OXYMORPHONE HYDROCHLORIDE- oxymorphone hydrochloride tablet, film coated, extended release
Quality Care Products, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use OXYMORPHONE HYDROCHLORIDE EXTENDED-RELEASE TABLETS safely and effectively. See full prescribing information for OXYMORPHONE HYDROCHLORIDE EXTENDED-RELEASE TABLETS.

OXYMORPHONE HYDROCHLORIDE extended-release tablets, for oral use, CII
Initial U.S. Approval: 1959

WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; INTERACTION WITH ALCOHOL; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES AND OTHER CNS DEPRESSANTS.

***See full prescribing information for complete boxed warning*.**

- **Oxymorphone hydrochloride extended-release tablets expose users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk before prescribing, and monitor regularly these behaviors and conditions. (5.1)**
- **To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for these products. (5.2)**
- **Serious life-threatening or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase. Instruct patients to swallow oxymorphone hydrochloride extended-release tablets whole to avoid exposure to a potentially fatal dose of oxymorphone. (5.3)**
- **Accidental ingestion of oxymorphone hydrochloride extended-release tablets, especially by children, can result in fatal overdose of oxymorphone. (5.3)**
- **Prolonged use of oxymorphone hydrochloride extended-release tablets during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. 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. (5.4)**
- **Instruct patients not to consume alcohol or any product containing alcohol while taking oxymorphone hydrochloride extended-release tablets because co-ingestion can result in fatal plasma oxymorphone levels. (5.5)**
- **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. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation. (5.5, 7)**

RECENT MAJOR CHANGES

Boxed Warning	6/2018
Warnings and Precautions (5.2)	6/2018

INDICATIONS AND USAGE

Oxymorphone hydrochloride extended-release tablets are an opioid agonist indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. (1)_

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve

oxymorphone hydrochloride extended-release tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. (1)
- Oxymorphone hydrochloride extended-release tablets are not indicated as an as-needed (prn) analgesic. (1)

DOSAGE AND ADMINISTRATION

- To be prescribed only by healthcare providers knowledgeable in use of potent opioids for management of chronic pain. (2.1)
- Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals. (2.1)
- Individualize dosing based on the severity of pain, patient response, prior analgesic experience, and risk factors for addiction, abuse, and misuse. (2.1)
- Administer on an empty stomach, at least 1 hour prior to or 2 hours after eating. (2.1)
- For opioid-naïve and opioid non-tolerant patients, initiate treatment with 5 mg tablets orally every 12 hours. (2.2)
- To convert to oxymorphone hydrochloride extended-release tablets from another opioid, use available conversion factors to obtain estimated dose. (2.2)
- Dose can be increased every 3 to 7 days, using increments of 5 mg to 10 mg every 12 hours (i.e., 10 mg to 20 mg per day). (2.3)
- Do not abruptly discontinue oxymorphone hydrochloride extended-release tablets in a physically dependent patient. (2.4, 5.14)
- Mild Hepatic Impairment: For opioid-naïve patients, initiate treatment with 5 mg and titrate slowly. For patients on prior opioid therapy, reduce starting dose by 50% and titrate slowly. Monitor for signs of respiratory and central nervous system depression. (2.5)
- Renal Impairment: For opioid-naïve patients, initiate treatment with 5 mg and titrate slowly. For patients on prior opioid therapy, reduce starting dose by 50% and titrate slowly. Monitor for signs of respiratory and central nervous system depression. (2.6)
- Geriatric Patients: Initiate dosing with 5 mg, titrate slowly, and monitor for signs of respiratory and central nervous system depression. (2.7)

DOSAGE FORMS AND STRENGTHS

Extended-release tablets: 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, and 40 mg (3)

CONTRAINDICATIONS

- Significant respiratory depression. (4)
- Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment. (4)
- Hypersensitivity to oxymorphone. (4)
- Moderate or severe hepatic impairment. (4)
- Known or suspected gastrointestinal obstruction, including paralytic ileus. (4)

WARNINGS AND PRECAUTIONS

See Boxed WARNINGS

- Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly Cachectic or Debilitated Patients: Monitor closely particularly during initiation and titration. (5.6)
- Anaphylaxis, Angioedema, and Other Hypersensitivity Reactions: If symptoms occur, stop administration immediately, discontinue permanently, and do not rechallenge with any other oxymorphone formulation. (5.7)
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid. (5.8)
- Severe Hypotension: Monitor during dose initiation and titration. Avoid use of oxymorphone hydrochloride extended-release tablets in patients with circulatory shock. (5.10)
- Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury or Impaired Consciousness: Monitor for sedation and respiratory depression. Avoid use of oxymorphone hydrochloride extended-release tablets in patients with impaired consciousness or coma. (5.11)

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 Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Serotonergic Drugs: Concomitant use may result in serotonin syndrome. Discontinue oxymorphone hydrochloride extended-release tablets if serotonin syndrome is suspected. (7)
- Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics: Avoid use with oxymorphone hydrochloride extended-release tablets because they may reduce analgesic effect of oxymorphone hydrochloride extended-release tablets or precipitate withdrawal symptoms. (7)
- Monoamine Oxidase Inhibitors (MAOIs): Can potentiate the effects of oxymorphone. Avoid concomitant use in patients receiving MAOIs or within 14 days of stopping treatment with an MAOI. (7)

USE IN SPECIFIC POPULATIONS

- Pregnancy: May cause fetal harm. (8.1)
- Lactation: Not recommended. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 9/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; INTERACTION WITH ALCOHOL; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

Oxymorphone hydrochloride extended-release tablets expose patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing oxymorphone hydrochloride extended-release tablets, and monitor all patients regularly for the development of these behaviors and conditions *[see Warnings and Precautions (5.1)].*

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)

To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a REMS for these products *[see Warnings and Precautions (5.2)]*. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to

- **complete a REMS-compliant education program,**
- **counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products,**
- **emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and**
- **consider other tools to improve patient, household, and community safety.**

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of oxymorphone hydrochloride extended-release tablets. Monitor for respiratory depression, especially during initiation of oxymorphone hydrochloride extended-release tablets or following a dose increase. Instruct patients to swallow oxymorphone hydrochloride extended-release tablets whole; crushing, chewing, or dissolving oxymorphone hydrochloride extended-release tablets can cause rapid release and absorption of a potentially fatal dose of oxymorphone *[see Warnings and Precautions (5.3)].*

Accidental Ingestion

Accidental ingestion of even one dose of oxymorphone hydrochloride extended-release tablets, especially by children, can result in a fatal overdose of oxymorphone *[see Warnings and Precautions (5.3)].*

Neonatal Opioid Withdrawal Syndrome

Prolonged use of oxymorphone hydrochloride extended-release tablets during pregnancy 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 *[see Warnings and Precautions (5.4)].*

Interaction with Alcohol

Instruct patients not to consume alcoholic beverages or use prescription or non-prescription products that contain alcohol while taking oxymorphone hydrochloride extended-release tablets. The co-ingestion of alcohol with oxymorphone hydrochloride extended-release tablets may result in increased plasma levels and a potentially fatal overdose of oxymorphone *[see Warnings and Precautions (5.5)].*

Risks from Concomitant Use With Benzodiazepines Or Other CNS Depressants

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 *[see Warnings and Precautions (5.5), Drug Interactions (7)].*

- **Reserve concomitant prescribing of oxymorphone hydrochloride extended-release tablets and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.**
- **Limit dosages and durations to the minimum required.**
- **Follow patients for signs and symptoms of respiratory depression and sedation.**

1 INDICATIONS AND USAGE

Oxymorphone hydrochloride extended-release tablets are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Usage

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations *[see Warnings and Precautions (5.1)]*, reserve oxymorphone hydrochloride extended-release tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
- Oxymorphone hydrochloride extended-release tablets are not indicated as an as-needed (prn) analgesic.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Instructions

Oxymorphone hydrochloride extended-release tablets should be prescribed only by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain.

- Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals *[see Warnings and Precautions (5)]*. Initiate the dosing regimen for each patient individually, taking into account the patient's severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse *[see Warnings and Precautions (5.1)]*.
- Monitor patients closely for respiratory depression, especially within the first 24 to 72 hours of initiating therapy and following dosage increases with oxymorphone hydrochloride extended-release tablets and adjust the dosage accordingly *[see Warnings and Precautions (5.3)].*

Instruct patients to swallow oxymorphone hydrochloride extended-release tablets whole *[see Patient Counseling Information (17)]*. Crushing, chewing, or dissolving oxymorphone hydrochloride extended-release tablets will result in uncontrolled delivery of oxymorphone and can lead to overdose or death *[see Warnings and Precautions (5.3)]*.

