



CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Effective Date 4/15/2010
Next Review Date..... 4/15/2011
Coverage Policy Number 5030

Subject **Butorphanol Nasal Spray**

Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	3
References	3
Policy History	4

Hyperlink to Related Coverage Policies

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

Coverage Policy

CIGNA covers more than TWO units of Butorphanol Nasal Spray per month as medically necessary for EITHER of the following indications:

- moderate-to-severe chronic pain with either an inability to take oral pain medications **OR** failure/contraindication/intolerance to any other pain management treatment option
- migraine headache with failure/contraindication/intolerance to two different classes of prophylactic therapy to fully control headache pain. Examples of migraine prophylaxis drug therapies include anticonvulsants (e.g., divalproex); beta blockers (e.g., propranolol, atenolol, metoprolol); tricyclic antidepressants (e.g., amitriptyline); calcium channel blockers (e.g., verapamil); monoamine oxidase Inhibitors (e.g., phenelzine)

FDA Approved Indications

Butorphanol Tartrate Nasal Spray USP is indicated for the management of pain when the use of an opioid analgesic is appropriate.

FDA Recommended Dosing

Factors to be considered in determining the dose are age, body weight, physical status, underlying pathological condition, the use of other drugs, type of anesthesia to be used, and surgical procedure involved. Use in the

elderly, in patients with hepatic or renal disease, or in labor requires extra caution. The following doses are for patients who do not have impaired hepatic or renal function and who are not on CNS active agents.

Use for Pain

The usual recommended dose for initial nasal administration is 1 mg (1 spray in one nostril). Adherence to this dose reduces the incidence of drowsiness and dizziness. If adequate pain relief is not achieved within 60 to 90 minutes, an additional 1 mg dose may be given. The initial dose sequence outlined above may be repeated in 3 to 4 hours as required after the second dose of the sequence. Depending on the severity of the pain, an initial dose of 2 mg (1 spray in each nostril) may be used in patients who will be able to remain recumbent in the event drowsiness or dizziness occurs. In such patients single additional 2 mg doses should not be given for 3 to 4 hours.

Use in Balanced Anesthesia

The use of butorphanol tartrate nasal spray is not recommended because it has not been studied in induction or maintenance of anesthesia. Butorphanol nasal spray is supplied as a 2.5 ml metered dose bottle containing 10 mg/ml. After initial priming, the nasal solution spray pump delivers 14–15 metered doses containing 1mg of butorphanol tartrate per spray. If repriming of the pump is necessary because of intermittent use, the spray pump will deliver about 8–10 metered doses, depending on the extent of the repriming.

General Background

Pharmacology

Butorphanol has analgesic and opiate antagonistic effects. The exact mechanisms of actions of the drug are not known. However, the analgesic effect is believed to result from an interaction with an opiate receptor site in the central nervous system (CNS); the opiate antagonistic effect may result from competitive inhibition at the opiate receptor, but other mechanisms are probably also involved. The drug exerts antagonistic or partially antagonistic effects at μ opiate receptor sites, while it is thought that butorphanol exerts its agonistic effects principally at the κ and Σ opiate receptors. On a weight basis, the analgesic activity of intramuscular (IM) butorphanol is approximately four to seven times that of IM morphine, 15–30 times that of IM pentazocine, and 30–50 times that of IM meperidine. Studies in animals indicate that, on a weight basis, subcutaneous butorphanol has 30 times the opiate antagonist activity of subcutaneous pentazocine and $1/40$ that of subcutaneous naloxone. The absolute bioavailability of butorphanol NS is 60–70% and is unchanged in patients with allergic rhinitis. In patients using a nasal vasoconstrictor (oxymetazoline), the fraction of the dose absorbed was unchanged, but the rate of absorption was slowed. The peak plasma concentrations were approximately half those achieved in the absence of the vasoconstrictor.

When treating chronic pain, narcotic opioids should be considered if pain cannot be otherwise controlled. Although these medications can be dangerous and addicting, they can also be extremely effective when used appropriately. One common mistake when treating chronic pain with opioid medications is using the short acting types of medication (e.g. Percocet, Morphine, Vicoden, etc.). While these medications are useful for acute pain, they are also associated with sedating and euphoric side-effects. The short acting nature of these medications encourages overuse and the development of tolerance. Long-acting opioids (morphine sustained release, methadone, OxyContin, fentanyl) have fewer cognitive side-effects, and better control of chronic pain.

Like opiate agonists, butorphanol produces respiratory depression, sedation, miosis and, in animals, antitussive effects. Some experts state that butorphanol nasal spray (NS) may be considered when other antimigraine drugs cannot be used or as rescue therapy when sedative effects will not place the patient at risk. In patients for whom butorphanol might be indicated for management of migraine headache, special attention should be given to the potential for overuse and dependence. When used to relieve postoperative pain, single intranasal butorphanol doses of 1 or 2 mg have been as effective as IM meperidine hydrochloride doses of 37.5 or 75 mg, respectively. When used to relieve migraine headache, butorphanol nasal solution administered as two 1-mg doses (given one hour apart) was as effective as a single 10-mg dose of IM methadone hydrochloride.

The effectiveness of opioid analgesics varies in different pain syndromes. Studies with butorphanol NS have been performed in postoperative (i.e., general, orthopedic, oral, cesarean section) pain, in postepiostomy pain, in pain of musculoskeletal origin, and in migraine headache pain.

