Pharmacy Policy Bulletin

Title: Opioid Policy

Policy #: Rx.01.197

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for prior authorization, morphine milligram equivalent (MME) limit, quantity limits, and days' supply for opioid analgesics, buprenorphine containing medication assistant treatments, and butalbital containing headache medications as provided under the member's prescription drug benefit.

Description:

Opioid analgesics are classified as full agonists, mixed agonist-antagonists, or partial agonists by their activity at opioid receptors. There are three major classes of opioid receptors in the central nervous system (CNS): mu, kappa, and delta. Mu-receptor activation causes analgesia, respiratory depression, miosis, reduced GI motility, and euphoria. Kappa-receptor activation also causes analgesia, but may also produce effects such as dysphoria and hallucinations, which limit use. Delta-receptor activation produces some analgesia but may also cause seizures at high doses and has some antidepressant effects. Morphine-like opioid agonists have activity at the mu, kappa, and delta receptors, but have the highest affinity for the mu receptors[1]. Opioid agonists include natural opium alkaloids (e.g., codeine, morphine), semisynthetic analogs (e.g., hydrocodone, hydromorphone, oxycodone, oxymorphone), and synthetic compounds (e.g., fentanyl, levorphanol, methadone, sufentanil, tapentadol, tramadol). There is no defined maximum dose for most opioids. The ceiling to analgesic effectiveness is imposed only by adverse reactions. Adverse effects of opioids include constipation, nausea and vomiting, dizziness, sedation, respiratory depression[2]. Long-term use of high dose narcotics may also have significant adverse effects including but not limited to endocrinological effects, such as, hypogonadism, impotence in males, menstrual irregularities, and galactorrhea in women; and opioid induced hyperanalgesia caused by damage to the nociceptors thus increasing pain sensitivity[3].

Opioid analgesics are commonly prescribed in pain management. Pain is classified into non-cancer and cancer related pain. Non-cancer related pain may be acute or chronic while cancer-related pain may be a mixture of both[2]. When using opioid agents to manage pain, the choice should be made based on patient acceptance, pain intensity, analgesic effectiveness, pharmacodynamic, pharmacokinetic and side effect profiles. Like the treatment of many disease states, pain treatment should be initiated with the most effective agent with minimal side effects. Prior to starting patient on opioid pain management, pain severity and intensity should be thoroughly assessed using patient medical history, physical examination and different pain assessment tools[4]. In the management of mild non-cancer pain, the American Pain Society recommends the use of non-opioid analgesics such as acetaminophen and NSAIDs as first line agents. If pain relief is not adequate, opioid analgesics could be considered as the next line of treatment. Combination treatments of opioid with acetaminophen or NSAIDs are recommended when treating moderate to severe non-cancer pain. Common opioid analgesics like oxycodone and hydrocodone are often co-formulated with acetaminophen or NSAIDs and have a maximum dose to limit the amount of acetaminophen and NSAIDs exposure. It is recommended not to exceed 4000 mg of acetaminophen per day, 3200 mg of ibuprofen or 4000 mg (3900mg for controlled-, extended-, and delayed-release products) of aspirin daily.

Pain that is associated with cancer or a malignant condition is known as cancer related pain. Cancer related pain may be acute and/or chronic. Pain related to cancer is usually the result of damage to parts of the body from cancer metastasis or therapies such as chemotherapy, radiation and surgical procedures. Opioid analgesics play an important role in pain management for oncology patients. The World Health Organization (WHO) developed a pain relief regimen known as the WHO's Pain Relief

Ladder which provides guidelines for pain management in cancer patients[5]. Like non-cancer related pain, opioid analgesics are reserved for moderate to severe cancer pain. Patients with mild pain should try non-opioid analgesics such as acetaminophen, ibuprofen, or naproxen first. Opioid agents or opioid combination are reserved for moderate to severe cancer pain or when inadequate pain relief is not achieved with non-opioid analgesics.

The potency of opioids is not consistent across all medications. Morphine milligram equivalents (MME) is a conversion factor used to standardize the dose of an opioid into the equivalent dose of morphine to easily compare doses of different opioid agents and assess the risk of the doses. Conversion factors are included in the table below.

Several utilization tools are in place to prevent abuse and overuse of opioids. These include MME limits, days' supply limits, and quantity limits.

1. MME limits: MME Limits are in place to limit the total dosage of opioids a patient can receive in a day. Regimens, whether single drug or multiple drugs, that exceed 90 MME are subject to MME limit. Higher doses of opioids, along with other factors, are associated with increased risk of opioid overdose. The threshold of 90 MME is based on the recommendations from the Centers for Disease Control and Prevention: "When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day."
2. Days' Supply Limits: Day supply limits are in place to limit the total days a patient can receive opioids. "The probability of long-term opioid use increases most sharply in the first days of therapy, particularly after 5 days or 1 month of opioids have been prescribed," according to the Centers for Disease Control and Prevention (CDC). Long-term opioid use often begins with treatment of acute pain. To address these statistics, all opioids individual opioids with a dose less than or equal to 90 morphine milligram equivalents (MME) are subject to 5 days' supply limit. Continuation beyond five days requires review.
3. Quantity Limits: Quantity limits are in place to optimize doses and achieve the prescribed dose using the least number of tablets, capsules, patches, films, liquids, suppositories, etc. that a patient can receive in a day. Opioids are subject to limits on the quantity per day. While opioid doses are variable and may have no true maximum, quantity limits are in place to address safety concerns, including abuse, addiction, and diversion. The limits in this policy restrict quantities to either the daily MME of 90 mg of a single agent or the FDA limit of additional product components such as 4 grams of acetaminophen, 3.2 grams of ibuprofen or 4 grams of aspirin

