# P.R.N.

ISSN # 1941-9481

www.prnnewsletter.com

**No. 65** | **The Newsletter for Community Pharmacists** | **Jan/Feb, 2019**


**What's Inside…**



## FDA NEWS

### FDA Issues New Warning on Fluoroquinolones

The Food and Drug Administration (FDA) is now warning that fluoroquinolone antibiotics may increase the risk of aortic dissection. Aortic dissection is a life-threatening rupture of an aortic aneurysm, a balloon-like bulge in the main artery in the body, which can lead to dangerous bleeding and death. The agency is recommending that fluoroquinolones should not be used in patients at risk for aortic aneurysm, unless there are no other treatment options available. People at risk include:

- **Patients with a history of aortic aneurysm**
- **Patient with hypertension**
- **The elderly**
- **Patients with certain genetic disorders that involve blood vessel changes, such as Marfan syndrome and Ehlers-Danlos syndrome**

The FDA will require that a new warning about the risk of aortic aneurysm be added to the prescribing information and patient medication guides for all systemic fluoroquinolones.

## ……RX NEWS……RX NEWS……RX NEWS……RX NEWS……

**MOTEGRITY** (Prucalopride).
**Category:** Serotonin receptor agonist for the treatment of chronic idiopathic constipation.
**Initial Dose:** 2 mg once daily, with or without food.
**MDD:** 2 mg once daily, with or without food.

Shire has announced FDA approval of Motegrity (prucalopride) for the treatment of chronic idiopathic constipation (CIC) in adults. Motegrity works by activating serotonin type 4 ($5\text{-}HT_4$) receptors to stimulate colonic peristalsis, which increases bowel motility. The recommended starting and maintenance dose of Motegrity is 2 mg once daily, with or without food. Patients with severe renal impairment (CrCL <30 mL/min) should receive 1 mg once daily. The FDA-approved labeling contains a warning about suicidal ideation and behavior. Patients should be monitored for persistent worsening of depression and emergence of suicidal thoughts and behavior.

**AEMCOLO** (Rifamycin).
**Category:** Antibacterial for the treatment of travelers' diarrhea.
**Initial Dose:** 388 mg (two tablets) twice daily for three days, with or without food.
**MDD:** 388 mg (two tablets) twice daily for three days, with or without food.

Cosmo Pharmaceuticals has been granted FDA approval to market Aemcolo (rifamycin) for the treatment of adults with travelers' diarrhea caused by noninvasive strains of *E. coli*, not complicated by fever or blood on the stool. Two 194 mg tablets should be taken with a glass of liquid twice daily for three days. Do not take Aemcolo concomitantly with alcohol.

**NUZYRA** (Omadacycline).
**Category:** Tetracycline-class antibacterial.
**Initial Dose:** 450 mg once daily on day 1 and 2, followed by 300 once daily on an empty stomach.
**MDD:** 450 mg once daily.

Paratek Pharmaceuticals has received approval for a new tetracycline antibiotic, Nuzyra (omadacycline). Nuzyra, available in both intravenous and oral tablet form, is indicated for the treatment of adult patients with community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI). Treatment of CABP begins with an IV infusion loading dose and can continue with 300 mg orally once daily for 7 to 14 days. For ABSSSI, the loading dose can be IV or oral. Patients must fast for at least 4 hours before taking Nuzyra tablets, and after oral dosing no food or drink (except water) may be consumed for 2 hours, and no dairy, antacids, or vitamins for 4 hours.

**SEYSARA** (Sarecycline).
**Category:** Tetracycline-class antibacterial.
**Initial Dose:** 60 to 150 mg once daily, with or without food, depending upon patient weight.
**MDD:** 150 mg once daily, with or without food.

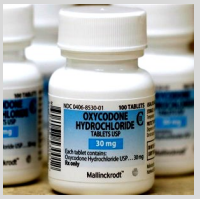
Allergan will market a new tetracycline-class antibiotic called Seysara (sarecycline). Seysara is indicated for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older. Dosing is based upon weight as follows:

| | |
|---|---|
| **33 to 54 kg** | **60 mg once daily** |
| **55 to 84 kg** | **100 mg once daily** |
| **85 to 136 kg** | **150 mg once daily** |

## FDA Issues Warning Letter to McKesson Over Illegitimate Products

On February 7, 2019, the Food and Drug Administration (FDA) delivered a warning letter to the McKesson Corporation, the nation's largest pharmaceutical drug distributor. The warning involved the drug wholesaler's alleged failure to take required action after being notified by pharmacies of illegitimate products received from McKesson. The key incidents described in the letter involved schedule II controlled substances:

