A%2F%2Faasm.org%2Fresources%2Fpracticeparameters%2Fpp_narcolepsy_update.pdf&group=__world__

Because of the importance of narcolepsy treatment, the American Academy of Sleep Medicine (AASM) sponsored a review paper on the use of stimulants for treatment of narcolepsy in 1994. Based on that review, the Standards of Practice Committee (SPC) of the AASM published practice parameters on narcolepsy therapy with stimulants.

In view of the new treatments, basic research advances, and the NGC protocol, the AASM decided to update the practice parameters for treatment of narcolepsy.

3. The following medications are effective treatments for narcolepsy. Comparative safety and efficacy of the stimulant medications are not defined. The rating of the recommendation is based on the grade of evidence for each. See Table 5 for dosages.

b. Amphetamine, methamphetamine, dextroamphetamine, and methylphenidate are effective for treatment of daytime sleepiness due to narcolepsy

Table 5.
MEDICATION: Amphetamine
Usual daily dose (maximum dose): 30 mg (100 mg)

Morgenthaler TI, Kapur VK, Brown T, Swick TJ, Alessi C, Aurora RN, Boehlecke B, Chesson AL Jr, Friedman L, Maganti R, Owens J, Pancer J, Zak R; Standards of Practice Committee of the American Academy of Sleep Medicine. **Practice parameters for the treatment of narcolepsy and other hypersomnias of**

central origin. Sleep. 2007 Dec;30(12):1705-11. doi: 10.1093/sleep/30.12.1705. Erratum in: Sleep. 2008 Feb 1;31(2):table of contents. PMID: 18246980; PMCID: PMC2276123.

> c. Amphetamine, methamphetamine, dextroamphetamine, and methylphenidate are effective for treatment of daytime sleepiness due to narcolepsy [4.1.1.1] (Guideline).
>
> This recommendation is unchanged from the previous recommendation. These medications have a long history of effective use in clinical practice

"AASM Updates Guidance on the Treatment of Narcolepsy & Other Hypersomnias", Sleep Review, Sep 5, 2021; https://sleepreviewmag.com/sleep-disorders/hypersomnias/narcolepsy/aasm-updates-guidance-treatment-narcolepsy-hypersomnias/

> It's been more than a decade since the American Academy of Sleep Medicine (AASM) last issued guidelines for the treatment of central disorders of hypersomnolence
>
> New AASM recommendations released in August 2021 on medications to treat these disorders
>
> "The prior set of treatment recommendations was published in 2007," says Lynn Marie Trotti, MD, MSc, an associate professor of neurology at Emory University School of Medicine in Atlanta. Trotti is on the board of directors at the AASM and co-authored the new hypersomnolence recommendations.
>
> "The biggest implication of this change is that we were not able to make any recommendation for some interventions that have been widely used in clinical practice and were recommended in the 2007 guideline…" Trotti says.

Maski K, Trotti LM, Kotagal S, Robert Auger R, Rowley JA, Hashmi SD, Watson NF. **Treatment of central disorders of hypersomnolence: an American Academy of Sleep Medicine clinical practice guideline**. J Clin Sleep Med. 2021 Sep 1;17(9):1881-1893. doi: 10.5664/jcsm.9328. PMID: 34743789; PMCID: PMC8636351.

> Recommendation 6: We suggest that clinicians use dextroamphetamine for the treatment of narcolepsy in adults….these studies demonstrated clinically significant improvements in excessive daytime sleepiness
>
> Different choices may be appropriate for different patients. The clinician must help each patient determine if the suggested course of action is clinically appropriate and consistent with his or her values and preferences. …. The ultimate judgment regarding the suitability of any specific recommendation must be made by the clinician and the patient

"Understanding Unapproved Use of Approved Drugs "Off Label", **United States Federal Drug Administration**, 02/05/2018; https://www.fda.gov/patients/learn-about-expanded-access-and-other-treatment-options/understanding-unapproved-use-approved-drugs-label

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- How to use the drug to treat those specific diseases and conditions.