Morphine Milligram Equivalent (MME) Conversion Factors for Commonly Prescribed Opioid Analgesics

Opioid Oral Morphine Milligram Equivalent (MME) Conversion Factors[12]	
Type of Opioid (strength units)	**MME Conversion Factor**
Buprenorphine film/tablet (mg)	30
Buprenorphine patch (mcg/hr)	12.6
Buprenorphine film* (mcg)	0.03
Butorphanol (mg)	7
Codeine (mg)	0.15
Dihydrocodeine (mg)	0.25
Fentanyl buccal or SL tablets, or lozenge/troche5 (mcg)	0.13
Fentanyl film or oral spray (mcg)	0.18
Fentanyl nasal spray (mcg)	0.16
Fentanyl patch** (mcg)	7.2
Hydrocodone (mg)	1
Hydromorphone (mg)	4
Levorphanol tartrate (mg)	11
Meperidine hydrochloride (mg)	0.1
Methadone (mg) >0, <= 20 >20, <=40 >40, <=60 >60	3 4 8 10 12
>0, <= 20	4
>20, <=40	8
>40, <=60	10
>60	12
Morphine (mg)	1

Opium (mg)	1
Oxycodone (mg)	1.5
Oxymorphone (mg)	3
Pentazocine (mg)	0.37
Tapentadol (mg)	0.4
Tramadol (mg)	0.1

These conversion factors will be used to determine the MME/day of all opioids being prescribed. Calculate the total daily dose of the opioid in the left column and multiply by the conversion factor to determine to MME/ day. If multiple agents are being used, add the MME of the individual agents to get the total MME of the regimen. These values do not constitute clinical guidance or recommendations for converting patients from one form of opioid analgesic to another. Extra caution applies to methadone (conversion factor depends on dose) and fentanyl (patches are dosed in mcg/hour rather than mg/day). Please consult the manufacturer's full prescribing information for such guidance.

[12] These conversion factors are based on CMS "Opioid Oral Morphine Milligram Equivalent (MME) Conversion Factors" found here: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-Aug-2017.pdf

[*]The MME conversion factor for buprenorphine patches is based on the assumption that one milligram of parenteral buprenorphine is equivalent to 75 milligrams of oral morphine and that one patch delivers the dispensed micrograms per hour over a 24 hour day. Example: 5 ug/hr buprenorphine patch X 24 hrs = 120 ug/day buprenorphine = 0.12 mg/day = 9 mg/day oral MME. In other words, the conversion factor not accounting for days of use would be 9/5 or 1.8. However, since the buprenorphine patch remains in place for 7 days, we have multiplied the conversion factor by 7 (1.8 X 7 = 12.6). In this example, MME/day for four 5 µg/hr buprenorphine patches dispensed for use over 28 days would work out as follows: Example: 5 ug/hr buprenorphine patch X (4 patches/28 days) X 12.6 = 9 MME/day. Please note that because this allowance has been made based on the typical dosage of one buprenorphine patch per 7 days, you should first change all Days Supply in your prescription data to follow this standard, i.e., Days Supply for buprenorphine patches= # of patches x 7

[**]The MME conversion factor for fentanyl patches is based on the assumption that one milligram of parenteral fentanyl is equivalent to 100 milligrams of oral morphine and that one patch delivers the dispensed micrograms per hour over a 24 hour day. Example: 25 ug/hr fentanyl patch X 24 hrs = 600 ug/day fentanyl = 60 mg/day oral morphine milligram equivalent. In other words, the conversion factor not accounting for days of use would be 60/25 or 2.4. However, since the fentanyl patch remains in place for 3 days, we have multiplied the conversion factor by 3 (2.4 X 3 = 7.2). In this example, MME/day for ten 25 µg/hr fentanyl patches dispensed for use over 30 days would work out as follows: Example: 25 ug/hr fentanyl patch X (10 patches/30 days) X 7.2 = 60 MME/day. Please note that because this allowance has been made based on the typical dosage of one fentanyl patch per 3 days, you should first change all Days Supply in your prescription data to follow this standard, i.e., Days Supply for fentanyl patches= # of patches X 3.

Butalbital containing products in tension-type headache

Butalbital is a barbiturate that is commonly prescribed in combination with acetaminophen and caffeine to treat different types of headaches such as tension-type and migraines. It works by decreasing motor activity and depress the sensory cortex causing CNS depression ranging from sedation to general anesthesia[6]. The analgesia effect of barbiturate is unknown. However, there are limited studies that show the efficacy of butalbital in the treatment of tension type headache and migraine[7]. In addition, overuse of barbiturate products could lead to dependency, withdrawal, and drug-induced headache. Therefore, when selecting a treatment for tension-type headache as well as other types of headaches, butalbital containing products should only be used if first line analgesics like acetaminophen or NSAIDs provide insufficient relief. In acute management, butalbital products should not be used more than 3 days[7].

Opioid Containing Cough and cold products

Opioid containing cough and cold products are thought to suppress cough via action on the central cough center. While the products are widely used, data are limited regarding efficacy. Like opioids used to treat pain, cough and cold products containing an opioid are subject to days' supply limits, quantity limits, and morphine milligram equivalent (MME) limits.

Days' Supply and Quantity limits

Quantity limits are designed to allow a sufficient supply of medication based upon FDA-approved or medically accepted maximum daily doses and length of therapy of a particular drug. Quantity limits may be expressed as quantity over time or maximum daily dose. Additionally, there are some medications to which a limit on the days' supply is applied.