- **Between September and October of 2016, three different Rite Aid pharmacies in Michigan received bottles of 100 oxycodone 30 mg tablets, made by Mallinckrodt, which were found to contain no oxycodone. The bottles instead contained 15 generic Aleve (naproxen) tablets.**
- **McKesson's own internal investigation concluded that the bottles were likely tampered with while in possession or control of McKesson.**




The FDA determined that the wholesaler failed to take the legally required corrective actions, including quarantining all products with identical lot numbers and notifying any other pharmacies that may have received products from those lots. McKesson has 15 days to notify the FDA of specific steps that have been taken to correct the violations identified in the warning letter.

# MEDICAID UPDATE

*Information Regarding the New York State Medicaid Program*

**Updates to the Dispense Brand Name Drug when Less Expensive than Generic Program**

There have recently been several updates to the Dispense Brand Name Drug when Less Expensive than Generic Program, including 2 additions and 1 deletion:

**Additions**
**Canasa**
**Elidel**

**Deletions**
**Adderall XR**

Prescriptions for drugs in the program **do not require** *"DAW"* or *"Brand Medically Necessary"* on the prescription, and have a generic copayment. If a drug is removed from the program, a new prescription is not required. The current list of drugs in the program is as follows:

**Adcirca**
**Aggrenox**
**Albenza**
**Alphagan P 0.15%**
**Androgel**
**Butrans**
**Canasa**
**Catapres-TTS**
**Cellcept Susp**
**Cipro oral suspension**
**Copaxone 20 mL SQ**
**Elidel**
**Exelon patch**
**Focalin**
**Focalin XR**
**Fosrenol chewable tablets**
**Gleevec**
**Hepsera**
**Kapvay**
**Kitabis**
**Lexiva tablets**
**Methylin solution**
**Norvir tablets**
**Protopic**
**Pulmicort respules 1 mg**
**Retin-A cream**
**Suboxone 8mg/2mg film**
**Suprax suspension**
**Sustiva tablets**
**Tegretol Suspension**
**Tobradex suspension**
**Transderm-Scop**
**Trizivir**
**Voltaren gel**
**Xeloda**
**Zyflo CR**

# LAW REVIEW

*Regulatory Issues Affecting Pharmacy in New York State*

## Medicare Part D Implements Opioid Overutilization Policies

Effective January 1, 2019, the Centers for Medicare and Medicaid Services (CMS) has implemented new policies for all Medicare Part D drug plans in an effort to address the ongoing opioid epidemic. The policies include both real-time safety alerts at the time of dispensing, and drug management programs aimed at reducing chronic high-risk opioid use.

### Real-time Safety Alerts at the Time of Dispensing

- **7 day supply limit for opioid naïve patients:** Part D plans will implement a hard stop edit to limit the initial dispensing of opioid medications to a 7 day supply or less. This policy will apply to Medicare patents who have not filled an opioid prescription recently (for example, within the past 60 days). A pharmacist can dispense partial quantities of an opioid prescription consistent with state and federal regulations (see this month's ***Ask PRN*** for a discussion of applicable New York State law), but if the prescriber believes that an opioid naïve patient will require more than a 7 day supply initially, they can request a coverage determination on behalf of the patient. Pharmacists in New York will already be familiar with this policy, as the 7 day limit for initial opioid prescriptions has been in effect for all patients in the state, not just those on Medicare, since July of 2016 (see ***PRN*** #55 in the archive section of our website for details).
- **Opioid care coordination alert:** This alert, not a hard stop, will be triggered whenever a patient presents a prescription which would cause their cumulative morphine milligram equivalent (MME) dose per day, across all of their opioid prescriptions, to reach or exceed 90 MME (for a discussion of MMEs and a dose conversion chart, see this month's ***Feature Article***). Regardless of whether individual prescriptions are written below the threshold, the alert will be activated by the fill of the prescription that causes the 90 MME threshold to be reached or exceeded, and it is the *prescriber who writes the prescription that triggers the alert who should be contacted by the pharmacy*. In reviewing the alert, the pharmacist may consult with the prescriber to confirm the need for the higher MME. The pharmacist can then indicate that the prescriber was consulted so that the prescription claim can pay.