Administer on an empty stomach, at least 1 hour prior to or 2 hours after eating.

Oxymorphone hydrochloride extended-release tablets are administered orally twice daily (every 12 hours).

2.2 Initial Dosing

Use of Oxymorphone Hydrochloride Extended-Release Tablets as the First Opioid Analgesic

Initiate treatment with oxymorphone hydrochloride extended-release tablets with the 5 mg tablet orally every 12-hours.

Use of Oxymorphone Hydrochloride Extended-Release Tablets in Patients who are not Opioid Tolerant

The starting dose for patients who are not opioid tolerant is oxymorphone hydrochloride extended-release tablets 5 mg orally every 12 hours. Patients considered opioid tolerant are those taking, for one week or longer, at least 60 mg oral morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid.

Use of higher starting doses in patients who are not opioid tolerant may cause fatal respiratory depression.

Conversion from Oxymorphone Hydrochloride Tablets to Oxymorphone Hydrochloride Extended-Release Tablets

Patients receiving oxymorphone hydrochloride tablets may be converted to oxymorphone hydrochloride extended-release tablets by administering half the patient's total daily oral oxymorphone hydrochloride tablets dose as oxymorphone hydrochloride extended-release tablets, every 12 hours.

Conversion from Parenteral Oxymorphone to Oxymorphone Hydrochloride Extended-Release Tablets

The absolute oral bioavailability of oxymorphone hydrochloride extended-release tablets are approximately 10%. Convert patients receiving parenteral oxymorphone to oxymorphone hydrochloride extended-release tablets by administering 10 times the patient's total daily parenteral oxymorphone dose as oxymorphone hydrochloride extended-release tablets in two equally divided doses (e.g., [intravenous dose × 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 Oxymorphone Hydrochloride Extended-Release Tablets

Discontinue all other around-the-clock opioid drugs when oxymorphone hydrochloride extended-release tablets therapy is initiated.

While there are useful tables of opioid equivalents readily available, there is substantial inter-patient variability in the relative potency of different opioid drugs and products. As such, it is preferable to underestimate a patient's 24-hour oral oxymorphone requirements and provide rescue medication (e.g., immediate-release opioid) than to overestimate the 24-hour oral oxymorphone requirements which could result in adverse reactions. In an oxymorphone hydrochloride extended-release tablets clinical trial with an open-label titration period, patients were converted from their prior opioid to oxymorphone hydrochloride extended-release tablets using the table below as a guide for the initial oxymorphone hydrochloride extended-release tablets dose.

Consider the following when using the information in the table below:

- This is **not** a table of equianalgesic doses.
- The conversion factors in this table are only for the conversion **from** one of the listed oral opioid analgesics **to** oxymorphone hydrochloride extended-release tablets.
- This table **cannot** be used to convert **from** oxymorphone hydrochloride extended-release tablets **to** another opioid. Doing so will result in an over-estimation of the dose of the new opioid and may result in fatal overdose.

CONVERSION FACTORS TO OXYMORPHONE HYDROCHLORIDE EXTENDED-RELEASE TABLETS	
Prior Oral Opioid	Approximate Oral Conversion Factor
Oxymorphone	1
Hydrocodone	0.5
Oxycodone	0.5
Methadone	0.5
Morphine	0.333

To calculate the estimated oxymorphone hydrochloride extended-release tablet dose using the table above:

- For patients on a single opioid, sum the current total daily dose of the opioid and then multiply the total daily dose by the conversion factor to calculate the approximate oral (active opioid) daily dose.
- For patients on a regimen of more than one opioid, calculate the approximate oral (active opioid) dose for each opioid and sum the totals to obtain the approximate total (active opioid) daily dose.
- For patients on a regimen of fixed-ratio opioid/non-opioid analgesic products, use only the opioid component of these products in the conversion.

Always round the dose down, if necessary, to the appropriate oxymorphone hydrochloride extended-release tablet strength(s) available.

Example conversion from a single opioid to oxymorphone hydrochloride extended-release tablets:

Step 1: Sum the total daily dose of the opioid oxycodone 20 mg BID

20 mg former opioid 2 times daily = 40 mg total daily dose of former opioid

Step 2: Calculate the approximate equivalent dose of oral (active opioid) based on the total daily dose of the current opioid using the table above 40 mg total daily dose of former opioid × 0.5 mg Conversion Factor = 20 mg of oral (active opioid) daily

Step 3: Calculate the approximate starting dose of oxymorphone hydrochloride extended-release tablets to be given every 12 hours. Round down, if necessary, to the appropriate oxymorphone hydrochloride extended-release tablets strengths available.

10 mg oxymorphone hydrochloride extended-release tablets every 12 hours

Conversion from Methadone to Oxymorphone Hydrochloride Extended-Release Tablets

Close monitoring is of particular importance when converting from methadone to other opioid agonists. The ratio between methadone and other opioid agonists may vary widely as a function of previous dose exposure. Methadone has a long half-life and can accumulate in the plasma.

2.3 Titration and Maintenance of Therapy

Individually titrate oxymorphone hydrochloride extended-release tablets to a dose that provides adequate analgesia and minimizes adverse reactions. Continually reevaluate patients receiving oxymorphone hydrochloride extended-release tablets to assess the maintenance of pain control and the relative incidence of adverse reactions, as well as monitoring for the development of addiction, abuse, and misuse. Frequent communication is important among the prescriber, other members of the healthcare team, the patient, and the caregiver/family during periods of changing analgesic requirements, including initial titration. During chronic therapy, 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 oxymorphone hydrochloride extended-release tablets dose to decrease the level of pain. Because steady-state plasma concentrations are approximated within 3 days, oxymorphone hydrochloride extended-release tablets dosage adjustments, preferably at increments of 5 mg to 10 mg every 12 hours, may be done every 3 to 7 days.

Patients who experience breakthrough pain may require a dose increase of oxymorphone hydrochloride extended-release tablets, or may need rescue medication with an appropriate dose of an immediate-release analgesic. If the level of pain increases after dose stabilization, attempt to identify the source of increased pain before increasing oxymorphone hydrochloride extended-release tablets dose.

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

2.4 Discontinuation of Oxymorphone Hydrochloride Extended-Release Tablets

When a patient no longer requires therapy with oxymorphone hydrochloride extended-release tablets, taper the dose gradually, by 25% to 50% every 2 to 4 days, while monitoring carefully for signs and symptoms of withdrawal. If the patient develops these signs or symptoms, raise the dose to the previous level and taper more slowly, either by increasing the interval between decreases, decreasing the amount of change in dose, or both. Do not abruptly discontinue oxymorphone hydrochloride extended-release tablets *[see Warnings and Precautions (5.14), Drug Abuse and Dependence (9.3)].*

2.5 Dosage Modifications in Patients with Mild Hepatic Impairment

Oxymorphone hydrochloride extended-release tablets are 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 oxymorphone hydrochloride extended-release tablets 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 (5.3), Use in Specific Populations (8.6)* and *Clinical Pharmacology (12.3)].*

2.6 Dosage Modifications in Patients with Renal Impairment

In patients with creatinine clearance rates less than 50 mL/min, start oxymorphone hydrochloride extended-release tablets in the opioid-naïve patient with the 5 mg dose. For patients on prior opioid therapy, start oxymorphone hydrochloride extended-release tablets 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 (5.3), Use in Specific Populations (8.7)* and *Clinical Pharmacology (12.3)].*

2.7 Dosage Modifications in Geriatric Patients

The steady-state plasma concentrations of oxymorphone are higher in elderly subjects than in young subjects. Initiate dosing with oxymorphone hydrochloride extended-release tablets 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 oxymorphone hydrochloride extended-release tablets to adequate analgesia *[see Warnings and Precautions (5.3), Use in Specific Populations (8.5)* and *Clinical Pharmacology (12.3)]*. For patients on prior opioid therapy, start oxymorphone

hydrochloride extended-release tablets at 50% lower than the starting dose for a younger patient on prior opioids and titrate slowly.

3 DOSAGE FORMS AND STRENGTHS

Oxymorphone hydrochloride extended-release tablets USP, 5 mg dosage form is a purple, round, film-coated extended-release tablet debossed with “G71” on one side and blank on the other side.