A. **Quantity over time:** This quantity limit is based on dosing guidelines over a rolling time period, usually 30 days.
B. **Maximum daily dose** (maximum quantity per day): This quantity limit is based on maximum number of units of the drug allowed per day.
C. **Days' supply limit:** This limits the numbers of days of therapy within a defined period of time. Maximum daily dose applies to days' supply limits.

Summary Of Utilization Managment

Summary Table of Criteria on Opioid Medications			
Criteria	**Short Acting Opioids**	**Long Acting Opioids (including opioid patches)**	**Transmucosal Immediate Release Fentanyl (TIRF)**
MME Limit	**Yes**	**Yes**	**Yes**
Day Supply Limit	**Yes***	**No**	**No**
Quantity Limit	**Yes**	**Yes**	**Yes**
Opioid Prior Authorization	**No***	**Yes**	**Yes**

***Note**: short-acting opioids are available without prior authorization for two 5-day supplies within 60 days or less. Greater than a total of a 10 day supply within 60 days requires prior authroization.

Policy:

PRIOR AUTHORIZATION

I. Transmucosal Immediate Release Fentanyl (TIRF) Product fentanyl citrate is considered medically necessary as follows:

A. INITIAL CRITERIA [Authorization duration: 1 year]: Transmucosal Immediate Release Fentanyl (TIRF) Products are considered medically necessary when there is documentation of ALL of the following:

a. Use for breakthrough pain associated with active cancer treatment or cancer not in remission in members who are receiving long-acting opioid therapy; and
b. Member is 18 years of age or older (16 years of age and older for fentanyl citrate); and
c. Member is tolerant to current opioid therapy (i.e., adherence to one of the following regimens for one week or longer: 25mcg of transdermal fentanyl hourly, 30mg of oxycodone daily, 60mg of oral morphine daily, 8mg of oral hydromorphone daily, 25mg of oral oxymorphone daily; or an equianalgesic dose of another opioid)

B. REAUTHORIZATION CRITERIA [Authorization duration: 1 year]: Transmucosal Immediate Release Fentanyl (TIRF) product is re-approved when there is documentation of continued use for breakthrough pain associated with active cancer treatment or cancer not in remission in members who are currently receiving long-acting opioid therapy

II. Opioid regimens containing greater than 90 morphine milligram equivalents per day, long acting opioids, and short acting opioids for continuation beyond 30 days [Authorization duration: 1 year] - are considered medically necessary as follows:

A. INITIAL CRITERIA: The requested product or regimen is considered medically necessary when there is ONE of the following

1. Pain associated with active cancer treatment, cancer not in remission, or sickle cell anemia OR
2. Severe, persistent chronic pain with documentation of diagnosis associated with pain and ALL of the following:

i. Documentation of a current patient-prescriber opioid treatment agreement (signed within one year of request); and

ii. ONE of the following
    1. Regimen prescribed by or in consultation with a pain management specialist within last 6 months. Must provide name of physician and date of last visit. Physician must be Board Certified by one of the following:
        a. American Board of Anesthesiology- Pain Management; or
        b. American Board of Psychiatry & Neurology- Pain Management; or
        c. American Board of Physical Medicine & Rehabilitation; or
        d. American Osteopathic Association- Pain Management

        OR

    2. The member has been evaluated for at least TWO of the following therapies:
        i. Physical therapy; or
        ii. Psychotherapy; or
        iii. Adjuvant medications specific to causative condition including but not limited to any of the following: antidepressants, anticonvulsants, muscle relaxants, anti-inflammatory agents;

B. REAUTHORIZATION CRITERIA [Authorization duration: 1 year]: Re-authorization of the requested opioid product or regimen containing greater than 90 morphine milligram equivalents per day, long acting opioids, and short acting opioids for continuation beyond 30 days is considered medically necessary when there is documentation of ONE of the following:

1. Pain associated with active cancer treatment, cancer not in remission, or sickle cell anemia AND documentation that a urine drug screen (UDS) will be performed by prescriber within 1 year of request.

OR

2. Severe, persistent chronic pain with documentation of diagnosis associated with pain and ALL of the following:

a. Documentation of a current patient-prescriber opioid treatment agreement (signed within one year of request); and
b. Documentation that a urine drug screen (UDS) will be performed by prescriber within 1 year of request.

III. Appropriate Utilization with Medication Assistant Treatments (MAT) for opioid use disorder
- [Authorization duration: 2 months] - Opioid analgesics will require prior authorization for medical necessity when filled within two months of a paid claim for either buprenorphine/naloxone (Bunavail®/Suboxone®/Zubsolv®) or buprenorphine sublingual tablet. Opioid analgesic products are approved in patients that have received buprenorphine/naloxone or buprenorphine in the previous two months when there is documentation of a treatment plan showing discontinuation of buprenorphine containing MAT.

DAYS' SUPPLY AND QUANTITY LIMITS

I. Day supply limit Criteria

A. Short-acting opioids for short term use (greater than two 5-day fills within 60 days for 18 and older, and greater than two 3-days fills within 60 days for age less than 18) [Authorization duration: 1 month for a 30 day supply] - an exception is approved when ALL of the following are met:

1. **INITIAL CRITERIA**

a. Diagnosis of acute pain; and
b. Prescriber reviewed member's history in state Prescription Drug Monitoring Program website; and
c. Prescriber counseled member (or member's representative) on risk of addiction; and
d. Substance abuse screening done by prescriber

2. **REAUTHORIZATION CRITERIA** see **Opioid regimens containing greater than 90 morphine milligram equivalents per day, long acting opioids, and short acting low dose opioids for continuation beyond additional 30 days Prior Authorization** criteria under section II.A above.