From the FDA perspective, once the FDA approves a drug, healthcare providers generally may prescribe the drug for an unapproved use when they judge that it is medically appropriate for their patient.

Unapproved use of an approved drug is often called "off-label" use. This term can mean that the drug is:

- Given in a different dose, such as when a drug is approved at a dose of one tablet every day, but a patient is told by their healthcare provider to take two tablets every day.

Multiple Post-Dated Scripts Can Be Written Up to 90-day Supply

Prevoznik, T. W., Deputy Assistant Administrator, Diversion Control Division, & **U.S. Department of Justice, Drug Enforcement Administration, www.dea.gov. (2020, March 20). (DEA065) Early RX Refill - OMB 3-20-20 2200 "early refills on prescriptions for controlled substances."** Usdoj.gov; U.S. DEPARTMENT OF JUSTICE, DRUG ENFORCEMENT ADMINISTRATION, Diversion Control Division. https://www.deadiversion.usdoj.gov/GDP/(DEA-DC-017)(DEA065)%20Early%20RX%20Refill%20-%20OMB%203-20-20%202200%20DAA%20approved.pdf (Annotated Link)

> Pursuant to 21 CFR 1306.12(b) "an individual **practitioner may issue multiple prescriptions authorizing the patient to receive a total of up to a 90-day supply of a schedule II controlled substance**, subject to specific conditions are met….the practitioner must sign and date the multiple prescriptions as of the date issued, (21 CFR 1306.05(a)); and, **write on each separate prescription the earliest date on which the prescription can be filled** (21 CFR 1306.12(b)(ii))….. This does not prohibit the practitioner from issuing one prescription for a 90-day supply if allowed by state law and regulation that otherwise comport with 21 CFR 1306.04(a)

Quantity Limits: No law/rule limits maximum supply; Medicaid pays for 30 days or 100 days if maintenance medication for chronic condition (Dr's discretion to define chronic)

McDermott, W. T., Assistant Administrator, Diversion Control Division, & **U. S. Department of Justice , Drug Enforcement Administration. (2020). (DEA-DC-021)(DEA073) Oral CII for regular CII scirpt (Final) +Esign a.pdf.** In *U.S. DEPARTMENT OF JUSTICE, DRUG ENFORCEMENT ADMINISTRATION, Diversion Control Division*. https://www.deadiversion.usdoj.gov/GDP/(DEA-DC-

021)(DEA073)%20Oral%20CII%20for%20regular%20CII%20scirpt%20(Final)%20+Esign%20a.pdf (Annotated Link)

> Please note that **DEA does not assign a numerical limit to the amount of schedule II controlled substance to be prescribed**. Instead, DEA recognizes that these **are medical decisions within the prescribing practitioner's sound medical discretion**

Health First Colorado Pharmacy Benefits Frequently Asked Questions - Health First Colorado. (2016, July 18). Health First Colorado. https://www.healthfirstcolorado.com/frequently-asked-questions/health-first-colorado-pharmacy-benefits/ (Annotated Link)

> Clients may receive up to a 100 day supply of maintenance medications and up to a 30 day supply of non-maintenance medications.

Early Refills: Medicaid refills CII currently after 50% of prior rx time has lapsed by default, or prior to 50% if necessary by phone request; at 85% prior to COVID19, 1x/lifetime/drug if lost; immediately if rx is a "dose increase"

Colorado Department of Health Care Policy and Financing. (2020, June 4). ***COVID-19 Guidance for Pharmacies 6/4/2020*.** https://hcpf.colorado.gov/sites/hcpf/files/COVID%20Guidance%20for%20Pharmacies%20060420.pdf (Annotated Link)

> **Early Refills**
>
> Pharmacies are able to override early refills at the point-of-sale (POS) after 50% of medication day supply has lapsed since last fill for reasons related to COVID-19. Use DUE response codes with reason for service code 'ER' at the POS to receive a paid claim. This override is not available for use by mail order pharmacies.
>
> If a member requires a refill before 50% of the day supply has lapsed, a POS override is not available. Please contact the Magellan Help Desk at 1-800-424-5725 for a one-time refill authorization.