Oxymorphone hydrochloride extended-release tablets USP, 7.5 mg dosage form is a gray, round, film-coated extended-release tablet debossed with “G75” on one side and blank on the other side.

Oxymorphone hydrochloride extended-release tablets USP, 10 mg dosage form is an orange, round, film-coated extended-release tablet debossed with “G72” on one side and blank on the other side.

Oxymorphone hydrochloride extended-release tablets USP, 15 mg dosage form is a white, round, film-coated extended-release tablet debossed with “G76” on one side and blank on the other side.

Oxymorphone hydrochloride extended-release tablets USP, 20 mg dosage form is a green, round, film-coated extended-release tablet debossed with “G73” on one side and blank on the other side.

Oxymorphone hydrochloride extended-release tablets USP, 30 mg dosage form is a brown, round, film-coated extended-release tablet debossed with “G77” on one side and blank on the other side.

Oxymorphone hydrochloride extended-release tablets USP, 40 mg dosage form is an orange, round, film-coated extended-release tablet debossed with “G74” on one side and blank on the other side.

4 CONTRAINDICATIONS

Oxymorphone hydrochloride extended-release tablets are contraindicated in patients with:

- Significant respiratory depression *[see Warnings and Precautions (5.3)]*
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment *[see Warnings and Precautions (5.6)]*
- Hypersensitivity (e.g. anaphylaxis) to oxymorphone, any other ingredients in oxymorphone hydrochloride extended-release tablets *[see Warnings and Precautions (5.7), Adverse Reactions (6)]*
- Moderate and severe hepatic impairment *[see Warnings and Precautions (5.9),Clinical Pharmacology (12.3)]*
- Known or suspected gastrointestinal obstruction, including paralytic ileus *[see Warnings and Precautions (5.12)]*

5 WARNINGS AND PRECAUTIONS

5.1 Addiction, Abuse, and Misuse

Oxymorphone hydrochloride extended-release tablet contains, oxymorphone, a Schedule II controlled substance. As an opioid, oxymorphone hydrochloride extended-release tablets exposes users to the risks of addiction, abuse, and misuse. Because extended-release products such as oxymorphone hydrochloride extended-release tablets deliver the opioid over an extended period of time, there is a greater risk for overdose and death due to the larger amount of oxymorphone present *[see Drug Abuse and Dependence (9)]*.

Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed oxymorphone hydrochloride extended-release tablets. Addiction can occur at recommended doses and if the drug is misused or abused.

Assess each patient's risk for opioid abuse or addiction, abuse, or misuse prior to prescribing oxymorphone hydrochloride extended-release tablets, and monitor all patients receiving oxymorphone hydrochloride extended-release tablets for the development of these behaviors and conditions. Risks are 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 depression). The potential for these risks should not, however, prevent the proper management of pain in any given patient. Patients at increased risk may be prescribed opioids such as oxymorphone hydrochloride extended-release tablets, but use in such patients necessitates intensive counseling about the risks and proper use of oxymorphone hydrochloride extended-release tablets along with intensive monitoring for signs of addiction, abuse, and misuse.

Abuse, or misuse of oxymorphone hydrochloride extended-release tablets by crushing, chewing, snorting, or injecting the dissolved product will result in the uncontrolled delivery of the oxymorphone and can result in overdose and death *[see Overdosage (10)]*.

Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing oxymorphone hydrochloride extended-release tablets. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper disposal of unused drug *[see Patient Counseling Information (17)]*. Contact local state professional licensing board or state controlled substances authority for information on how to prevent and detect abuse or diversion of this product.

5.2 Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)

To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to do all of the following:

- Complete a REMS-compliant education program offered by an accredited provider of continuing education (CE) or another education program that includes all the elements of the FDA Education Blueprint for Health Care Providers Involved in the Management or Support of Patients with Pain.
- Discuss the safe use, serious risks, and proper storage and disposal of opioid analgesics with patients and/or their caregivers every time these medicines are prescribed. The Patient Counseling Guide (PCG) can be obtained at this

link: www.fda.gov/OpioidAnalgesicREMSPCG.
- Emphasize to patients and their caregivers the importance of reading the Medication Guide that they will receive from their pharmacist every time an opioid analgesic is dispensed to them.
- Consider using other tools to improve patient, household, and community safety, such as patient-prescriber agreements that reinforce patient-prescriber responsibilities.

To obtain further information on the opioid analgesic REMS and for a list of accredited REMS CME/CE, call 1-800-503-0784, or log on to www.opioidanalgesicrems.com. The FDA Blueprint can be found at www.fda.gov/OpioidAnalgesicREMSBlueprint.

5.3 Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression from opioid use, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status *[see Overdosage (10)]*. Carbon dioxide (CO_2) retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of oxymorphone hydrochloride extended-release tablets, the risk is greatest during the initiation of therapy or following a dose increase. Monitor patients closely for respiratory depression, especially within the first 24 to 72 hours of initiating therapy and following dose increases of oxymorphone hydrochloride extended-release tablets.

To reduce the risk of respiratory depression, proper dosing and titration of oxymorphone hydrochloride extended-release tablets are essential *[see Dosage and Administration (2.1, 2.2)]*. Overestimating the oxymorphone hydrochloride extended-release tablets dosage when converting patients from another opioid product can result in fatal overdose with the first dose.

Accidental ingestion of even one dose of oxymorphone hydrochloride extended-release tablets, especially by children, can result in respiratory depression and death due to an overdose of oxymorphone.

5.4 Neonatal Opioid Withdrawal Syndrome

Prolonged use of oxymorphone hydrochloride extended-release tablets during pregnancy can result in withdrawal signs in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available *[see Use in Specific Populations (8.1), Patient Counseling Information (17)]*.

5.5 Risks from Concomitant Use with Benzodiazepines or Other CNS

Depressants

Patients must not consume alcoholic beverages or prescription or non-prescription products containing alcohol while on oxymorphone hydrochloride extended-release tablets therapy. The co-ingestion of alcohol with oxymorphone hydrochloride extended-release tablets may result in increased plasma levels and a potentially fatal overdose of oxymorphone *[see Clinical Pharmacology (12.3)]*.

Profound sedation, respiratory depression, coma, and death may result from the concomitant use of oxymorphone hydrochloride extended-release tablets with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with opioid analgesics *[see Drug Interactions (7)].*

If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant than indicated in the absence of an opioid and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking a benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid analgesic, and titrate based on clinical response. Follow patients closely for signs and symptoms of respiratory depression and sedation.

Advise both patients and caregivers about the risks of respiratory depression and sedation when oxymorphone hydrochloride extended-release tablets are used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressant have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs *[see Drug Interactions (7)* and *Patient Counseling Information (17)].*

5.6 Risks of Life-Threatening Respiratory Depression in Patients with Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients

The use of oxymorphone hydrochloride extended-release tablets in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

Patients with Chronic Pulmonary Disease: Oxymorphone hydrochloride extended-release tablets treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased

respiratory drive including apnea, even at recommended dosages of oxymorphone hydrochloride extended-release tablets *[see Warnings and Precautions (5.3)].*

Elderly, Cachectic, or Debilitated Patients: Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients *[see Warnings and Precautions (5.3)]*.

Monitor such patients closely, particularly when initiating and titrating oxymorphone hydrochloride extended-release tablets and when oxymorphone hydrochloride extended-release tablets are given concomitantly with other drugs that depress respiration *[see Warnings and Precautions (5.3)]*. Alternatively, consider the use of non-opioid analgesics in these patients.

5.7 Anaphylaxis, Angioedema, and Other Hypersensitivity Reactions

Potentially life-threatening hypersensitivity reactions, including anaphylaxis and angioedema, have occurred in patients treated with oxymorphone hydrochloride extended-release tablets in the postmarket setting. The most commonly described clinical features in these reports were swelling of the face, eyes, mouth, lips, tongue, hands, and/or throat; dyspnea; hives, pruritus, and/or rash; and nausea/vomiting. If anaphylaxis or other hypersensitivity occurs, stop administration of oxymorphone hydrochloride extended-release tablets immediately, discontinue oxymorphone hydrochloride extended-release tablets permanently, and do not rechallenge with any formulation of oxymorphone. Advise patients to seek immediate medical attention if they experience any symptoms of a hypersensitivity reaction *[see Patient Counseling Information (17)]*.

