HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use OPANA® ER safely and effectively. See full prescribing information for OPANA® ER.

OPANA® ER (oxymorphone hydrochloride) Extended-Release tablets, for oral use, CII

Initial U.S. Approval: 1959

WARNING: ABUSE POTENTIAL, LIFE-THREATENING RESPIRATORY DEPRESSION, ACCIDENTAL EXPOSURE, and INTERACTION WITH ALCOHOL

See full prescribing information for complete boxed warning.

- **OPANA ER contains oxymorphone, a Schedule II controlled substance. Monitor for signs of misuse, abuse, and addiction during OPANA ER therapy. (5.1, 9)**
- **Fatal respiratory depression may occur, with highest risk at initiation and with dose increases. Instruct patients on proper administration of OPANA ER tablets to reduce the risk. (5.2)**
- **Accidental ingestion of OPANA ER can result in fatal overdose of oxymorphone, especially in children. (5.3)**
- **Instruct patients not to consume alcoholic beverages or use prescription or non-prescription products containing alcohol while taking OPANA ER because of the risk of increased, and potentially fatal, plasma oxymorphone levels. (5.4)**

----------RECENT MAJOR CHANGES----------

Boxed Warning	07/2012
Indications and Usage (1)	07/2012
Dosage and Administration (2)	07/2012
Contraindications (4)	07/2012
Warnings and Precautions (5)	07/2012

----------INDICATIONS AND USAGE----------

OPANA ER is an opioid agonist indicated for the relief of moderate to severe pain in patients requiring continuous around-the-clock opioid treatment for an extended period of time. (1)

Limitations of Use

- OPANA ER is not for use:
  - As an as-needed (prn) analgesic (1)
  - For pain that is mild or not expected to persist for an extended period of time (1)
  - For acute pain (1)
  - For postoperative pain, unless the patient is already receiving chronic opioid therapy prior to surgery, or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time (1)

----------DOSAGE AND ADMINISTRATION----------

- Individualize dosing based on patient's prior analgesic treatment experience, and titrate as needed to provide adequate analgesia and minimize adverse reactions. (2.1, 2.2,)
- Administer on an empty stomach, at least 1 hour prior to or 2 hours after eating. (2.1)
- Instruct patients to swallow OPANA ER tablets intact. (2.4)
- Do not abruptly discontinue OPANA ER in a physically dependent patient. (2.3, 5.13)
- Reduce the dose of OPANA ER in patients with mild hepatic impairment and patients with renal impairment. (2.5, 2.6)

----------DOSAGE FORMS AND STRENGTHS----------

- Extended-Release Tablets, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, and 40 mg

----------CONTRAINDICATIONS----------

- Significant respiratory depression (4)
- Acute or severe bronchial asthma (4)
- Known or suspected paralytic ileus (4)
- Hypersensitivity to oxymorphone (4)
- Moderate or severe hepatic impairment (4)

----------WARNINGS AND PRECAUTIONS----------

See Boxed WARNINGS

- Elderly, cachectic, and debilitated patients, and patients with chronic pulmonary disease: Monitor closely because of increased risk of respiratory depression. (5.5, 5.6)
- Interaction with CNS depressants: Consider dose reduction of one or both drugs because of additive effects. (5.7, 7.2)
- Hypotensive effect: Monitor during dose initiation and titration. (5.9)
- Patients with head injury or increased intracranial pressure: Monitor for sedation and respiratory depression. Avoid use of OPANA ER in patients with impaired consciousness or coma susceptible to intracranial effects of CO_2 retention. (5.10)
- Respiratory depression: Increased risk in elderly, debilitated patients, and those suffering from conditions accompanied by hypoxia, hypercapnia, or decreased respiratory reserve. (5.2)

----------ADVERSE REACTIONS----------

Adverse reactions in ≥2% of patients in placebo-controlled trials: nausea, constipation, dizziness, somnolence, vomiting, pruritus, headache, sweating increased, dry mouth, sedation, diarrhea, insomnia, fatigue, appetite decreased, and abdominal pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Endo Pharmaceuticals Inc. at 1-800-462-3636 or FDA at 1-800 FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- CNS depressants: Increased risk of respiratory depression, hypotension, profound sedation, coma or death. When combined therapy with CNS depressant is contemplated, the dose of one or both agents should be reduced. (7.2)
- Mixed agonist/antagonist opioids (i.e., pentazocine, nalbuphine, and butorphanol): May reduce analgesic effect and/or precipitate withdrawal symptoms. (7.3)

----------USE IN SPECIFIC POPULATIONS----------

- Pregnancy: Based on animal data, may cause fetal harm. (8.1)
- Nursing mothers: Closely monitor infants of nursing women receiving OPANA ER. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 07/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