B. Opioid containing cough and cold products are limited to two five (5) day fills within 60 days for 18 and older and two three (3) day fills within 60 days for age less than 18 - an exception is approved when

1. INITIAL CRITERIA: there is documentation of inadequate response or inability to tolerate non-opioid therapies for the indication [Authorization duration 1 month]

2. REAUTHORIZATION CRITERIA: Documentation the underlying etiology of cough has been identified and treated, if applicable (e.g. allergic rhinitis, asthma, GERD) [Authorization duration 6 months]

C. Butalbital containing headache products are limited to one five (5) day fill within 30 days. Opioid containing headache products are limited to one three (3) day fill within 30 days for less than 18 years of age - an exception is approved as follows:

1. **INITIAL CRITERIA** [Authorization duration: 3 months]: All of the following:

    a. Diagnosis of one of the following:

        i. Tension-type or muscular headache

        ii. Migraine headache

    b. Member is 12 years of age or older

    c. Inadequate response or inability to tolerate TWO of the following:

        i. At least two triptans

        ii. Non-steroid anti-inflammatory drugs (e.g. ibuprofen, naproxen)

        iii. Neuroleptics (e.g. prochlorperazine, metoclopramide)

        iv. Dihydroergotamine

2. **REAUTHORIZATION CRITERIA:** [Authorization duration: 1 year]: All of the following:

    a. Diagnosis of one of the following:

        i. Tension-type or muscular headache

        ii. Migraine headache

    b. Member is 12 years of age or older

    c. Prescribed by or in consultation with a neurologist or a headache specialist, or pain specialist

    d. Inadequate response or inability to tolerate NSAIDs

    e. Ongoing assessment of medication-overuse headache

II. Quantity limit Criteria

A. Opioid pain products [authorization duration= 1 year] An increased quantity of an opioid medication is approved when there is documentation of ALL of the following:

1. Current patient-prescriber opioid treatment agreement (signed within one year of request); and

2. The requested dose and frequency do not exceed FDA approved dosing or are supported by compendia; and

3. ONE of the following:

a. The dose cannot be achieved with commercially available clinical dosage forms; or

b. Documentation indicating medical necessity for a quantity that exceeds the plan limit (e.g. GI malabsorption)

B. Cough and cold products [Authorization duration: 1 month for initial; 6 months for reauthorizations] - An increased quantity of an opioid containing cough and cold medication is approved when there is documentation of ALL of the following:

1. The requested dose and frequency do not exceed FDA approved dosing or are supported by compendia; and
2. Documentation of diagnosis requiring long-term therapy with requested cough/ cold medications; and
3. Inadequate response or inability to tolerate non-opioid therapies for the indication

C. Butalbital containing headache products [Authorization duration:1 year] - An increased quantity of a butalbital containing headache medication is approved when there is documentation of ALL of the following:

1. The requested dose and frequency do not exceed FDA approved dosing or are supported by compendia; and
2. Inadequate response or inability to tolerate prophylactic therapy; and
3. Prescribed by or in consultation with a neurologist, headache specialist or pain specialist

D. Buprenorphine/ naloxone (Bunavail®/Suboxone®/Zubsolv®) and buprenorphine sublingual tablet [Authorization duration: 6 months]**:** buprenorphine/ naloxone or buprenorphine for the treatment of opioid use disorder are approved in quantities greater than those specified in the policy when ALL of the following are met:

1. The requested dose and frequency do not exceed FDA approved dosing or are supported by compendia; and
2. The dose cannot be achieved with commercially available dosage forms; and
3. Inadequate response to lower doses

Black Box Warning:

1. Respiratory depression: [21, 22, 30, 31, 32, 33, 34, 35, 40, 43] **TIRFs (Actiq®, Fentora®, Subsys®), Lazanda®, Duragesic®, Hydromorphone (Dilaudid, Exalgo®), Methadone, Morphine Sulfate: Arymo™ ER, Avinza®, Kadian®, and MS Contin®, Morphabond ER®, Nucynta ER®/ Opana ER®, Oxycodone (Oxycontin®, oxycodone concentrate, Oxaydo™, Roxybond®), Zohydro ER™ (hydrocodone ER), Buprenorphine (Belbuca and Butrans), benzhydrocodone/acetaminophen (Apadaz®), codeine polistirex and chlorpheniramine (Tuzistra XR), codeine phosphate and chlorpheniramine maleate (Tuxarin®), levorphanol, Qdolo® (tramadol), Seglentis® (tramadol/celecoxib)**

Fatal respiratory depression has occurred in patients treated with the above listed opioid products, including following use in opioid-intolerant patients and improper dosing. Be sure to monitor for sign and symptoms of respiratory depression, especially during initiation of the drugs. The substitution of fentanyl sublingual/buccal for any other fentanyl product may result in fatal overdose. Because of the risk of respiratory depression, fentanyl products are contraindicated for use as an as-needed analgesic, or in the management of acute or postoperative pain, including headache/migraine and in opioid-intolerant patients. In addition, the concomitant use of fentanyl sublingual with CYP3A4 inhibitors may result in an increase in fentanyl plasma concentrations and may cause potentially fatal respiratory depression.

For hydromorphone and ER products like morphine ER, oxycodone ER, hydrocodone ER, tapentadol ER, and oxymorphone ER products, instruct patients to swallow a whole tablet. Crushing, chewing, snorting, or dissolving tablets can cause rapid release and absorption that could lead to fatal overdose and even death. Note: Avinza® capsule contents may be sprinkled on applesauce and swallowed without chewing[19]. Hydromorphone is a potent Schedule II controlled opioid agonist. Schedule II opioid agonists have the highest potential for abuse and risk of producing respiratory depression. Alcohol, other opioids, and CNS depressants (sedative-hypnotics) potentiate the respiratory depressant effects of hydromorphone, increasing the risk of respiratory depression that might result in death.