5.8 Adrenal Insufficiency

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

5.9 Use in Patients with Hepatic Impairment

A study of oxymorphone hydrochloride extended-release tablets in patients with hepatic disease indicated greater plasma concentrations than those with normal hepatic function *[see Clinical Pharmacology (12.3)]*. Oxymorphone hydrochloride extended-release tablets are contraindicated in patients with moderate or severe hepatic impairment. In patients with mild hepatic impairment reduce the starting dose to the lowest dose and monitor for signs of respiratory and central nervous system depression *[see Dosage and Administration (2.5)]*.

5.10 Severe Hypotension

Oxymorphone hydrochloride extended-release tablets may cause severe hypotension including orthostatic hypotension and syncope in ambulatory patients. There is an increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (e.g. phenothiazines or general anesthetics) *[see Drug Interactions (7)]*. Monitor these patients for signs of hypotension after initiating or titrating the dosage of oxymorphone hydrochloride extended-release tablets. In patients with circulatory shock, oxymorphone hydrochloride extended-release tablets may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of oxymorphone hydrochloride extended-release tablets in patients with circulatory shock.

5.11 Risks of Use in Patients with Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness

In patients who may be susceptible to the intracranial effects of CO_2 retention (e.g., those with evidence of increased intracranial pressure or brain tumors), oxymorphone hydrochloride extended-release tablets may reduce respiratory drive, and the resultant CO_2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with oxymorphone hydrochloride extended-release tablets.

Opioids may also obscure the clinical course in a patient with a head injury. Avoid the use of oxymorphone hydrochloride extended-release tablets in patients with impaired consciousness or coma.

5.12 Risks of Use in Patients with Gastrointestinal Conditions

Oxymorphone hydrochloride extended-release tablets are contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus.

The oxymorphone in oxymorphone hydrochloride extended-release tablets may cause spasm of the sphincter of Oddi. Opioids may cause increases in serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.

5.13 Increased Risk of Seizures in Patients with Convulsive or Seizure Disorders

The oxymorphone in oxymorphone hydrochloride extended-release tablets may increase the frequency of seizures in patients with seizure disorders and may increase the risk of seizures occurring in other clinical settings associated with seizures. Monitor patients with a history of seizure disorders for worsened seizure control during oxymorphone hydrochloride extended-release tablets therapy.

5.14 Withdrawal

Avoid the use of mixed agonist/antagonist (e.g., pentazocine, nalbuphine, and butorphanol) and partial agonist (e.g., buprenorphine) analgesics in patients who are receiving a full opioid agonist analgesic, including oxymorphone hydrochloride extended-release tablets. In these patients, mixed agonist/antagonist and partial agonist analgesics may reduce the analgesic effect and/or may precipitate withdrawal symptoms.

When discontinuing oxymorphone hydrochloride extended-release tablets, gradually

taper the dose *[see Dosage and Administration (2.4)]*. Do not abruptly discontinue oxymorphone hydrochloride extended-release tablets.

5.15 Risks of Driving and Operating Machinery

Oxymorphone hydrochloride extended-release tablets may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to the effects of oxymorphone hydrochloride extended-release tablets and know how they will react to the medication.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the labeling:

- Addiction, Abuse, and Misuse *[see Warnings and Precautions (5.1)]*
- Life-Threatening Respiratory Depression *[see Warnings and Precautions (5.3)]*
- Neonatal Opioid Withdrawal Syndrome *[see Warnings and Precautions (5.4)]*
- Interactions with Benzodiazepines or Other CNS Depressants *[see Warnings and Precautions (5.5)]*
- Anaphylaxis and Angioedema *[see Warnings and Precautions (5.7)]*
- Adrenal Insufficiency *[see Warnings and Precautions (5.8)]*
- Severe Hypotension *[see Warnings and Precautions (5.10)]*
- Gastrointestinal Adverse Reactions *[see Warnings and Precautions (5.12)]*
- Seizures *[see Warnings and Precautions (5.13)]*
- Withdrawal *[see Warnings and Precautions (5.14)]*

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The safety of oxymorphone hydrochloride extended-release tablets was evaluated in a total of 2011 patients in open-label and controlled clinical trials. The clinical trials enrolled of patients with moderate to severe chronic non-malignant pain, cancer pain, and post surgical pain. The most common serious adverse events reported with administration of oxymorphone hydrochloride extended-release tablets were chest pain, pneumonia and vomiting.

Tables 1 and 2 list the most frequently occurring adverse reactions (in at least 5% of patients) from the placebo-controlled trials in patients with low back pain.

Table 1: Treatment-Emergent Adverse Reactions Reported in ≥ 5% of Patients During the Open-Label Titration Period and Double-Blind Treatment Period by Preferred Term — Number (%) of Treated Patients (12-Week Study In Opioid-Naïve Patients with Low Back Pain)

	Open-Label Titration Period	**Double-Blind Treatment Period**	
	Oxymorphone Hydrochloride	**Oxymorphone Hydrochloride**	**Placebo**

	Extended-Release Tablets	Extended-Release Tablets	Placebo
Preferred Term	**(N = 325)**	**(N = 105)**	**(N = 100)**
Constipation	26%	7%	1%
Somnolence	19%	2%	0%
Nausea	18%	11%	9%
Dizziness	11%	5%	3%
Headache	11%	4%	2%
Pruritus	7%	3%	1%

Table 2: Treatment-Emergent Adverse Reactions Reported in ≥ 5% of Patients During the Open-Label Titration Period and Double-Blind Treatment Period by Preferred Term – Number (%) of Treated Patients (12-Week Study In Opioid-Experienced Patients with Low Back Pain)

	Open-Label Titration Period	Double-Blind Treatment Period	
	Oxymorphone Hydrochloride Extended-Release Tablets	Oxymorphone Hydrochloride Extended-Release Tablets	Placebo
Preferred Term	**(N = 250)**	**(N = 70)**	**(N = 72)**
Nausea	20%	3%	1%
Constipation	12%	6%	1%
Headache	12%	3%	0%
Somnolence	11%	3%	0%
Vomiting	9%	0%	1%
Pruritus	8%	0%	0%
Dizziness	6%	0%	0%

The following table lists adverse reactions that were reported in at least 2% of patients in placebo-controlled trials (N=5).

Table 3: Adverse Reactions Reported in Placebo-Controlled Clinical Trials with Incidence ≥ 2% in Patients Receiving Oxymorphone Hydrochloride Extended-Release Tablets

MedDRA Preferred Term	Oxymorphone Hydrochloride Extended-Release Tablets (N=1259)	Placebo (N=461)
Nausea	33%	13%
Constipation	28%	13%
Dizziness (Excl Vertigo)	18%	8%
Somnolence	17%	2%
Vomiting	16%	4%
Pruritus	15%	8%
Headache	12%	6%

Sweating increased	9%	9%
Dry mouth	6%	< 1%
Sedation	6%	8%
Diarrhea	4%	6%
Insomnia	4%	2%
Fatigue	4%	1%
Appetite decreased	3%	< 1%
Abdominal pain	3%	2%

The **common** (≥ 1% to < 10%) adverse drug reactions reported at least once by patients treated with oxymorphone hydrochloride extended-release tablets in the clinical trials organized by MedDRA's (Medical Dictionary for Regulatory Activities) System Organ Class and not represented in Table 1 were:

Eye disorders: vision blurred

Gastrointestinal disorders: diarrhea, abdominal pain, dyspepsia

General disorders and administration site conditions: dry mouth, appetite decreased, fatigue, lethargy, weakness, pyrexia, dehydration, weight decreased, edema

Nervous system disorders: insomnia

Psychiatric disorders: anxiety, confusion, disorientation, restlessness, nervousness, depression

Respiratory, thoracic and mediastinal disorders: dyspnea

Vascular disorders: flushing and hypertension

Other **less common** adverse reactions known with opioid treatment that were seen < 1% in the oxymorphone hydrochloride extended-release tablet trials include the following: Bradycardia, palpitation, syncope, tachycardia, postural hypotension, miosis, abdominal distention, ileus, hot flashes, allergic reactions, hypersensitivity, urticaria, oxygen saturation decreased, central nervous system depression, depressed level of consciousness, agitation, dysphoria, euphoric mood, hallucination, mental status changes, difficult micturition, urinary retention, hypoxia, respiratory depression, respiratory distress, clamminess, dermatitis, hypotension.

6.2 Post-marketing Experience

The following adverse reactions have been identified during post approval use of opioids. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Nervous system disorder: amnesia, convulsion, memory impairment.