Pharmacy Billing Manual | Colorado Department of Health Care Policy & Financing. (2022). Colorado.gov. https://hcpf.colorado.gov/pharmacy-billing-manual#rtsPol

> [Prior to COVID19] **Refill Too Soon Policy**
> For DEA Schedule 2 through 5 drugs, 85 percent of the days' supply of the last fill must lapse before a drug can be filled again. For non-scheduled drugs, 75 percent of the days' supply of the last fill must lapse before a drug can be filled again.

OTC Drugs Paid For: Aspirin and various others labeled "OTC" in the PDL

Health First Colorado Pharmacy Benefits Frequently Asked Questions - Health First Colorado. (2016, July 18). Health First Colorado. https://www.healthfirstcolorado.com/frequently-asked-questions/health-first-colorado-pharmacy-benefits/

> **Are over-the-counter (OTC) medications covered?**
> Insulin and aspirin are covered without a prior authorization. All other over-the-counter (OTC) medications require a prior authorization before approval unless an OTC is a preferred product on the Preferred Drug List (PDL).

Paper Scripts Can Be Written for CII Drugs

Electronic prescribing of controlled substances: **What physicians and practices need to know**. (2021, August 16). Cms.org; **Colorado Medical Society**. https://www.cms.org/articles/electronic-prescribing-of-controlled-substances-what-physicians-and-practic (Annotated Link)

> Physicians are exempt from the new law, 12-30-111. Electronic prescribing of controlled substances - exceptions - rules - definitions, if:
>
> - The prescriber reasonably determines that the patient would be unable to obtain controlled substances prescribed electronically in a timely manner and that the delay would adversely affect the patient's medical condition.

Pharmacist Authority: CAN dispense alternative dose; CAN dispense a substitute (non-psychotropic) drug; CAN dispense emergency refill w/o an rx

C.R.S. § 12-280-125.5 (Lexis Advance through Chapter 49 from the 2023 Regular Session and effective as of March 31, 2023. The text of this section is not final. It will not be final until compared to, and updated from, the text provided by the Colorado Office of Legislative Legal Services later this year)

> 12-280-125.5. Pharmacists' authority to dispense chronic maintenance drugs - rules - liability.
> **(1)** In accordance with board rules adopted under subsection (2) of this section, on and after January 1, 2020, a pharmacist may dispense an emergency supply of a chronic maintenance drug to a patient without a current, valid **prescription** if:

(a) The pharmacist makes every reasonable attempt but is unable to obtain authorization to refill the **prescription** from the **prescribing** health-care provider or another health-care provider responsible for the patient's care;
(b)
(I) The pharmacist has a record of a **prescription** at the pharmacy or has been presented proof of a recent **prescription** for the chronic maintenance drug in the name of the patient who is requesting the emergency supply; or
(II) In the pharmacist's professional judgment, the refusal to dispense an emergency supply of the chronic maintenance drug will endanger the patient's health or disrupt essential drug therapy for a chronic condition of the patient;
(c) The amount of the chronic maintenance drug dispensed does not exceed the amount of the most recent **prescription** or the standard **quantity** or unit of use package of the drug;
(d) The pharmacist has not dispensed an emergency supply of the chronic maintenance drug to the same patient in the previous twelve-month period; and
(e) The prescriber of the drug has not indicated that no emergency refills are authorized.

(3) A pharmacist, the pharmacist's employer, and the original prescriber of the drug **are not civilly liable** for an act or omission in connection with the dispensing of a chronic maintenance drug pursuant to this section unless the act or omission constitutes negligence, recklessness, or willful or wanton misconduct.