2. Medication errors: [32, 33] **TIRFs (Actiq®, Fentora®, Subsys®), Lazanda®, codeine phosphate and chlorpheniramine maleate (Tuxarin®), codeine polistirex and chlorpheniramine (Tuzistra XR), Qdolo® (tramadol)**

Substantial differences exist in the pharmacokinetic profile of fentanyl sublingual/buccal compared with other fentanyl products that result in clinically important differences in the extent of absorption of fentanyl that could result in fatal overdose. When prescribing, do not convert patients on a mcg-per-mcg basis from any other fentanyl products to fentanyl sublingual/buccal. When dispensing, do not substitute a fentanyl sublingual/buccal prescription for other fentanyl products.

3. Addiction and Abuse potential: [21, 22, 30, 31, 32, 33, 34, 42, 43] **TIRFs (Actiq®, Fentora®, Subsys®), Lazanda®, Duragesic®, Hydromorphone (Dilaudid, Exalgo®), Methadone, Morphine Sulfate: Arymo™ ER, Avinza®, Kadian®, and MS Contin®, Morphabond ER®, Nucynta ER®/ Opana ER®, Oxycodone (Oxycontin®, oxycodone concentrate, Oxaydo™, Roxybond®), Zohydro ER™ (hydrocodone ER), Buprenorphine (Belbuca and Butrans), benzhydrocodone/acetaminophen (Apadaz®), codeine phosphate and chlorpheniramine maleate (Tuxarin®), codeine polistirex and chlorpheniramine (Tuzistra XR), levorphanol, Qdolo® (tramadol), Seglentis® (tramadol/celecoxib)**

All opioid analgesics regardless of formulation are classified as Schedule II controlled substance, with high abuse liability. They expose patients and drug users to the risk of opioid addiction, abuse, and misuse, which can lead to overdose and death. Diversion, addiction, and abuse potential should be considered when prescribing or dispensing opioid analgesics. Providers must monitor all patients regularly for the development of these behaviors or conditions. Due to the risk for misuse, abuse, addiction, and overdose, some products such as fentanyl sublingual/buccal is available only through a restricted program required by the Food and Drug Administration, called a Risk Evaluation and Mitigation Strategy (REMS). Under the Transmucosal Immediate Release Fentanyl (TIRF) REMS Access Program, outpatients, health care providers who prescribe to outpatients, pharmacies, and distributors must enroll in the program. Further information is available at http://www.TIRFREMSaccess.com or by calling 1-866-822-1483.

4. Cytochrome P450 3A4 interaction: [30, 31] **TIRFs (Actiq®, Fentora®, Subsys®), Lazanda®, Duragesic®, Oxycodone (Oxycontin®, oxycodone concentrate, Oxaydo™ ,Roxybond®), Zohydro ER™ (hydrocodone ER), benzhydrocodone/acetaminophen (Apadaz®), codeine polistirex and chlorpheniramine (Tuzistra XR), codeine phosphate and chlorpheniramine maleate (Tuxarin®), Qdolo® (tramadol), Seglentis® (tramadol/celecoxib)**

The concomitant use of fentanyl, oxycodone ER and hydrocodone ER with all cytochrome P450 3A4 (CYP3A4) inhibitors may result in an increase in oxycodone plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in oxycodone plasma concentration. Monitor patients receiving oxycodone ER and any CYP3A4 inhibitor or inducer.

5. Accidental exposure [21, 22, 30, 31, 32, 33, 34, 42, 43]**: Duragesic®, Hydromorphone (Dilaudid, Exalgo®), Methadone, Morphine Sulfate: Arymo™ ER, Avinza®, Kadian®, and MS Contin®, Morphabond ER®, Nucynta ER®/ Opana ER®, Oxycodone (Oxycontin®, oxycodone concentrate, Oxaydo™ Roxybond®), Zohydro ER™, Buprenorphine (Belbuca and Butrans), benzhydrocodone/acetaminophen (Apadaz®), codeine polistirex and chlorphniramine (Tuzistra XR), codeine phosphate and chlorpheniramine maleate (Tuxarin®), levorphanol, Qdolo® (tramadol), Seglentis® (tramadol/celecoxib)**

Deaths due to a fatal overdose of the above listed opioid analgesics have occurred when children and adults were accidentally exposed to the drugs. Strict adherence to the recommended handling and disposal instructions is of the utmost importance to prevent accidental exposure. Accidental ingestion of even 1 dose, especially in children, can result in a fatal overdose and death.

6. Neonatal opioid withdrawal syndrome: [21, 22, 30, 31, 32, 33, 34, 44, 43]
Prolonged use of opioid analgesics especially **Duragesic®, Hydromorphone (Dilaudid, Exalgo®), Methadone, Morphine Sulfate: Arymo™ ER, Avinza®, Kadian®, and MS Contin®, Morphabond ER®, Nucynta ER®/ Opana ER®** (**tapentadol ER, and oxymorphone ER), Zohydro ER™, Oxycodone (Oxycontin®, oxycodone concentrate, Oxaydo™, Roxybond®), Buprenorphine (Belbuca and Butran), benzhydrocodone/acetaminophen (Apadaz®), codeine phosphate and chlorpheniramine maleate (Tuxarin®), codeine polistirex and chlorpheniramine (Tuzistra XR), Qdolo® (tramadol), levorphanol, Seglentis® (tramadol/celecoxib)** can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

7. Exposure to heat: Duragesic® [31]

Exposure of the fentanyl application site and surrounding area to direct external heat sources, such as heating pads or electric blankets, heat or tanning lamps, sunbathing, hot baths, saunas, hot tubs, and heated water beds may increase fentanyl absorption and has resulted in fatal overdose of fentanyl and death. Patients wearing fentanyl systems who develop fever or increased core body temperature due to strenuous exertion are also at risk for increased fentanyl exposure and may require an adjustment in the dose of fentanyl to avoid overdose and death.