Serotonin syndrome: Cases of serotonin syndrome, a potentially life-threatening condition, have been reported during concomitant use of opioids with serotonergic drugs.

Adrenal insufficiency: Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use.

Anaphylaxis: Anaphylaxis has been reported with ingredients contained in oxymorphone hydrochloride extended-release tablets.

Androgen deficiency: Cases of androgen deficiency have occurred with chronic use of opioids *[see Clinical Pharmacology (12)].*

7 DRUG INTERACTIONS

Table 4 includes clinically significant drug interactions with oxymorphone hydrochloride extended-release tablets.

Table 4: Clinically Significant Drug Interactions with Oxymorphone Hydrochloride Extended-Release Tablets

Alcohol	
Clinical Impact:	The concomitant use of alcohol with oxymorphone hydrochloride extended-release tablets can result in an increase of oxymorphone plasma levels and potentially fatal overdose of oxymorphone.
Intervention:	Instruct patients not to consume alcoholic beverages or use prescription or non-prescription products containing alcohol while on oxymorphone hydrochloride extended-release tablets therapy *[see Clinical Pharmacology (12.3)]*.
Benzodiazepines and other Central Nervous System (CNS) Depressants	
Clinical Impact:	Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants including alcohol, can increase the risk of hypotension, respiratory depression, profound sedation, coma, and death.
Intervention:	Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients closely for signs of respiratory depression and sedation *[see Warnings and Precautions (5.5)]*.
Examples:	Benzodiazepines and other sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol.
Serotonergic Drugs	
Clinical Impact:	The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Intervention:	If concomitant use is warranted, carefully observe the patient, particularly during treatment initiation and dose adjustment. Discontinue oxymorphone hydrochloride extended-release tablets if serotonin syndrome is suspected.
	Selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors

Examples:	(SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 receptor antagonists, drugs that affect the serotonin neurotransmitter system (e.g., mirtazapine, trazodone, tramadol), monoamine oxidase (MAO) inhibitors (those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue).
Monoamine Oxidase Inhibitors (MAOIs)	
Clinical Impact:	MAOI interactions with opioids may manifest as serotonin syndrome or opioid toxicity (e.g., respiratory depression, coma) *[see Warnings and Precautions (5.3)].*
Intervention:	The use of oxymorphone hydrochloride extended-release tablets are not recommended for patients taking MAOIs or within 14 days of stopping such treatment.
Examples:	phenelzine, tranylcypromine, linezolid
Mixed Agonist/Antagonist and Partial Agonist Opioid Analgesics	
Clinical Impact:	May reduce the analgesic effect of oxymorphone hydrochloride extended-release tablets and/or precipitate withdrawal symptoms.
Intervention:	Avoid concomitant use.
Examples:	butorphanol, nalbuphine, pentazocine, buprenorphine
Diuretics	
Clinical Impact:	Opioids can reduce the efficacy of diuretics by inducing the release of antidiuretic hormone.
Intervention:	Monitor patients for signs of diminished diuresis and/or effects on blood pressure and increase the dosage of the diuretic as needed.
Muscle Relaxants	
Clinical Impact:	Oxymorphone may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.
Intervention:	Monitor patients for signs of respiratory depression that may be greater than otherwise expected and decrease the dosage of oxymorphone hydrochloride extended-release tablets and/or the muscle relaxant as necessary.
Anticholinergic Drugs	
Clinical Impact:	The concomitant use of anticholinergic drugs may increase risk of urinary retention and/or severe constipation, which may lead to paralytic ileus.
Intervention:	Monitor patients for signs of urinary retention or reduced gastric motility when oxymorphone hydrochloride extended-release tablets are used concomitantly with anticholinergic drugs.
Cimetidine	
Clinical Impact:	Cimetidine can potentiate opioid-induced respiratory depression.

Intervention:	Monitor patients for respiratory depression when oxymorphone hydrochloride extended-release tablets and cimetidine are used concurrently.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Prolonged use of opioid analgesics during pregnancy may cause neonatal opioid withdrawal syndrome *[see Warnings and Precautions (5.4)]*. Available data with oxymorphone hydrochloride extended-release tablets in pregnant women are insufficient to inform a drug-associated risk for major birth defects and miscarriage.

In animal reproduction studies, reduced postnatal survival of pups and an increased incidence of stillborn pups were observed following oral treatment of pregnant rats with oxymorphone during gestation and through lactation at doses 2.4 and 12 times the human daily dose of 20 mg/day (HDD), respectively. Reduced fetal weights were observed with oral administration of oxymorphone to pregnant rats and rabbits during organogenesis at exposures up to 4.9 and 48.8 times the HDD, respectively *[see Data]*. Based on animal data, advise pregnant women of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinical recognized pregnancies is 2% to 4% and 14% to 20%, respectively.

Clinical Considerations

Fetal/Neonatal adverse reactions

Prolonged use of opioid analgesics during pregnancy for medical or nonmedical purposes may cause fetal-neonatal physical dependence and neonatal withdrawal syndrome shortly after birth. Neonatal opioid withdrawal syndrome presents as irritability, hyperactivity and abnormal sleep pattern, high pitched cry, tremor, vomiting, diarrhea, and failure to gain weight. The onset, duration, and severity of neonatal opioid withdrawal syndrome vary based on the specific opioid used, duration of use, timing and amount of last maternal use, and rate of elimination of the drug by the newborn. Observe newborns for symptoms of neonatal opioid withdrawal syndrome, and manage accordingly *[see Warnings and Precautions (5.4)]*.

Labor or delivery

Opioids cross the placenta and may produce respiratory depression and psycho-physiologic effects in neonates. An opioid antagonist, such as naloxone must be available for reversal of opioid-induced respiratory depression in the neonate. Oxymorphone hydrochloride extended-release tablets are not recommended for use in women during and immediately prior to labor, when use of shorter acting analgesics or other analgesic techniques are more appropriate. Opioid analgesics, including oxymorphone hydrochloride extended-release tablets, can prolong labor through actions which temporarily reduce the strength, duration, and frequency of uterine

contractions. However this effect is not consistent and may be offset by an increased rate of cervical dilatation, which tends to shorten labor. Monitor neonates exposed to opioid analgesics during labor for signs of excess sedation and respiratory depression.

Data

Animal data

Pregnant rats were treated with oxymorphone hydrochloride from Gestation Day 6 to 17 via oral gavage doses of 5, 10, or 25 mg/kg/day (2.4, 4.9, or 12.2 times the HDD based on body surface area, respectively). Reduced mean fetal weights were observed at 4.9 times the HDD. Maternal toxicity was noted in all treatment groups (reduced food consumption and body weights in all groups and mortality in the high dose group).

Pregnant rabbits were treated with oxymorphone hydrochloride from Gestation Day 7 to 20 via oral gavage doses of 10, 25, or 50 mg/kg/day (9.8, 24.4, or 48.8 times the HDD based on body surface area, respectively). Decreased mean fetal weights were noted at 48.8 times the HDD. Maternal toxicity was noted in all treatment groups (reduced food consumption and body weights).

Pregnant rats were treated with oxymorphone hydrochloride from Gestation Day 6 to Lactation Day 20 via oral gavage doses of 1, 5, 10, or 25 mg/kg/day (0.5, 2.4, 4.9, or 12.2 times the HDD based on body surface area, respectively). Increased neonatal death (postnatal day 0 to 1) was noted at 2.4 times the HDD. Decreased pup survival over the first week of life, reduced pup birth weight, and reduced postnatal weight gain were noted at 4.9 times the HDD. Maternal toxicity was noted in all treatment groups (reduced food consumption and body weights in all groups and mortality in the 10 and 25 mg/kg/day groups).

In a published study, neural tube defects (exencephaly and cranioschisis) were noted following subcutaneous administration of 153 mg/kg oxymorphone hydrochloride (62.2 times the HDD) on Gestation Day 8 to pregnant hamsters. This dose also produced significant maternal toxicity (20% maternal deaths).

8.2 Lactation

Risk Summary

There is no information regarding the presence of oxymorphone in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions, including excess sedation and respiratory depression in a breastfed infant, advise patients that breastfeeding is not recommended during treatment with oxymorphone hydrochloride extended-release tablets.

Clinical Considerations

Monitor infants exposed to oxymorphone hydrochloride extended-release tablets through breast milk for excess sedation and respiratory depression. Withdrawal symptoms can occur in breastfed infants when maternal administration of an opioid analgesic is stopped, or when breast-feeding is stopped.

