



CIGNA PHARMACY COVERAGE POLICY

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

Subject Fentanyl Transdermal System (Duragesic®)

Effective Date 2/15/2011
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Coverage Policy Number 5029

Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	4
References	4
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. Please note, the terms of a customer'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 customer'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 customer'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 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 ©2011 CIGNA

Coverage Policy

CIGNA covers fentanyl transdermal system (Duragesic®) as medically necessary for the management of persistent, moderate to severe chronic pain in an individual who is already receiving and is tolerant to opioid therapy AND has EITHER of the following:

- requirement for continuous, around-the-clock opioid administration for an extended period of time
- inability to be managed by other means such as non-steroidal analgesics, opioid combination products, or immediate-release opioids

CIGNA does not cover fentanyl transdermal system (Duragesic®) for the following indications because it is considered experimental, investigational, or unproven (this list may not be all-inclusive):

- management of acute or postoperative pain
- management of mild or intermittent pain that can otherwise be managed by lesser means such as non-steroidal analgesics, opioid combination products, or immediate-release opioids

Note: The quality limit for any strength of Duragesic is 15 patches per 30 days for one co-pay.

FDA Approved Indications

Duragesic is indicated for management of persistent, moderate to severe chronic pain that requires continuous, around-the-clock opioid administration for an extended period of time and cannot be managed by other means such as non-steroidal analgesics, opioid combination products, or immediate-release opioids. Duragesic should only be used in patients who are already receiving opioid therapy, who have demonstrated opioid tolerance, and who require a total daily dose at least equivalent to Duragesic 25 mcg/h. Patients who are considered opioid-tolerant are those who have been taking, for a week or longer, at least 60 mg of morphine daily, or at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily, or an equianalgesic dose of another opioid. Because serious or life-threatening hypoventilation could result, Duragesic is contraindicated for use on an as needed basis (i.e., prn), for the management of post-operative or acute pain, or in patients who are not opioid-tolerant or who require opioid analgesia for a short period of time.

FDA Recommended Dosing

Duragesic patches are intended for transdermal use (on intact skin) only. The Duragesic patch should not be used if the seal is broken, or the patch is cut, damaged, or changed in any way. Using a patch that is cut, damaged, or changed in any way can expose the patient or caregiver to the contents of the patch, which can result in an overdose of fentanyl that may be fatal. Each Duragesic patch may be worn continuously for 72 hours. The next patch should be applied to a different skin site after removal of the previous transdermal system. If problems with adhesion of the patch occur, the edges of the patch may be taped with first aid tape. If problems with adhesion persist, the patch may be overlaid with a transparent adhesive film dressing (e.g., Bioclusive or Tegaderm). If the patch falls off before 72 hours, dispose of it by folding in half and flushing down the toilet. A new patch may be applied to a different skin site.

Black Box Warning

The FDA has placed a "Black Box Warning" for transdermal fentanyl regarding the specific indication, occurrence of serious or life-threatening hypoventilation in certain conditions, drug interaction, and signs of misuse, abuse, and addiction. This drug is indicated for management of persistent, moderate to severe chronic pain that requires continuous, around-the-clock opioid administration for an extended period of time, and cannot be managed by other means such as nonsteroidal analgesics, opioid combination products, or immediate-release opioids. Since the use of Transdermal fentanyl in non-opioid tolerant patients may lead to fatal respiratory depression, this drug should only be used in patients who are already receiving opioid therapy and who have demonstrated opioid tolerance. Patients who are considered opioid-tolerant are those who have been taking, for a week or longer, at least 60 mg of morphine daily, or at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid.

Drug Availability

Duragesic (fentanyl transdermal system) is supplied in cartons containing 5 individually packaged systems as: Duragesic 25; Duragesic 50; Duragesic 75; and Duragesic 100.

General Background

Pharmacology

Transdermal fentanyl contains a high concentration of a potent Schedule II opioid agonist, similar to hydromorphone, morphine, oxycodone, and oxymorphone. These drugs have the highest potential for abuse and associated risk of fatal overdose due to respiratory depression. The high content of fentanyl in the patches may be a particular target for abuse and diversion.

Opioid analgesics such as fentanyl bind with stereospecific receptors at many sites within the central nervous system (CNS) to alter processes affecting both the perception of and emotional response to pain. Although the precise sites and mechanisms of action have not been fully determined, alterations in the release of various neurotransmitters from afferent nerves sensitive to painful stimuli may be partially responsible for the analgesic effects.

On a weight basis, fentanyl is considerably more potent than morphine. Transdermal administration of fentanyl at a delivery rate of 100 mcg per hour (mcg/hr) is therapeutically equivalent to intramuscular administration of 60 mg of morphine. Fentanyl, like other opioid analgesics, may cause respiratory depression (characterized by

decreases in respiratory rate, tidal volume, minute ventilation, and ventilatory response to carbon dioxide), increased biliary tone, increased smooth muscle tone in the urinary tract, decreased gastrointestinal motility, euphoria, miosis, hypotension, and bradycardia. However, unlike many other opioid analgesics, fentanyl does not cause clinically significant histamine release with therapeutic doses (as determined by intravenous administration of single doses of up to 50 mcg per kg of body weight [mcg/kg]).