***Sections or subsections omitted from the full prescribing information are not listed.**

FULL PRESCRIBING INFORMATION

WARNING: ABUSE POTENTIAL, LIFE-THREATENING RESPIRATORY DEPRESSION, ACCIDENTAL EXPOSURE, and INTERACTION WITH ALCOHOL

Abuse Potential

OPANA ER contains oxymorphone, an opioid agonist and Schedule II controlled substance with an abuse liability similar to other opioid agonists, legal or illicit *[see Warnings and Precautions (5.1)]*. Assess each patient's risk for opioid abuse or addiction prior to prescribing OPANA ER. The risk for opioid abuse is increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depressive disorder). Routinely monitor all patients receiving OPANA ER for signs of misuse, abuse, and addiction during treatment *[see Drug Abuse and Dependence (9)]*.

Life-threatening Respiratory Depression

Respiratory depression, including fatal cases, may occur with use of OPANA ER, even when the drug has been used as recommended and not misused or abused *[see Warnings and Precautions (5.2)]*. Proper dosing and titration are essential and OPANA ER should only be prescribed by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain. Monitor for respiratory depression, especially during initiation of OPANA ER or following a dose increase. Instruct patients to swallow OPANA ER tablets whole. Crushing, dissolving, or chewing OPANA ER can cause rapid release and absorption of a potentially fatal dose of oxymorphone.

Accidental Exposure

Accidental ingestion of OPANA ER, especially in children, can result in a fatal overdose of oxymorphone *[see Warnings and Precautions (5.3)]*.

Interaction with Alcohol

The co-ingestion of alcohol with OPANA ER may result in an increase of plasma levels and potentially fatal overdose of oxymorphone *[see Warnings and Precautions (5.4)]*. Instruct patients not to consume alcoholic beverages or use prescription or non-prescription products that contain alcohol while on OPANA ER.

1 INDICATIONS AND USAGE

OPANA ER is indicated for the relief of moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time.

Limitations of Usage

OPANA ER is not intended for use:

- As an as-needed (prn) analgesic
- For pain that is mild or not expected to persist for an extended period of time
- For acute pain
- For postoperative pain unless the patient is already receiving chronic opioid therapy prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time.

2 DOSAGE AND ADMINISTRATION

2.1 Initial Dosing

Initiate the dosing regimen for each patient individually, taking into account the patient's prior analgesic treatment experience. Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy with OPANA ER *[see Warnings and Precautions (5.2)]*.

Consider the following factors when selecting an initial dose of OPANA ER:

- Total daily dose, potency, and any prior opioid the patient has been taking previously;
- Reliability of the relative potency estimate used to calculate the equivalent dose of oxymorphone needed (Note: potency estimates may vary with the route of administration);
- Patient's degree of opioid experience and opioid tolerance;
- General condition and medical status of the patient;
- Concurrent medication;
- Type and severity of the patient's pain.

OPANA ER is administered at a frequency of twice daily (every 12 hours). Administer on an empty stomach, at least 1 hour prior to or 2 hours after eating.

Use of OPANA ER as the First Opioid Analgesic
Initiate Opana ER therapy with the 5 mg tablet twice daily (at 12-hour intervals). Adjust the dose of OPANA ER in increments of 5-10 mg every 12 hours every 3 to 7 days.

Conversion from OPANA to OPANA ER
Patients receiving OPANA may be converted to OPANA ER by administering half the patient's total daily oral OPANA dose as OPANA ER, every 12 hours.

Conversion from Parenteral Oxymorphone to OPANA ER
The absolute oral bioavailability of OPANA ER is approximately 10%. Convert patients receiving parenteral oxymorphone to OPANA ER by administering 10 times the patient's total daily parenteral oxymorphone dose as OPANA ER in two equally divided doses (e.g., [IV dose x 10] divided by 2). Due to patient variability with regards to opioid analgesic response, upon conversion monitor patients closely to evaluate for adequate analgesia and side effects.

Conversion from Other Oral Opioids to OPANA ER
While there are useful tables of oral and parenteral equivalents, there is substantial inter-patient variability in the relative potency of different opioid drugs and formulations. As such, it is safer to underestimate a patient's 24-hour oral oxymorphone dose and provide rescue medication (e.g. immediate-release oxymorphone) than to overestimate the 24-hour oral oxymorphone dose and manage an adverse reaction. Consider the following general points:

In a Phase 3 clinical trial with an open-label titration period, patients were converted from their prior opioid to OPANA ER using the following table as a guide for the initial OPANA ER dose.

- **The table is not a table of equianalgesic doses.**
- **The conversion ratios in this table are only to be used for the conversion from oral therapy with one of the listed opioid analgesics to OPANA ER.**
- **Do not use this table to convert from OPANA ER to another opioid. Doing so will result in an over-estimation of the dose of the new opioid and may result in fatal overdose.**

For example, a patient receiving oxycodone at a total daily dose of 40 mg would then be converted to a total daily dose of 20 mg of oxymorphone (40 mg x 0.5), dosed as OPANA ER 10 mg twice daily.