The analgesic efficacy of butorphanol NS was evaluated (approximately 35 patients per treatment group) in a general and orthopedic surgery trial. Single doses of butorphanol NS (1 or 2 mg) and IM meperidine (37.5 or 75 mg) were compared. Analgesia provided by 1 and 2 mg doses of butorphanol NS was similar to 37.5 and 75 mg meperidine, respectively, with onset of analgesia within 15 minutes and peak analgesic effect within one hour. The median duration of pain relief was 2.5 hours with 1 mg butorphanol NS, 3.5 hours with 2 mg butorphanol NS, and 3.3 hours with either dose of meperidine.

In a postcesarean section trial, butorphanol NS administered to 35 patients as two 1 mg doses 60 minutes apart was compared with a single 2 mg dose of butorphanol NS or a single 2 mg IV dose of butorphanol injection (37 patients each). Onset of analgesia was within 15 minutes for all butorphanol regimens. Peak analgesic effects of 2 mg intravenous butorphanol injection and butorphanol NS were similar in magnitude. The duration of pain relief provided by both 2 mg butorphanol NS regimens was approximately 4.5 hours and was greater than intravenous butorphanol injection (2.6 hours).

The analgesic efficacy of two 1 mg doses one hour apart of butorphanol NS in migraine headache pain was compared with a single dose of 10 mg IM methadone (31 and 32 patients, respectively). Significant onset of analgesia occurred within 15 minutes for both butorphanol NS and IM methadone. Peak analgesic effect occurred at two hours for butorphanol NS and 1.5 hours for methadone. The median duration of pain relief was six hours with butorphanol NS and four hours with methadone as judged by the time when approximately half of the patients re-medicated.

In two other trials in patients with migraine headache pain, a 2 mg initial dose of butorphanol NS followed by an additional 1 mg dose one hour later (76 patients) was compared with either 75 mg IM meperidine (24 patients) or placebo (72 patients). Onset, peak activity, and duration were similar with both active treatments; however, the incidence of adverse experiences (e.g., nausea, vomiting, dizziness) was higher in these two trials with the 2 mg initial dose of butorphanol NS than in the trial with the 1 mg initial dose.

Adverse Reactions/Contraindications

Because of its opioid antagonist properties, butorphanol is not recommended for use in patients dependent on narcotics. Such patients should have an adequate period of withdrawal from opioid drugs prior to beginning butorphanol therapy. In patients taking opioid analgesics chronically, butorphanol has precipitated withdrawal symptoms such as anxiety, agitation, mood changes, hallucinations, dysphoria, weakness, and diarrhea. Because of the difficulty in assessing opioid tolerance in patients who have recently received repeated doses of narcotic analgesic medication, caution should be used in the administration of butorphanol to such patients. Butorphanol may produce respiratory depression; therefore, this drug is not recommended for use in patients with decreased respiratory capacity such as asthma or chronic obstructive pulmonary disease (COPD).

The most frequently reported adverse experiences across all clinical trials with butorphanol NS were somnolence, dizziness, nausea and/or vomiting. In long-term trials, nasal congestion and insomnia were also frequently reported.

Coding/Billing Information

Note: This section is not in use.

References

1. Hoffert MJ, Couch JR, Diamond S, et al. Transnasal Butorphanol in the Treatment of Acute Migraine Headache. 1995; 35: 65-69.
2. McEvoy GK, ed. AHFS 2009 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2009.
3. Roxane Laboratories, Inc. Butorphanol Tartrate Nasal Spray package insert. Columbus, OH: Roxane Laboratories, Inc. Oct 2007.

Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	3/15/2008	5030	Butorphanol Nasal Spray
Great-West Healthcare	1/2007	MDL98.101.2	Butorphanol Nasal Spray

“CIGNA” and the “Tree of Life” logo are registered service marks of CIGNA Intellectual Property, Inc., licensed for use by CIGNA Corporation and its operating subsidiaries. All products and services are provided exclusively by such operating subsidiaries and not by CIGNA Corporation. Such operating subsidiaries include Connecticut General Life Insurance Company, CIGNA Behavioral Health, Inc., Intracorp, and HMO or service company subsidiaries of CIGNA Health Corporation and CIGNA Dental Health, Inc. In Arizona, HMO plans are offered by CIGNA HealthCare of Arizona, Inc. In California, HMO plans are offered by CIGNA HealthCare of California, Inc. and Great-West Healthcare of California, Inc. In Connecticut, HMO plans are offered by CIGNA HealthCare of Connecticut, Inc. In North Carolina, HMO plans are offered by CIGNA HealthCare of North Carolina, Inc. In Virginia, HMO plans are offered by CIGNA HealthCare Mid-Atlantic, Inc. All other medical plans in these states are insured or administered by Connecticut General Life Insurance Company.

Connecticut General Life Insurance Company has acquired the business of Great-West Healthcare from Great-West Life & Annuity Insurance Company (GWLA). Certain products continue to be provided by GWLA (Life, Accident and Disability, and Excess Loss). GWLA is not licensed to do business in New York. In New York, these products are sold by GWLA’s subsidiary, First Great-West Life & Annuity Insurance Company, White Plains, N.Y.