### Drug Management Programs

- **Patient-specific point of sale (POS) claim edit:** this is an individualized POS edit for specific patients ("at risk") and specific drugs ("frequently abused"). The limitation could be a restriction on all frequently abused drugs or limitations to specific drugs and/or specific amounts, which the plan will determine on a case-by-case basis. For 2019, CMS has identified opioids and benzodiazepines as frequently abused drugs, and potential at-risk patients are identified by their opioid use which involves multiple doctors and pharmacies.
- **Pharmacy limitation (also known as "pharmacy lock-in"):** this limitation will require the patient to obtain prescriptions for frequently abused drugs at a particular pharmacy. Before implementing this limitation, the plan must verify with a prescriber that a patient is at risk, but is not required to obtain a prescriber's agreement to the limitation. Patients can choose which pharmacy they prefer to use and may update their preference as needed.
- **Prescriber limitation (also known as "prescriber lock-in"):** this limitation will require the patient to obtain their prescriptions for frequently abused drugs from a certain prescriber. The plan must obtain the prescriber's agreement to be a prescriber and confirm the prescriber's selection for this limitation. Patients can choose which prescriber they prefer to use and may update those preferences as needed.

FEATURE ARTICLE...

# Morphine Milligram Equivalents: Rationale and Calculation

**In March of 2016,** the Centers for Disease Control and Prevention (CDC) released guidelines for prescribing opioids for chronic pain. Among other recommendations, the guidelines set specific parameters for opioid dosing based upon morphine milligram equivalents/day (MME). Those parameters have now been used as the basis for the new Medicare Part D opioid overutilization policies discussed in this month's ***Law Review*** (see page 3). Below is a discussion of the rationale behind limiting MME, as well as information on calculating MME for a variety of opioid medications.

## CDC Recommendations on Opioid Use

The 2016 Guideline for Prescribing Opioids for Chronic Pain, published by the CDC, contained a number of recommendations for prescribers. If it is determined that opioids are appropriate, the CDC suggests the following:

- **Use immediate-release opioids when starting therapy**
- **Start low and go slow**
- **When opioids are needed for acute pain, prescribe no more than needed**
- **Do not prescribe ER/LA opioids for acute pain**
- **Follow-up and re-evaluate risk of harm; reduce dose or taper and discontinue if needed**

The Guideline then discussed evidence on the dangers associated with increasing MME dosing.

## Rationale for Limiting MME Dose/Day

In their 2016 guideline, the CDC cited clinical evidence reviews which assessed the risks involved in increasing the number of morphine milligram equivalents per day prescribed to patients. The highlights of these reviews included:

- **A randomized trial found no difference in pain or function between a more liberal opioid dose escalation strategy and maintenance of current dosage (these groups were prescribed average doses of 52 and 40 MME/day respectively).**
- **Higher opioid doses are associated with increased risk for motor vehicle injury, opioid use disorder, and overdose.**
- **Dosages of 50 to <100 MME/day increase risk for overdose by factors of 1.9 to 4.6 compared with doses of 1 to <20 MME/day.**
- **Dosages ≥100 MME/day increase risk of overdose up to 8.9 times the risk at 1 to <20 MME/day.**
- **A Veteran's Administration study showed that the mean opioid dosage of patients who died from overdose was 98 MME/day.**

## Calculating MME/day

Using the chart on the right hand side of this page, pharmacists may easily calculate a patient's MME/day dosage. Simply multiply the total milligrams per day of each opioid by the conversion factor given, then add them together (if more than one opioid is prescribed). For example, if a patient is prescribed **Oxycodone ER 10 mg twice a day** and **Oxycodone IR 10 mg four times a day**:

**20 mg ER x 1.5 = 30 MME/day *plus* 40 mg IR x 1.5 = 60 MME/day**

**Total MME/day is 90**

## MME Conversion Chart

| Opioid Drug | Conversion factor |
|---|---|
| Butorphanol | 7 |
| Codeine | 0.15 |
| Dihydrocodeine | 0.25 |
| Fentanyl patch (mcg/hour)[1] | 2.4 |
| Hydrocodone | 1 |
| Hydromorphone | 4 |
| Levorphanol tartrate | 11 |
| Meperidine hydrochloride | 0.1 |
| Methadone[2] | 3 |
| > 0 mg to ≤ 20 mg | 4 |
| > 20 mg to ≤ 40 mg | 8 |
| > 40 mg to ≤ 60 mg | 10 |
| > 60 mg | 12 |
| Morphine | 1 |
| Opium | 1 |
| Oxycodone | 1.5 |
| Oxymorphone | 3 |
| Pentazocine | 0.37 |
| Tapentadol | 0.4 |
| Tramadol | 0.1 |

1. The MME conversion factor for fentanyl is based on the assumption that 1 mg of parenteral fentanyl is equal to 100 mg of morphine. Therefore a 25 mcg/hour patch x 24 hours = 600 mcg/day of fentanyl is equivalent to 60 MME/day and 60/25 = 2.4 conversion factor.