8. Life-threatening QT prolongation: Methadone [29]

QT interval prolongation and serious arrhythmia like torsades de pointes have occurred during treatment with methadone. Most cases involve patients being treated for pain with large, multiple daily doses of methadone, although cases have been reported in patients receiving doses commonly used for maintenance treatment of opioid addiction. Closely monitor patients for changes in cardiac rhythm during initiation and titration of methadone.

9. Treatment of opioid addiction: Methadone[29]

For detoxification and maintenance of opioid dependence, methadone should be administered in accordance with the treatment standards cited in 42 CFR Section 8, including limitations on unsupervised administration.

10. Interaction with alcohol [21, 22, 30, 31, 32, 33, 34, 35, 40]: Morphine Sulfate: Avinza®, Kadian®, and MS Contin®, Nucynta ER®/ Opana ER®, Zohydro ER™, Oxycodone (Oxycontin®, oxycodone concentrate, Oxaydo™, Roxybond®), Buprenorphine (Belbuca and Butran), benzhydrocodone/acetaminophen (Apadaz®)

When using with alcohol, all opioid analgesic products have the potential to cause excessive sedation and may increase blood concentration of certain opioids like tapentadol, oxymorphone, and morphine. This could lead to fatal overdose and death. Instruct patients to avoid alcoholic beverages or use prescription or nonprescription products that contain alcohol while taking opioid analgesics.

11. Information about oral morphine and oxycodone solution[23, 29] : Morphine Sulfate: Avinza®, Kadian®, and MS Contin®, Oxycodone (Oxycontin®, oxycodone concentrate, Oxaydo™, Roxybond®)

Morphine oral solution is available in 10 mg per 5 mL, 20 mg per 5 mL, and 100 mg per 5 mL (20 mg/mL) concentrations. The 100 mg per 5 mL (20 mg/mL) concentration is indicated for use in opioid-tolerant patients only. Take care when prescribing and administering morphine oral solution to avoid dosing errors due to confusion between different concentrations and between milligrams and milliliters, which could result in accidental overdose and death. Take care to ensure the proper dose is communicated and dispensed. Keep morphine oral solution out of the reach of children. In case of accidental ingestion, seek emergency medical help immediately.

Oxycodone concentrated oral solution is available as a 20 mg/mL concentration and is indicated for use in opioid-tolerant patients only. Take care when prescribing and administering oxycodone concentrated oral solution to avoid dosing errors due to confusion between milligram and milliliter, and other oxycodone solutions with different concentrations, which could result in accidental overdose and death. Take care to ensure the proper dose is communicated and dispensed. Keep oxycodone out of the reach of children. In case of accidental ingestion, seek emergency medical help immediately.

12. Abuse Deterrent Technology: Oxaydo™ [37]

This formulation incorporates Acura's patented AVERSION® (abuse-deterrent) Technology which Acura states is a patented mixture of gelling ingredients and nasal irritants designed to address common forms of opioid abuse. OXAYDO can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing in situations where there is concern about an increased risk of misuse or abuse. OXAYDO™ may be abused by crushing, chewing, snorting or injecting the product and these practices pose a significant risk to the abuser that could result in overdose and death.

A Risk Evaluation and Mitigation Strategy (REMS) is included in the label of the several medications. A REMS is a safety strategy to manage known or potential serious risks associated with a medication and to enable patients to have continued access to such medicines by managing their safe use. Refer to the individual product labels for details on the REMS programs.

13. Risks from Concomitant Use with Benzodiazepines or other CNS Depressants: **Arymo^{TM} ER [42], Morphabond ER®[43], benzhydrocodone/acetaminophen (Apadaz®), codeine polistirex and chlorphniramine (Tuzistra XR), codeine phosphate and chlorpheniramine maleate (Tuxarin®), levorphanol, Qdolo® (tramadol), Seglentis® (tramadol/celecoxib)**

Concomitant use of opioid with benzodiazepines or other CNS depressants may result in profound sedation, respiratory depressions, coma, and death.

14. Life threatening respiratory depression and death have occurred in children who received codeine; most cases followed tonsillectomy and/or adenoidectomy and many of the children had evidence of being an ultra-rapid metabolizer of codeine due to a CYP2D6 polymorphism. **TUXARIN ER, TUZISTRA XR** are contraindicated in children younger than 12 years of age and in children younger than 18 years of age following tonsillectomy and/or adenoidectomy. Avoid the use of **TUXARIN ER, TUZISTRA XR** for adolescents 12 to 18 years of age who have other risk factors that may increase their sensitivity to the respiratory depressant effects of codeine. Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Avoid use of opioid cough medications in patients taking benzodiazepines, other CNS depressants, or alcohol.

Life-threatening respiratory depression and death have occurred in children who received **Qdolo® (tramadol).** Some of the reported cases followed tonsillectomy and/or adenoidectomy; in at least one case, the child had evidence of being an ultra-rapid metabolizer of tramadol due to a CYP2D6 polymorphism. **Qdolo®** is contraindicated in children younger than 12 years of age and in children younger than 18 years of age following tonsillectomy and/or adenoidectomy. Avoid the use of **Qdolo®** in adolescents 12 to 18 years of age who have other risk factors that may increase their sensitivity to the respiratory depressant effects of tramadol.