Following application of a transdermal system, some fentanyl is released relatively rapidly from the adhesive layer of the system. Most of the fentanyl is located in a reservoir layer within the system, from which it is released gradually at a rate controlled by a restrictive copolymer membrane located between the reservoir and adhesive layers. Absorption of fentanyl after application of a transdermal system is initially slow because a depot of fentanyl, from which the medication is subsequently absorbed into the systemic circulation, must first form in the upper skin layers. Approximately 92% of the fentanyl contained in a transdermal system is absorbed into the systemic circulation over 72 hours. Effective concentrations were reached between 1.2 and 37.3 hours after application of a transdermal system in various postoperative pain studies. The elimination half-life of transdermal fentanyl is 17 hours.

Guidelines

The National Comprehensive Cancer Network (NCCN) recommendations include maintenance therapy for the management of chronic persistent pain in cancer patients when 24-hr opioid requirement is stable. Used in conjunction with specific treatment for oncologic emergency as clinically indicated.

Clinical Efficacy

Transdermal fentanyl has been studied in patients with acute and chronic pain (postoperative and cancer pain models); however, transdermal fentanyl is contraindicated for postoperative analgesia. The analgesic efficacy of transdermal fentanyl was demonstrated in an acute pain model with surgical procedures expected to produce various intensities of pain (e.g., hysterectomy, major orthopedic surgery). Clinical use and safety was evaluated in patients experiencing chronic pain due to malignancy. Based on the results of these trials, transdermal fentanyl was determined to be effective in both populations but safe only for use in patients with chronic pain. Because of the risk of hypoventilation (4% incidence) in postoperative patients with acute pain, transdermal fentanyl is contraindicated for postoperative analgesia.

Transdermal fentanyl as therapy for pain due to cancer has been studied in 153 patients. In this patient population, transdermal fentanyl has been administered in doses of 25–600 mcg/h. Individual patients have used transdermal fentanyl continuously for up to 866 days. At one month after initiation of transdermal fentanyl therapy, patients generally reported lower pain intensity scores as compared to a prestudy analgesic regimen of oral morphine.

Adverse Reactions/Contraindications

The safety of transdermal fentanyl was evaluated in three open-label trials in 291 pediatric patients, 2–18 years of age, with chronic pain. Starting doses of 25 mcg/h and higher were used by 181 patients. Approximately 90% of the total daily opioid requirement (transdermal fentanyl plus rescue medication) was provided by transdermal fentanyl.

Because serious or life-threatening hypoventilation could occur, transdermal fentanyl is contraindicated in the following: the management of acute or postoperative pain, including use in out-patient surgeries because there is no opportunity for proper dose titration; the management of mild or intermittent pain that can otherwise be managed by lesser means such as acetaminophen-opioid combinations, nonsteroidal analgesics, or as needed dosing with short-acting opioids; in doses exceeding 25 mcg/h at the initiation of opioid therapy because of the need to individualize dosing by titrating to the desired analgesic effect.

Transdermal fentanyl doses greater than 25 mcg/h are too high for initiation of therapy in non-opioid-tolerant patients and should not be used to begin transdermal fentanyl therapy in these patients. Children converting to transdermal fentanyl should be opioid-tolerant. Transdermal fentanyl may impair mental and/or physical ability required for the performance of potentially hazardous tasks (e.g., driving, operating machinery). Patients who have been given transdermal fentanyl should not drive or operate dangerous machinery unless they are tolerant to the side effects of the drug.

Hypoventilation may occur at any time during the use of transdermal fentanyl. Because significant amounts of fentanyl are absorbed from the skin for 17 hours or more after the system is removed, hypoventilation may persist beyond the removal of transdermal fentanyl. Consequently, patients with hypoventilation should be carefully observed for degree of sedation and their respiratory rate monitored until respiration has stabilized.

In post-marketing experience, deaths from hypoventilation due to inappropriate use of transdermal fentanyl have been reported. In adults, the safety of transdermal fentanyl has been evaluated in 357 postoperative patients and 153 cancer patients for a total of 510 patients. Patients with acute pain used Duragesic for one to three days. The duration of transdermal fentanyl use varied in cancer patients; 56% of patients used transdermal fentanyl for over 30 days; 28% continued treatment for more than four months; and 10% used transdermal fentanyl for more than one year. Hypoventilation was the most serious adverse reaction observed in 13 (4%) postoperative patients and in three (2%) of the cancer patients. Hypotension and hypertension were observed in 11 (3%) and four (1%) of the opioid-naive patients.

Most patients in the clinical trials were converted to transdermal fentanyl from other narcotics. Therefore, there has been no systematic evaluation of transdermal fentanyl as an initial opioid analgesic in the management of chronic pain. In addition, patients who are not opioid-tolerant have experienced hypoventilation and death during use of transdermal fentanyl. Therefore, transdermal fentanyl should be used only in patients who are opioid-tolerant.

Coding/Billing Information

Note: This section is not in use.

References

1. Alza Coporation. Duragesic® Product Information. Vacaville, CA: Alza Coporation. July 2009.
 2. Farrar JT, Cleary J, Rauck R: Oral transmucosal fentanyl citrate: randomized, double-blinded, placebo-controlled trial for treatment of breakthrough pain in cancer patients, J Natl Cancer Inst 1998 90: 611-6.
 3. McEvoy GK, ed. AHFS 2011 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2011.
 4. NCCN Drugs & Biologics Compendium™. Duragesic® (fentanyl transdermal system). Copyright 2011, National Comprehensive Cancer Network (NCCN).
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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare (Duragesic®)	2/15/2008	5028	Fentanyl Transdermal System
Great-West Healthcare	6/2006	MDL05.100.2	Duragesic

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