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Section:	Prescription Drugs	**Effective Date:**	April 1, 2021
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	March 27, 2020
Subject:	Opioid Injectables	**Page:**	1 of 6

Last Review Date: March 12, 2021

Opioid Injectables

Description

Buprenex (buprenorphine), Butorphanol, Demerol (meperidine), Fentanyl, Hydromorphone, Morphine, Nalbuphine

Background
Buprenex (buprenorphine) is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor. Butorphanol is a partial opioid agonist at the mu opioid receptor and a full agonist at the kappa opioid receptor. Demerol (meperidine), fentanyl, hydromorphone, and morphine are full opioid agonists. Nalbuphine is a synthetic opioid agonist-antagonist analgesic. Buprenex (buprenorphine) is a Schedule III narcotic. Butorphanol is a Schedule IV narcotic. Demerol, fentanyl, hydromorphone, and morphine are a Schedule II narcotics. The principal actions of therapeutic value are analgesia and sedation (1-7).

Methadone injection is reserved for patients in an inpatient clinical setting and is not FDA approved for the outpatient treatment of opioid dependence. Thus, methadone injection is medical benefit only and not included in this policy.

Regulatory Status
FDA-approved indications (1-7):

1. Buprenex (buprenorphine) Injection: for the management of pain severe enough to require an opioid analgesic and for which alternate treatments are inadequate
2. Butorphanol Tartrate Injection: as a preoperative or pre-anesthetic medication, as a supplement to balanced anesthesia, for the relief of pain during labor, and for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate

3. Demerol (meperidine) Injection: for preoperative medication, support of anesthesia, for obstetrical analgesia, and for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate
4. Fentanyl Injection: analgesic action of short duration during the anesthetic periods, premedication, induction and maintenance, and in the immediate postoperative period (recovery room) as the need arises; use as an opioid analgesic supplement in general or regional anesthesia; administration with a neuroleptic as an anesthetic premedication, for the induction of anesthesia and as an adjunct in the maintenance of general and regional anesthesia; use as an anesthetic agent with oxygen in selected high risk patients, such as those undergoing open heart surgery or certain complicated neurological or orthopedic procedures
5. Hydromorphone Injectable: for the management of pain severe enough to require an opioid analgesic and for which alternate treatments are inadequate
6. Morphine Injectable: for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate
7. Nalbuphine Injectable: for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate

CDC guidelines find that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31%–61% of decedents (8). The FDA also states that benzodiazepines “are also commonly abused and misused, often together with opioid pain relievers and other medicines” (9).

The safety and effectiveness of opioid injectables in pediatric patients below the age of 18 have not been established. The safety and effectiveness of fentanyl and Buprenex (buprenorphine) in pediatric patients below the age of 2 have not been established (1-7).

Related policies

Abstral, Actiq, Butrans, Duragesic, Extended Release Opioid Drugs, Fentanyl Powder, Fentora, Immediate Release Opioid Drugs, IR Opioid Combo Drugs, Methadone, Olinvyk, Opioid Powders, Suboxone Drug Class, Subsys

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Opioid injectables may be considered **medically necessary** for patients with pain or as a preoperative or pre-anesthetic medication and if the conditions below are met.

Opioid injectables may be considered **investigational** for all other indications.

Prior-Approval Requirements

Prior authorization is not required if prescribed by an oncologist and/or the member has paid pharmacy claims for an oncology medication(s) in the past 6 months

Age
2 years of age or older – Buprenex (buprenorphine) and Fentanyl
18 years of age or older – Butorphanol, Demerol (meperidine), Hydromorphone, Morphine, Nalbuphine

Diagnoses

Butorphanol, Demerol (meperidine), and Fentanyl ONLY

Patient must be using for the following:

1. Induction or maintenance of anesthesia

Buprenex (buprenorphine), Butorphanol, Demerol (meperidine), Hydromorphone, Morphine, and Nalbuphine ONLY

Patient must have the following:

1. Pain severe enough to require an opioid analgesic

AND ALL of the following:

1. **NO** dual therapy with other immediate release opioid analgesic(s)
2. Alternative treatment options have been ineffective, not tolerated or inadequate for controlling the pain
    a. These include: non-opioid analgesics and other treatment modalities
3. Prescriber agrees to assess patient for signs and symptoms of serotonin syndrome
4. Prescriber agrees to participate in the Opioid Analgesic REMS program and to monitor for abuse, misuse, addiction, and overdose and discontinue if necessary (*https://opioidanalgesicrems.com*)
5. **NO** other opioid at prior authorization limits

6. **NO** dual therapy with opioid addiction treatment or methadone
7. **NO** dual therapy with an anti-anxiety benzodiazepine(s)
    a. Alprazolam (Xanax)
    b. Clonazepam (Klonopin)
    c. Diazepam (Valium)
    d. Lorazepam (Ativan)
    e. Oxazepam (Serax)
    f. Chlordiazepoxide (Librium)
    g. Clorazepate dipotassium (Tranxene)

Prior–Approval *Renewal* Requirements

Age 2 years of age or older – Fentanyl and Buprenex (buprenorphine)
18 years of age or older – Demerol (meperidine), hydromorphone, morphine, nalbuphine, and butorphanol

Diagnoses

Butorphanol, Demerol (meperidine), and Fentanyl ONLY

Patient must be using for the following:

1. Induction or maintenance of anesthesia

Buprenex (buprenorphine), Butorphanol, Demerol (meperidine), Hydromorphone, Morphine, and Nalbuphine ONLY

Patient must have the following:

1. Pain severe enough to require an opioid analgesic

AND ALL of the following:

1. **NO** dual therapy with other immediate release opioid analgesic(s)
2. Prescriber agrees to assess patient for signs and symptoms of serotonin syndrome
3. Prescriber agrees to participate in the Opioid Analgesic REMS program and to monitor for abuse, misuse, addiction, and overdose and discontinue if necessary (*https://opioidanalgesicrems.com*)
4. **NO** other opioid at prior authorization limits
5. **NO** dual therapy with opioid addiction treatment or methadone

6. **NO** dual therapy with an anti-anxiety benzodiazepine(s)
    a. Alprazolam (Xanax)
    b. Clonazepam (Klonopin)
    c. Diazepam (Valium)
    d. Lorazepam (Ativan)
    e. Oxazepam (Serax)
    f. Chlordiazepoxide (Librium)
    g. Clorazepate dipotassium (Tranxene)

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Duration 6 months

Prior–Approval *Renewal* Limits

Same as above

Rationale

Summary

Buprenex (buprenorphine) is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor. Butorphanol is a partial opioid agonist at the mu opioid receptor and a full agonist at the kappa opioid receptor. Demerol (meperidine), fentanyl, hydromorphone, and morphine are full opioid agonists. Nalbuphine is a synthetic opioid agonist-antagonist analgesic. Buprenex (buprenorphine) is a Schedule III narcotic. Butorphanol is a Schedule IV narcotic. Demerol, fentanyl, hydromorphone, and morphine are a Schedule II narcotics. The principal actions of therapeutic value are analgesia and sedation (1-7). Prior approval is required to ensure the safe, clinically appropriate and cost effective use of opioid injectables while maintaining optimal therapeutic outcomes. The safety and effectiveness of opioid injectables in pediatric patients below the age of 18 have not been established. The safety and effectiveness of Fentanyl and Buprenex (buprenorphine) in pediatric patients below the age of 2 have not been established (1-7).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of opioid injectables while maintaining optimal therapeutic outcomes.

References

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2. Butorphanol [package insert]. Eatontown, NJ. West-Ward Pharmaceuticals Corp. December 2018.
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5. Hydromorphone [package insert]. Lake Zurich, IL. Fresenius Kabi USA, LLC. January 2020.
6. Morphine [package insert]. Lake Zurich, IL. Fresenius Kabi USA, LLC. November 2019.
7. Nalbuphine [package insert]. Lake Forest, IL. Hospira, Inc. February 2020.
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Policy History

Date	Action
March 2020	Addition to PA
June 2020	Annual review
March 2021	Annual review

Keywords

This policy was approved by the FEP® Pharmacy Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.