15. Hepatotoxicity: benzhydrocodone/acetaminophen (Apadaz®)

APADAZ contains acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed 4000 milligrams per day, and often involve more than one acetaminophen-containing product.

16. Cardiovascular thrombotic events (Seglentis®)

Nonsteroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction, and stroke, which can be fatal. This risk may occur early in the treatment and may increase with duration of use. SEGLENTIS is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.

17. Gastrointestinal bleeding, ulceration, and perforation (Seglentis®)

NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious (GI) events.

18. Ultra-rapid metabolism of tramadol and other risk factors for life-threatening respiratory depression in children (Seglentis®)

Life-threatening respiratory depression and death have occurred in children who received tramadol. Some of the reported cases followed tonsillectomy and/or adenoidectomy; in at least one case, the child had evidence of being an ultra-rapid metabolizer of tramadol due to a CYP2D6 polymorphism. SEGLENTIS is contraindicated in children younger than 12 years of age and in children younger than 18 years of age following tonsillectomy and/or adenoidectomy. Avoid the use of SEGLENTIS in adolescents 12 to 18 years of age who have other risk factors that may increase their sensitivity to the respiratory depressant effects of tramadol.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company’s products when the medical necessity criteria listed in this

pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

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Cross References:

Applicable Age Edits Rx.01.2

Prior Authorization Requirements for Select Drugs Rx.01.202

Off-Label Use Rx.01.33

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

All products containing the active ingredients in the chart below are subject to the following:

II. Opioid regimens containing greater than 90 morphine milligram equivalents per day
III. Appropriate Utilization with Medication Assistant Treatments (MAT) for opioid use disorder

Active ingredient
Benzhydrocodone
Codeine
Dihydrocodeine

Fentanyl
Hydrocodone
Hydromorphone
Levorphanol
Meperidine
Methadone
Morphine
Opium
Oxycodone
Oxymorphone
Tapentadol
Tramadol

The table below identifies medications that are found in the following sections of this policy:

- I. Transmucosal Immediate Release Fentanyl (TIRF) Products (**¥ identifies impacted medications**)
- II. Opioid regimens containing greater than 90 morphine milligram equivalents per day, long acting opioids, and short acting low dose opioids for continuation beyond 30days (***identifies impacted long acting opioids**)
- Days' Supply and Quantity Limits

Drug Name	Days' Supply Limit	Maximum Quantity per Day	Quantity limit per rolling 30 days, unless otherwise specified (tablet, capsule)
Acetaminophen/codeine #2 300/15mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	
Acetaminophen/codeine #3 300/30mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	
Acetaminophen/codeine #4 300/60mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Acetaminophen/codeine liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	90mL	
Aspirin/codeine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Benzhydrocodone/acetaminophen (Apadaz®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	
Buprenorphine film* (Belbuca®)	No	2	
Buprenorphine patch* (Butrans®)	No		4 patches

Buprenorphine sublingual tablet 2mg	No	4	
Buprenorphine sublingual tablet 8mg	No	3	
Buprenorphine/naloxone (Suboxone® 2/0.5mg, 4/1mg)	No	4	
Buprenorphine/ naloxone (Suboxone® 8/2mg)	No	3	
Buprenorphine/ naloxone (Suboxone® 12/3mg)	No	2	
Buprenorphine/naloxone (Zubsolv® 1.4/0.36mg, 2.9-0.71mg)	No	4	
Buprenorphine/naloxone (Zubsolv® 5.7/1.4mg, 0.7/0.18mg)	No	3	
Buprenorphine/naloxone (Zubsolv® 8.6/2.1mg)	No	2	
Buprenorphine/naloxone (Zubsolv® 11.4-2.9mg)	No	1	
Buprenorphine/naloxone (Bunavail® 2.1/0.3mg)	No	4	
Buprenorphine/naloxone (Bunavail® 4.2/0.7mg)	No	3	
Buprenorphine/naloxone (Bunavail® 6.3/1mg)	No	1	
Butalbital/apap (Allzital®, Marten®)	one 5-day fill per 30 days	6	
Butalbital/apap/caffeine without codeine (Esgic®, Fioricet®)	one 5-day fill per 30 days	6	
Butalbital/apap/caffeine with codeine (Esgic®, Fioricet®/codeine)	one 5-day fill per 30 days for 18 and over; one 3-day fill per 30 days for less than 18	6	
Butalbital/asa/caffeine without codeine (Fiorinal®)	one 5-day fill per 30 days	6	
Butalbital/asa/caffeine with codeine (Fiorinal®/Codeine)	one 5-day fill per 30 days for 18 and over; one 3-day fill per 30 days for less than 18	6	
Carisoprodol/ aspirin/ codeine (Soma® compound with codeine)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	8	
Codeine sulfate tablets 15mg, 30mg	two 5-day fills per 60 for 18 and older; two 3-day fills per 60 days for less than 18	12	
Codeine sulfate tablets 60mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Codeine sulfate solution	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Codeine/chlorpheniramine (Tuxarin® ER)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	2	
Codeine/chlorpheniramine tablets (Tuzistra® XR)	two 5-day fills per 60 days for 18 and older; two 3-day	20mL	