8.3 Females and Males of Reproductive Potential

Infertility

Chronic use of opioids may cause reduced fertility in females and males of reproductive

potential. It is not known whether these effects on fertility are reversible *[Clinical Pharmacology (12.2), Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of oxymorphone hydrochloride extended-release tablets in patients below the age of 18 years have not been established.

8.5 Geriatric Use

Of the total number of subjects in clinical studies of oxymorphone hydrochloride extended-release tablets, 27% were 65 and over, while 9% were 75 and over. No overall differences in effectiveness were observed between these subjects and younger subjects. There were several adverse events that were more frequently observed in subjects 65 and over compared to younger subjects. These adverse events included dizziness, somnolence, confusion, and nausea. On average, age greater than 65 years was associated with an increase in oxymorphone AUC and C_{max}. Initiate dosing with oxymorphone hydrochloride extended-release tablets 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 oxymorphone hydrochloride extended-release tablets. For patients on prior opioid therapy, start at 50% of the starting dose for a younger patient on prior opioids and titrate slowly.

Oxymorphone is known to be substantially excreted by the kidney and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because the elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

8.6 Hepatic Impairment

Patients with mild hepatic impairment have an increase in oxymorphone bioavailability compared to the subjects with normal hepatic function. In opioid-naïve patients with mild hepatic impairment, initiate oxymorphone hydrochloride extended-release tablets using the 5 mg dose and monitor closely for respiratory and central nervous system depression. Oxymorphone hydrochloride extended-release tablets are contraindicated for patients with moderate and severe hepatic impairment *[see Dosage and Administration (2.5), Contraindications (4)*, *Warnings and Precautions (5.9),* and *Clinical Pharmacology (12.3)]*. For patients on prior opioid therapy, start at the 50% of the dose for that a patient with normal hepatic function on prior opioids and titrate slowly.

8.7 Renal Impairment

Patients with moderate to severe renal impairment were shown to have an increase in oxymorphone bioavailability compared to the subjects with normal renal function *[see Clinical Pharmacology (12.3)]*. Start opioid-naïve patients with the 5 mg dose of oxymorphone hydrochloride extended-release tablets and titrate slowly while closely monitoring for respiratory and central nervous system depression *[see Dosage and Administration (2.6)]*. For patients on prior opioid therapy, start at 50% of the dose for a patient with normal renal function on prior opioids and titrate slowly.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

Oxymorphone hydrochloride extended-release tablets contain oxymorphone, a Schedule II controlled substance.

9.2 Abuse

Oxymorphone hydrochloride extended-release tablets contains oxymorphone a substance with a high potential for abuse similar to other opioids fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, and tapentadol. Oxymorphone hydrochloride extended-release tablets can be abused and is subject to misuse, addiction, and criminal diversion *[see Warnings and Precautions (5.1)]*.

The high drug content in extended-release formulations adds to the risk of adverse outcomes from abuse and misuse.

All patients treated with opioids require careful monitoring for signs of abuse and addiction, since use of opioid analgesic products carries the risk of addiction even under appropriate medical use.

Prescription drug abuse is the intentional non-therapeutic use of a prescription drug, even once, for its rewarding psychological or physiological effects.

Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use and includes: a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal.

“Drug seeking" behavior is very common in persons with substance use disorders. Drug-seeking tactics include emergency calls or visits near the end of office hours, refusal to undergo appropriate examination, testing, or referral, repeated “loss” of prescriptions, tampering with prescriptions and reluctance to provide prior medical records or contact information for other treating healthcare provider(s). "Doctor shopping" (visiting multiple prescribers to obtain additional prescriptions) is common among drug abusers and people suffering from untreated addiction. Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control.

Abuse and addiction are separate and distinct from physical dependence and tolerance. Healthcare providers should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction.

Oxymorphone hydrochloride extended-release tablets, like other opioids, can be diverted for non-medical use into illicit channels of distribution. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests as required by state and federal law, is strongly advised.

Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to reduce abuse of opioid drugs.

<u>Risks Specific to Abuse of Oxymorphone Hydrochloride Extended-Release Tablets</u>

Oxymorphone hydrochloride extended-release tablets are for oral use only. Abuse of

oxymorphone hydrochloride extended-release tablets pose a risk of overdose and death. This risk is increased with concurrent abuse of oxymorphone hydrochloride extended-release tablets with alcohol and other substances. Taking cut, broken, chewed, crushed, or dissolved oxymorphone hydrochloride extended-release tablets enhance drug release and increases the risk of over dose and death.

Parenteral drug abuse is commonly associated with transmission of infectious diseases such as hepatitis and HIV.

9.3 Dependence

Both tolerance and physical dependence can develop during chronic opioid therapy. Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia (in the absence of disease progression or other external factors). Tolerance may occur to both the desired and undesired effects of drugs, and may develop at different rates for different effects.

Physical dependence results in withdrawal symptoms after abrupt discontinuation or a significant dose reduction of a drug. Withdrawal also may be precipitated through the administration of drugs with opioid antagonist activity, (e.g., naloxone, nalmefene), mixed agonist/antagonist analgesics (e.g., pentazocine, butorphanol, nalbuphine), or partial agonists (e.g., buprenorphine). Physical dependence may not occur to a clinically significant degree until after several days to weeks of continued opioid usage.

Oxymorphone hydrochloride extended-release tablets should not be abruptly discontinued *[see Dosage and Administration (2.4)].* If oxymorphone hydrochloride extended-release tablets are abruptly discontinued in a physically-dependent patient, withdrawal syndrome may occur. Some or all of the following can characterize this syndrome: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other signs and symptoms also may develop, including: irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, or increased blood pressure, respiratory rate, or heart rate.

Infants born to mothers physically dependent on opioids will also be physically dependent and may exhibit respiratory difficulties and withdrawal signs *[see Use in Specific Populations (8.2)].*

10 OVERDOSAGE

Clinical Presentation

Acute overdosage with oxymorphone hydrochloride extended-release tablets can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, and in some cases, pulmonary edema, bradycardia, hypotension, partial or completed airway obstruction, atypical snoring, and death. Marked mydriasis rather than miosis may be seen with severe hypoxia in overdose situations *[see Clinical Pharmacology (12.2)]*.

Treatment of Overdose

In case of overdose, priorities are the re-establishment of a patent and protected airway and institution of assisted or controlled ventilation if needed. Employ other supportive measures (including oxygen, vasopressors) in the management of circulatory shock and

pulmonary edema as indicated. Cardiac arrest or arrhythmias will require advanced life support techniques.

The opioid antagonists, naloxone or nalmefene, are specific antidotes to respiratory depression resulting from opioid overdose. For clinically significant respiratory or circulatory depression secondary to oxymorphone overdose, administer an opioid antagonist. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxymorphone overdose.

Because the duration of opioid reversal is expected to be less than the duration of action of oxymorphone in oxymorphone hydrochloride extended-release tablets, carefully monitor the patient until spontaneous respiration is reliably re-established. Oxymorphone hydrochloride extended-release tablets will continue to release oxymorphone and add to the oxymorphone load for 24 to 48 hours or longer following ingestion, necessitating prolonged monitoring. If the response to opioid antagonists is suboptimal or only brief in nature, administer additional antagonists as directed by product's prescribing information.

In an individual physically dependent on opioids, administration of the recommended usual dosage of the antagonist will precipitate an acute withdrawal syndrome. The severity of the withdrawal symptoms experienced will depend on the degree of physical dependence and the dose of the antagonist administered. If a decision is made to treat serious respiratory depression in the physically dependent patient, administration of the antagonist should be initiated with care and by titration with smaller than usual doses of the antagonist.

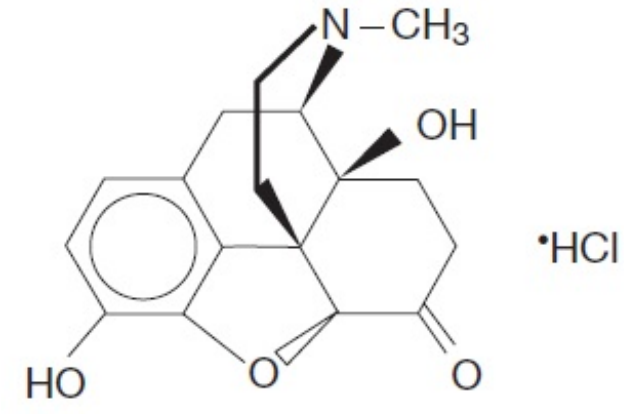
11 DESCRIPTION

Oxymorphone hydrochloride extended-release tablets, USP are for oral use and contain oxymorphone, a semi-synthetic opioid analgesic. Oxymorphone hydrochloride extended-release tablets, USP are supplied in 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, and 40 mg tablet strengths for oral administration. The tablet strength describes the amount of oxymorphone hydrochloride per tablet.