2. The CDC conversion factor for methadone is 3, but calculating the MME in clinical practice involves using a sliding scale whereby the conversion factor increases with increasing dose.

P.R.N.

**P.R.N.** (ISSN # 1941-9481)
is published bi-monthly by:
PRN Publishing LLC
7636 113th Street
Suite 6C
Forest Hills, New York 11375
Phone & Fax (718) 263-4632

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# ASK PRN...

**The new Medicare Part D opioid overutilization policies limit initial opioid prescriptions to a 7-day supply. In the case of a prescription that is rejected by a Part D plan due to a quantity greater than 7 days, what options does the pharmacist have in filling the prescription?**

In such an instance, the pharmacist may, of course, contact the prescriber to request that a new prescription be issued for a 7-day supply only. However, the CDC states in their guidance that "*a pharmacist can dispense partial quantities of an opioid prescription consistent with state and federal regulations*[1]." In New York State, regulations differ depending upon the schedule of the medication. For schedule II opioids, reducing the quantity of the prescription to a 7-day supply would require authorization from the prescriber, and the remainder of the original quantity would be voided.

For opioids in schedules 3 through 5, partial filling of the prescription (e.g., a 7-day supply) is permitted under section 80.74 of thr Rules and Regulations on Controlled Substances in New York State, which states the following:

1. **Each partial filling is recorded in the same manner as a refill.**
2. **The total quantity dispensed does not exceed the total quantity prescribed for a 30 day period.**

Note that "recorded in the same manner as a refill" refers to documentation, but *does not add any refills*. Any quantity remaining from a partial fill or partial refill must be dispensed within the 30 day life of that fill or refill; after 30 days any remaining quantity on that particular fill or refill is voided.

**GOT QUESTIONS? WE HAVE ANSWERS!**
**Send your questions to us at:**
***askprn@prnnewsletter.com***

*PRN welcomes your questions on any topics relating to the practice of pharmacy. All answers are researched by our staff and, when necessary, discussed with the appropriate regulatory agencies. The information provided is not intended as legal advice, nor is it a substitute for professional judgment in clinical practice.*

## DID YOU KNOW?

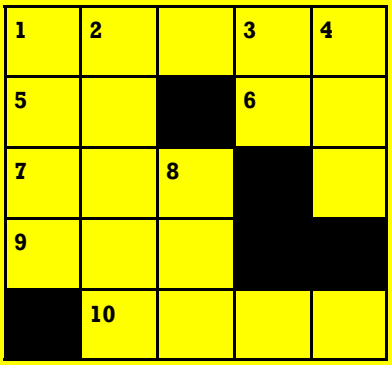
**DID YOU KNOW** that the opium trade in the 19th century led to not one, but two wars (the "opium wars" of 1839 and 1856), and resulted in Hong Kong becoming a British colony? In the early 1800s foreign traders, chiefly British, had been illegally importing opium into China from India, leading to widespread addiction (an earlier version of the opioid crisis?). When the ruling Qing dynasty attempted to cut off this lucrative trade, the British navy intervened and was eventually successful, leading to the Treaty of Nanjing, in which China ceded Hong Kong island to the victors, a territory Britain ruled for 156 years before returning it to Chinese control on July 1, 1997.

## PHARMACY FUN

**It's crossword puzzle time here at *Pharmacy Fun*! The first reader to submit the correct answers to *puzzle@prnnewsletter.com* wins a set of *PRN* stylus pens.**

***Across:***
**1. The mother of all narcotics**
**5. Doctor of osteopathy**
**6. OTC morphine derivative**
**7. Office of professional discipline**
**9. Pharmacist, in other words**
**10. Both Goodman *and* Gilman taught here**

***Down:***
**1. Spironolactone's is minty!**
**2. *Papaver somniferum***
**3. Ut dictum**
**4. No more than 90 a day, according to Medicare**
**8. Docosohexaenoic acid**




Answers to last month's **PHARMACY FUN**:
1. Voltaren 2. Maalox 3. Soma 4. Colcrys 5. Geodon 6. Montelukast

**References:**
1. https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/SE18016.pdf (page 2).