	fills per 60 days for less than 18		
Codeine/ chlorpheniramine solution (Z-Tuss® AC)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Dihydrocodeine/ acetaminophen/ caffeine (Trezix®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	10	
Fentanyl IR¥ (Actiq®, Fentora®, Subsys®)	No	4	
Fentanyl nasal solution¥ (Lazanda®)	No	1	
Fentanyl patch* (Duragesic®)	No		15 patches
Guaifenesin/ codeine (GG/codeine, Coditussin® AC)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Guaifenesin/ codeine (MAR-COF® CG, Trymine® CG)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	45mL	
Guaifenesin/ codeine (M-Clear® WC)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	90mL	
Hydrocodone bitartrate ER* (Hysingla® ER)	No	1	
Hydrocodone bitartrate ER* (Zohydro® ER)	No	2	
Hydrocodone/acetaminophen 2.5/325mg, 5/300mg,7.5/300mg, 5/325mg, 7.5/325mg tab (Vicodin®, Norco®, Lortab®, Xodol®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	
Hydrocodone/apap 10/325mg, 10/300mg tab (Vicodin®, Norco®, Lortab®, Xodol®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Hydrocodone/apap liquid (10mg/325mg/15ml, 2.5mg/167mg/5ml, 5mg/333mg/10ml, 7.5mg/325mg/15ml, 10mg/300mg/15ml)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	90mL	
Hydrocodone/chlorpheniramine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	10mL	
Hydrocodone/chlorpheniramine (TussiCaps®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	2	
Hydrocodone/ homatropine (Hydromet®)	two 5-day fills per 60 days for 18 and older; two 3-day	30mL	

	fills per 60 days for less than 18		
Hydrocodone/ homatropine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Hydrocodone/ibuprofen	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	5	
Hydromorphone (Dilaudid®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Hydromorphone 1mg/1ml liquid (Dilaudid®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12mL	
Hydromorphone extended release* (Exalgo®)	No	2	
Levorphanol tartrate 2mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Levorphanol tartrate 3mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	4	
Meperidine 50mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	67mL	
Meperidine HCL (Demerol®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Methadone* tabs 5mg, 10mg	No	6	
Methadone solution* 5mg/5ml	No	60mL	
Methadone solution* 10mg/5ml	No	30mL	
Methadone solution* (Methadose concentrate, Methadose sugar-free concentrate) 10mg/1ml	No	6mL	
Morphine 10mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	45 mL	
Morphine 20mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	23 mL	
Morphine concentrate 20mg/1ml, 10mg/0.5ml, 5mg/0.25ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6mL	

Morphine sulfate IR (MSIR®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Morphine sulfate ER capsules* (Avinza®)	No	1	
Morphine sulfate ER capsules* (Kadian®)	No	2	
Morphine sulfate SR* (Morphabond®)	No	3	
Morphine sulfate SR* (MS Contin® Arymo® ER)	No	3	
Morphine sulfate/naltrexone* (Embeda®)	No	2	
Morphine suppositories 5mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	18	
Morphine suppositories 10mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Morphine suppositories 20mg, 30mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Opium tincture	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	N/A	
Oxycodone 7.5mg tab (Oxaydo®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	8	
Oxycodone HCL (Oxy® IR/Roxicodone®/Oxaydo®, Roxybond®) 5mg caps/tabs	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	
Oxycodone HCL (Oxy® IR/Roxicodone®, Roxybond®), 10mg, 15 mg, 30mg caps/tabs	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Oxycodone 5mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60 mL	
Oxycodone highly concentrated liquid 20mg/1ml liquid (Eth-Oxydose®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6mL	
Oxycodone HCL ER* (Oxycontin®)	No	3	
Oxycodone ER* (Xtampza® ER)	No	2	
Oxycodone/Acetaminophen, Endocet® (Percocet®,Primlev®, Nalocet®, Prolate®) 2.5/325mg tab, 2.5/300mg tab, 5/300mg, 5/325mg tab	two 5-day fills per 60 days for 18 and older; two 3-day	12	

	fills per 60 days for less than 18		
Oxycodone/Acetaminophen (Primlev®, Prolate®) 7.5/300mg tab, 10/300mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Oxycodone/acetaminophen 7.5/325mg tab (Endocet®/Percocet®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	8	
Oxycodone/acetaminophen 10/325mg tab (Endocet®/Percocet®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Oxycodone/acetaminophen 5mg/325mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60	
Oxycodone/aspirin 4.8355/325mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	
Oxycodone/Acetaminophen (Prolate®) 10-300mg/5ml soln	Two 5-days fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	30 ml	
Oxycodone/ibuprofen tablets 5/400mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	4	
Oxymorphone HCL (Opana®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Oxymorphone HCL ER* (Opana® ER)	No	3	
Phenylephrine/ brompheniramine/ codeine (M-End® PE)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	90mL	
Phenylephrine/ chlorpheniramine/ codeine (Capcof®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Phenylephrine/ dexchlorpheniramine/ codeine (Pro-red® AC)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Promethazine/codeine 6.25-10mg/5mL syrup	two 5-day fills per 60 days for 18 and older; two 3-day	30mL	

	fills per 60 days for less than 18		
Promethazine/ phenylephrine/ codeine 6.25-5-10mg/5mL	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	30mL	
Pseudoephedrine/ brompheniramine/ codeine (MAR-COF® BP)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Pseudoephedrine/codeine/ guaifenesin (Virtussin DAC) solution 30-10-100 MG/5ML	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	40mL	
Pseudoephedrine/ dexbrompheniramine/ codeine (M-End® Max D)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Tapentadol (Nucynta®) 50mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	4	
Tapentadol (Nucynta®) 75mg, 100mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Tapentadol ER* (Nucynta® ER)	No	2	
Tramadol (Ultram®)		8	
Tramadol (Ultram® ER and Conzip®)		1	
Tramadol/acetaminophen (Ultracet®)		8	
Tramadol/celecoxib (Seglentis®)	No	4	
Tramadol 100 mg		4	
Tramadol (Qdolo®)		80ml	

Policy Version Number: 21.00

P&T Approval Date: December 08, 2022

Policy Effective Date: April 01, 2023

Next Required Review Date: December 08, 2023