The tablets contain the following inactive ingredients: microcrystalline cellulose, lactose monohydrate, hypromellose, xanthan gum, magnesium stearate, polyvinyl alcohol - partially hydrolyzed, polyethylene glycol, talc, and titanium dioxide. The 5 mg, 7.5 mg, 10 mg, 20 mg, and 40 mg tablets contain FD&C Yellow No. 6 Aluminum Lake. In addition, the 5 mg tablets contain FD&C Blue No. 2 and D&C Red No. 27. The 7.5 mg tablets contain FD&C Blue No. 2 and FD&C Red No. 40. The 10 mg tablets contain FD&C Red No. 40. The 20 mg tablets contain D&C Yellow No. 10 Aluminum Lake, FD&C Blue No. 1, and FD&C Blue No. 2. The 30 mg tablets contain Iron Oxide Yellow and Iron Oxide Black. The 40 mg tablets contain D&C Yellow No. 10 Aluminum Lake.

The chemical name of oxymorphone hydrochloride is 4,5α-epoxy-3, 14-dihydroxy-17-methylmorphinan-6-one hydrochloride. Oxymorphone hydrochloride, USP is a white or slightly off-white, odorless powder, which is sparingly soluble in alcohol and ether, but freely soluble in water. The molecular weight of oxymorphone hydrochloride is 337.80. The pKa1 and pKa2 of oxymorphone at 37°C are 8.17 and 9.54, respectively. The octanol/aqueous partition coefficient at 37°C and pH 7.4 is 0.98.

The structural formula for oxymorphone hydrochloride is as follows:



FDA approved dissolution test specifications differ from USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Oxymorphone is a full opioid agonist and is relatively selective for the mu-opioid receptor, although it can bind to other opioid receptors at higher doses. The principal therapeutic action of oxymorphone is analgesia. Like all full opioid agonists, there is no ceiling effect for analgesia with oxymorphone. Clinically, dosage is titrated to provide adequate analgesia and may be limited by adverse reactions, including respiratory and CNS depression.

The precise mechanism of the analgesic action is unknown. However, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and are thought to play a role in the analgesic effects of this drug.

12.2 Pharmacodynamics

CNS Depressant/Alcohol Interaction

Additive pharmacodynamic effects may be expected when oxymorphone hydrochloride extended-release tablets are used in conjunction with alcohol, other opioids, or illicit drugs that cause central nervous system depression.

Effects on the Central Nervous System

Oxymorphone produces respiratory depression by direct action on brain stem respiratory centers. The respiratory depression involves a reduction in the responsiveness of the brain stem respiratory centers to both increases in carbon dioxide tension and electrical stimulation.

Oxymorphone causes miosis, even in total darkness. Pinpoint pupils are a sign of opioid overdose but are not pathognomonic (e.g., pontine lesions of hemorrhagic or ischemic origin may produce similar findings). Marked mydriasis rather than miosis may be seen with hypoxia in overdose situations.

Effects on the Gastrointestinal Tract and on Other Smooth Muscle

Oxymorphone causes a reduction in motility associated with an increase in smooth muscle tone in the antrum of the stomach and duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased. Propulsive peristaltic waves in the colon are decreased, while tone is increased to the point of spasm, resulting in constipation. Other opioid-induced effects may include a reduction in biliary and pancreatic secretions, spasm of sphincter of Oddi, and transient elevations in serum amylase.

Effects on the Cardiovascular System

Oxymorphone produces peripheral vasodilation which may result in orthostatic hypotension or syncope. Release of histamine can occur and may contribute to opioid-induced hypotension. Manifestations of histamine release and/or peripheral vasodilation may include pruritis, flushing, red eyes, sweating, and/or orthostatic hypotension.

Effects on the Endocrine System

Opioids inhibit the secretion of adrenocorticotropic hormone (ACTH), cortisol, and luteinizing hormone (LH) in humans *[see Adverse Reactions (6.2)]*. They also stimulate prolactin, growth hormone (GH) secretion, and pancreatic secretion of insulin and glucagon.

Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility. The causal role of opioids in the clinical syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological stressors that may influence gonadal hormone levels have not been adequately controlled for in studies conducted to date *[see Adverse Reactions (6.2)].*

Effects on the Immune System

Opioids have been shown to have a variety of effects on components of the immune system in *in vitro* and animal models. The clinical significance of these findings is unknown. Overall, the effects of opioids appear to be modestly immunosuppressive.

Concentration-Efficacy Relationships

The minimum effective plasma concentration of oxymorphone varies widely among patients, especially among patients who have been previously treated with agonist opioids. The minimum effective analgesic concentration of oxymorphone for any individual patient may increase over time due to an increase in pain, development of a new pain syndrome and/or development of analgesic tolerance *[see Dosage and Administration (2.1, 2.2, 2.3)]*.

Concentration-Adverse Reaction Relationships

There is a relationship between increasing oxymorphone plasma concentration and increasing frequency of dose-related opioid adverse reactions such as nausea, vomiting, CNS effects, and respiratory depression. In opioid-tolerant patients, the situation may be altered by the development of tolerance to opioid-related adverse reactions *[see Dosage and Administration (2.1, 2.2, 2.3)]*.

12.3 Pharmacokinetics

Absorption

The absolute oral bioavailability of oxymorphone is approximately 10%.

Steady-state levels are achieved after three days of multiple-dose administration. Under both single-dose and steady-state conditions, dose proportionality has been established for the 5 mg, 10 mg, 20 mg, and 40 mg doses of oxymorphone hydrochloride extended-release tablets, for both peak plasma levels (C_{max}) and extent of absorption (AUC) (see Table 5).

Table 5: Mean (±SD) Oxymorphone Hydrochloride Extended-Release Tablets Pharmacokinetic Parameters

Regimen	**Dosage**	**C_{max} (ng/mL)**	**AUC (ng·hr/mL)**	**$T_{½}$ (hr)**
Single-Dose	5 mg	0.27±0.13	4.54±2.04	11.30±10.81
	10 mg	0.65±0.29	8.94±4.16	9.83±5.68
	20 mg	1.21±0.77	17.81±7.22	9.89±3.21
	40 mg	2.59±1.65	37.90±16.20	9.35±2.94
Multiple-Dose*	5 mg	0.70±0.55	5.60±3.87	NA
	10 mg	1.24±0.56	9.77±3.52	NA
	20 mg	2.54±1.35	19.28±8.32	NA
	40 mg	4.47±1.91	36.98±13.53	NA
NA = not applicable * Results after 5 days of q12h dosing.				

Food Effect

Two studies examined the effect of food on the bioavailability of single doses of 20 mg and 40 mg of oxymorphone hydrochloride extended-release tablets in healthy volunteers. In both studies, after the administration of oxymorphone hydrochloride extended-release tablets, the C_{max} was increased by approximately 50% in fed subjects compared to fasted subjects. A similar increase in C_{max} was also observed with oxymorphone solution.

The AUC was unchanged in one study and increased by approximately 18% in the other study in fed subjects following the administration of oxymorphone hydrochloride extended-release tablets. Examination of the AUC suggests that most of the difference between fed and fasting conditions occurs in the first four hours after dose administration. After oral dosing with a single-dose of 40 mg, a peak oxymorphone plasma level of 2.8 ng/ml is achieved at 1 hour in fasted subjects and a peak of 4.25 ng/ml is achieved at 2 hours in fed subjects and that beyond the 12 hour time point, there is very little difference in the curves. As a result, oxymorphone hydrochloride extended-release tablets should be dosed at least one hour prior to or two hours after eating *[see Dosage and Administration (2.1, 2.2)]*.

Distribution

Formal studies on the distribution of oxymorphone in various tissues have not been conducted. Oxymorphone is not extensively bound to human plasma proteins; binding is in the range of 10% to 12%.