Law, B. (2019, October 7). **Dispensing an Emergency Supply of a Chronic Maintenance Drug Without a Prescription. Baer Law.** https://baerlaw.com/dispensing-an-emergency-supply-of-a-chronic-maintenance-drug-without-a-prescription/

Earlier this year, Colorado Governor Jared Polis signed House Bill 19-1077 Concerning Authorization for a Pharmacist to Dispense a Chronic Maintenance Drug to a Patient Without a Current Prescription in Limited Circumstances (HB 19-1077).

The new law, slated to go into effect on January 1, 2020, allows a Colorado pharmacist to dispense an emergency supply of a chronic maintenance drug to a patient without a current, valid prescription

Pharmacy Billing Manual | Colorado Department of Health Care Policy & Financing. (2022). Colorado.gov. https://hcpf.colorado.gov/pharmacy-billing-manual#rtsPol

[Medicaid pays 3 days by default] In an emergency, when a PAR cannot be obtained in time to fill the prescription, pharmacies may dispense a 72-hour supply (3 days) of covered outpatient prescription drugs to an eligible member by calling the Pharmacy Support Center (1-800-424-5725)

C.R.S. § 12-280-125.3 (Lexis Advance through Chapter 49 from the 2023 Regular Session and effective as of March 31, 2023. The text of this section is not final. It will not be final until

compared to, and updated from, the text provided by the Colorado Office of Legislative Legal Services later this year)

12-280-125.3. Pharmacists' authority - minor prescription adaptions.

(1) Except as provided in subsection (3) of this section, a pharmacist who is acting in good faith and is using professional judgment and exercising reasonable care may make the following minor adaptions to an order if the pharmacist has the informed consent of the patient for whom the **prescription** was provided:

(a) A change in the **prescribed** dosage form or directions for use of the **prescription** drug if the change achieves the intent of the **prescribing** practitioner;

(b) A change in the **prescribed quantity** of the **prescription** drug if the **prescribed quantity** is not a package size commercially available from the manufacturer;

(c) An extension of the **quantity** of a maintenance drug for the limited **quantity** necessary to achieve medication refill synchronization for the patient; and

(d) Completion of missing information on the order if there is sufficient evidence to support the change.

(2) A pharmacist who adapts an order in accordance with subsection (1) of this section shall document the adaption and the justification for the change in the patient's pharmacy record with the original **prescription** and shall notify the **prescribing** practitioner of the adaption.

(3) A pharmacist shall not adapt an order if the **prescribing** practitioner has written "do not adapt" on the **prescription** or has otherwise communicated to the pharmacist that the **prescription** must not be adapted.

C.R.S. § 12-280-125 (Lexis Advance through Chapter 49 from the 2023 Regular Session and effective as of March 31, 2023. The text of this section is not final. It will not be final until compared to, and updated from, the text provided by the Colorado Office of Legislative Legal Services later this year)

12-280-125. Substitution of prescribed drugs and biological products authorized - when - conditions.

(1)

(a) A pharmacist filling a **prescription** order for a specific drug by brand or proprietary name may substitute an equivalent drug product if the substituted drug product is the same generic drug type and, in the pharmacist's professional judgment, the substituted drug product is therapeutically equivalent, is interchangeable with the **prescribed** drug, and is permitted to be moved in interstate commerce. A pharmacist making a substitution shall assume the same responsibility for selecting the dispensed drug product as he or she would incur

in filling a **prescription** for a drug product **prescribed** by a generic name; except that the pharmacist is charged with notice and knowledge of the FDA list of approved drug substances and manufacturers that is published periodically.

(a.5)

(I) A pharmacist filling a **prescription** order for a specific drug may substitute a drug in the same therapeutic class as long as the patient agrees to the substitution and the substitution is made to replace a drug that is on back order, to ensure formulary compliance with the patient's health insurance plan, or, in the case of an uninsured patient, to lower the cost to the patient for the drug while maintaining safety.

(II) This subsection (1)(a.5) does not authorize:

(A) The substitution of biological products, narrow therapeutic index drugs, or psychotropic drugs