CONVERSION RATIOS TO OPANA ER

Opioid	Total Daily Oral Dose	Oral Conversion Ratio
Oxymorphone	10 mg	1
Hydrocodone	20 mg	0.5
Oxycodone	20 mg	0.5
Methadone	20 mg	0.5
Morphine	30 mg	0.333

2.2 Titration and Maintenance of Therapy
Individually titrate OPANA ER to a dose that provides adequate analgesia and minimizes adverse reactions. Continually reevaluate patients receiving OPANA ER to assess the maintenance of pain control and the relative incidence of adverse reactions. During chronic therapy, especially for non-cancer-related pain (or pain associated with other terminal illnesses), periodically reassess the continued need for the use of opioid analgesics.
If the level of pain increases, attempt to identify the source of increased pain, while adjusting the OPANA ER dose to decrease the level of pain. Because steady-state plasma concentrations are approximated within 3 days, OPANA ER dosage adjustments, preferably at increments of 5-10 mg every 12 hours, may be done every 3 to 7 days. Patients who experience breakthrough pain may require dosage adjustment or rescue medication with a small dose of an immediate-release medication (e.g. immediate-release oxymorphone).

During chronic, around-the-clock opioid therapy, especially for non-cancer pain syndromes, reassess the continued need for around-the-clock opioid therapy periodically (e.g., every 6 to 12 months) as appropriate.

If signs of excessive opioid-related adverse reactions are observed, the next dose may be reduced. Adjust the dose to obtain an appropriate balance between management of pain and opioid-related adverse reactions.

2.3 Discontinuation of OPANA ER

When a patient no longer requires therapy with OPANA ER, use a gradual downward titration of the dose every two to four days, to prevent signs and symptoms of withdrawal in the physically-dependent patient. Do not abruptly discontinue OPANA ER.

2.4 Administration of OPANA ER

Instruct patients to swallow OPANA ER tablets intact. The tablets are not to be crushed, dissolved, or chewed due to the risk of rapid release and absorption of a potentially fatal dose of oxymorphone *[see Warnings and Precautions (5.2)]*. Administer on an empty stomach, at least 1 hour prior to or 2 hours after eating.

2.5 Patients with Hepatic Impairment

OPANA ER is contraindicated in patients with moderate or severe hepatic impairment.

In opioid-naïve patients with mild hepatic impairment, initiate treatment with the 5 mg dose. For patients on prior opioid therapy, start OPANA ER at 50% lower than the starting dose for a patient with normal hepatic function on prior opioids and titrate slowly. Monitor patients closely for signs of respiratory or central nervous system depression *[see Warnings and Precautions (5.2), Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)]*.

2.6 Patients with Renal Impairment

In patients with creatinine clearance rates less than 50 mL/min, start OPANA ER in the opioid-naïve patient with the 5 mg dose. For patients on prior opioid therapy, start OPANA ER at 50% lower than the starting dose for a patient with normal renal function on prior opioids and titrate slowly. Monitor patients closely for signs of respiratory or central nervous system depression *[see Warnings and Precautions (5.2), Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)]*.

2.7 Geriatric Patients

The steady-state plasma concentrations of oxymorphone are approximately 40% higher in elderly subjects than in young subjects. Initiate dosing with OPANA ER in patients 65 years of age and over using the 5 mg dose and monitor closely for signs of respiratory and central nervous system depression when initiating and titrating OPANA ER to adequate analgesia *[see Warnings and Precautions (5.2), Use in Specific Populations (8.5) and Clinical Pharmacology (12.3)]*. For patients on prior opioid therapy, start OPANA ER at 50% lower than the starting dose for a younger patient on prior opioids and titrate slowly.

3 DOSAGE FORMS AND STRENGTHS

The 5 mg dosage form is a pink, octagon shape, film coated, convex extended-release tablets debossed with "5" on one side and plain on the other.

The 7.5 mg dosage form is a gray, octagon shape, film coated, convex extended-release tablets debossed with "7 ½" on one side and plain on the other.

The 10 mg dosage form is a light orange, octagon shape, film coated, convex extended-release tablets debossed with "10" on one side and plain on the other.

The 15 mg dosage form is a white, octagon shape, film coated, convex extended-release tablets debossed with "15" on one side and plain on the other.

The 20 mg dosage form is a light green, octagon shape, film coated, convex extended-release tablets debossed with "20" on one side and plain on the other.

The 30 mg dosage form is a red, octagon shape, film coated, convex extended-release tablets debossed with "30" on one side and plain on the other.

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