Elimination

Metabolism

Oxymorphone is highly metabolized, principally in the liver, and undergoes reduction or conjugation with glucuronic acid to form both active and inactive metabolites. The two major metabolites of oxymorphone are oxymorphone-3-glucuronide and 6-OH-oxymorphone. The mean plasma AUC for oxymorphone-3-glucuronide is approximately 90-fold higher than the parent compound. The pharmacologic activity of the glucuronide metabolite has not been evaluated. 6-OH-oxymorphone has been shown in animal studies to have analgesic bioactivity. The mean plasma 6-OH-oxymorphone AUC is approximately 70% of the oxymorphone AUC following single oral doses, but is essentially equivalent to the parent compound at steady-state.

Excretion

Because oxymorphone is extensively metabolized, < 1% of the administered dose is excreted unchanged in the urine. On average, 33% to 38% of the administered dose is excreted in the urine as oxymorphone-3-glucuronide and less than 1% excreted as 6-OH-oxymorphone in subjects with normal hepatic and renal function. In animals given radiolabeled oxymorphone, approximately 90% of the administered radioactivity was recovered within 5 days of dosing. The majority of oxymorphone-derived radioactivity was found in the urine and feces.

Specific Populations

Geriatric Patients

The steady-state plasma concentrations of oxymorphone, 6-OH-oxymorphone, and oxymorphone-3-glucuronide are approximately 40% higher in elderly subjects (≥ 65 years of age) than in young subjects (18 to 40 years of age). On average, age greater than 65 years was associated with a 1.4-fold increase in oxymorphone AUC and a 1.5-fold increase in C_{max}. This observation does not appear related to a difference in body weight, metabolism, or excretion of oxymorphone *[see Use in Specific Populations (8.5)].*

Sex

The effect of sex was evaluated following single- and multiple-doses of oxymorphone hydrochloride extended-release tablets in male and female adult volunteers. There was a consistent tendency for female subjects to have slightly higher AUC_{ss} and C_{max} values than male subjects; however, sex differences were not observed when AUC_{ss} and C_{max} were adjusted by body weight.

Hepatic Impairment

The bioavailability of orally administered oxymorphone is markedly increased in patients with moderate to severe liver disease. The disposition of oxymorphone was compared in six patients with mild, five patients with moderate, and one patient with severe hepatic impairment and 12 subjects with normal hepatic function. The bioavailability of oxymorphone was increased by 1.6-fold in patients with mild hepatic impairment and by 3.7-fold in patients with moderate hepatic impairment. In one patient with severe hepatic impairment, the bioavailability was increased by 12.2-fold. The half-life of oxymorphone was not significantly affected by hepatic impairment.

Renal Impairment

Data from a pharmacokinetic study involving 24 patients with renal dysfunction show an increase of 26%, 57%, and 65% in oxymorphone bioavailability in mild (creatinine clearance 51 mL/min to 80 mL/min; n=8), moderate (creatinine clearance 30 mL/min to 50 mL/min; n=8), and severe (creatinine clearance < 30 mL/min; n=8) patients, respectively, compared to healthy controls.

Drug Interaction Studies

Alcohol Interaction

An *in vivo* study of the effect of alcohol (40%, 20%, 4% and 0%) on the bioavailability of a single-dose of 40 mg of oxymorphone hydrochloride extended-release tablets in healthy, fasted volunteers demonstrated a highly variable effect on C_{max} with concomitant administration of alcohol and oxymorphone hydrochloride extended-release tablets. The change in C_{max} ranged from a decrease of 50% to an increase of 270% across all conditions studied. Following administration of 240 mL of 40% ethanol, the C_{max} increased on average by 70% and up to 270% in individual subjects. Following the concomitant administration of 240 mL of 20% ethanol, the C_{max} increased on average by 31% and up to 260% in individual subjects. Following the concomitant administration of 240 mL of 4% ethanol, the C_{max} increased 7% on average and by as much as 110% for individual subjects. After oral dosing with a single-dose of 40 mg in fasted subjects, the mean peak oxymorphone plasma level is 2.4 ng/mL and the median T_{max} is 2 hours. Following co-administration of oxymorphone hydrochloride extended-release tablets and alcohol (240 mL of 40% ethanol) in fasted subjects, the mean peak oxymorphone level is 3.9 ng/mL and the median T_{max} is 1.5 hours (range 0.75 to 6 hours). The oxymorphone mean AUC was 13% higher after co-administration of 240 mL of 40% alcohol. The AUC was essentially unaffected in subjects following the co-administration of oxymorphone hydrochloride extended-release tablets and ethanol (240 mL of 20% or 4% ethanol).

In vitro studies have demonstrated that oxymorphone hydrochloride extended-release tablets do not release oxymorphone more rapidly in 500 mL of 0.1N HCl solutions containing ethanol (4%, 20%, and 40%).

Instruct patients to avoid use of alcohol when taking oxymorphone hydrochloride extended-release tablets.

In vitro studies revealed little to no biotransformation of oxymorphone to 6-OH-oxymorphone by any of the major cytochrome P450 (CYP P450) isoforms at therapeutically relevant oxymorphone plasma concentrations.

No inhibition of any of the major CYP P450 isoforms was observed when oxymorphone was incubated with human liver microsomes at concentrations of ≤ 15.1 mcg/mL. An inhibition of CYP3A4 activity occurred at oxymorphone concentrations ≥ 45.3 mcg/mL. Therefore, it is not expected that oxymorphone, or its metabolites will act as inhibitors of any of the major CYP P450 enzymes *in vivo*.

Increases in the activity of the CYP 2C9 and CYP 3A4 isoforms occurred when oxymorphone was incubated with human hepatocytes. However, clinical drug interaction studies with oxymorphone hydrochloride extended-release tablets showed no induction of CYP450 3A4 or 2C9 enzyme activity, indicating that no dose adjustment for CYP 3A4-

or 2C9-mediated drug-drug interactions is required.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

No evidence of carcinogenic potential was observed in long-term animal studies in mice and rats. Oxymorphone hydrochloride was administered to Sprague Dawley rats (2.5, 5, and 10 mg/kg/day in males and 5, 10, and 25 mg/kg/day in females) for 2 years by oral gavage. Systemic drug exposure (AUC) at the highest doses tested in male and female rats was 4.8 times and 21.2 times the human exposure at a dose of 20 mg/day, respectively. Oxymorphone hydrochloride was administered to male and female CD-1 mice (10, 25, 75 and 150 mg/kg/day) for 2 years by oral gavage. Systemic drug exposure (AUC) at 150 mg/kg/day in male and female mice was 205 times and 243 times the human exposure at a dose of 20 mg/day, respectively.

Mutagenesis

Oxymorphone hydrochloride was not mutagenic when tested in the *in vitro* bacterial reverse mutation assay (Ames test), or in an *in vitro* mammalian cell chromosome aberration assay performed with human peripheral blood lymphocytes. Oxymorphone hydrochloride tested positive in both the rat and mouse *in vivo* micronucleus assays. An increase in micronucleated polychromatic erythrocytes occurred in mice given doses ≥ 250 mg/kg and in rats given doses of 20 and 40 mg/kg. A subsequent study demonstrated that oxymorphone hydrochloride was not aneugenic in mice following administration of up to 500 mg/kg. Additional studies indicate that the increased incidence of micronucleated polychromatic erythrocytes in rats may be secondary to increased body temperature following oxymorphone administration. Doses associated with increased micronucleated polychromatic erythrocytes also produce a marked, rapid increase in body temperature. Pretreatment of animals with sodium salicylate minimized the increase in body temperature and prevented the increase in micronucleated polychromatic erythrocytes after administration of 40 mg/kg oxymorphone.

Impairment of Fertility

Female rats were treated with oxymorphone hydrochloride beginning 14 days prior to mating through Gestation Day 7 via oral gavage doses of 5, 10, or 25 mg/kg/day (2.4, 4.9, or 12.2 times the human daily dose of 20 mg/day based on body surface area, respectively). Male rats were treated via oral gavage with the same oxymorphone hydrochloride doses beginning 28 days prior to and throughout mating. In female rats, an increase in the length of the estrus cycle and decrease in the mean number of viable embryos, implantation sites and corpora lutea were observed at 4.9 times the human dose of 20 mg/day. No adverse effects of oxymorphone on male reproductive function or sperm parameters were observed.

14 CLINICAL STUDIES

The efficacy and safety of oxymorphone hydrochloride extended-release tablets have

been evaluated in double-blind, controlled clinical trials in opioid-naïve and opioid-experienced patients with moderate to severe pain including low back pain.

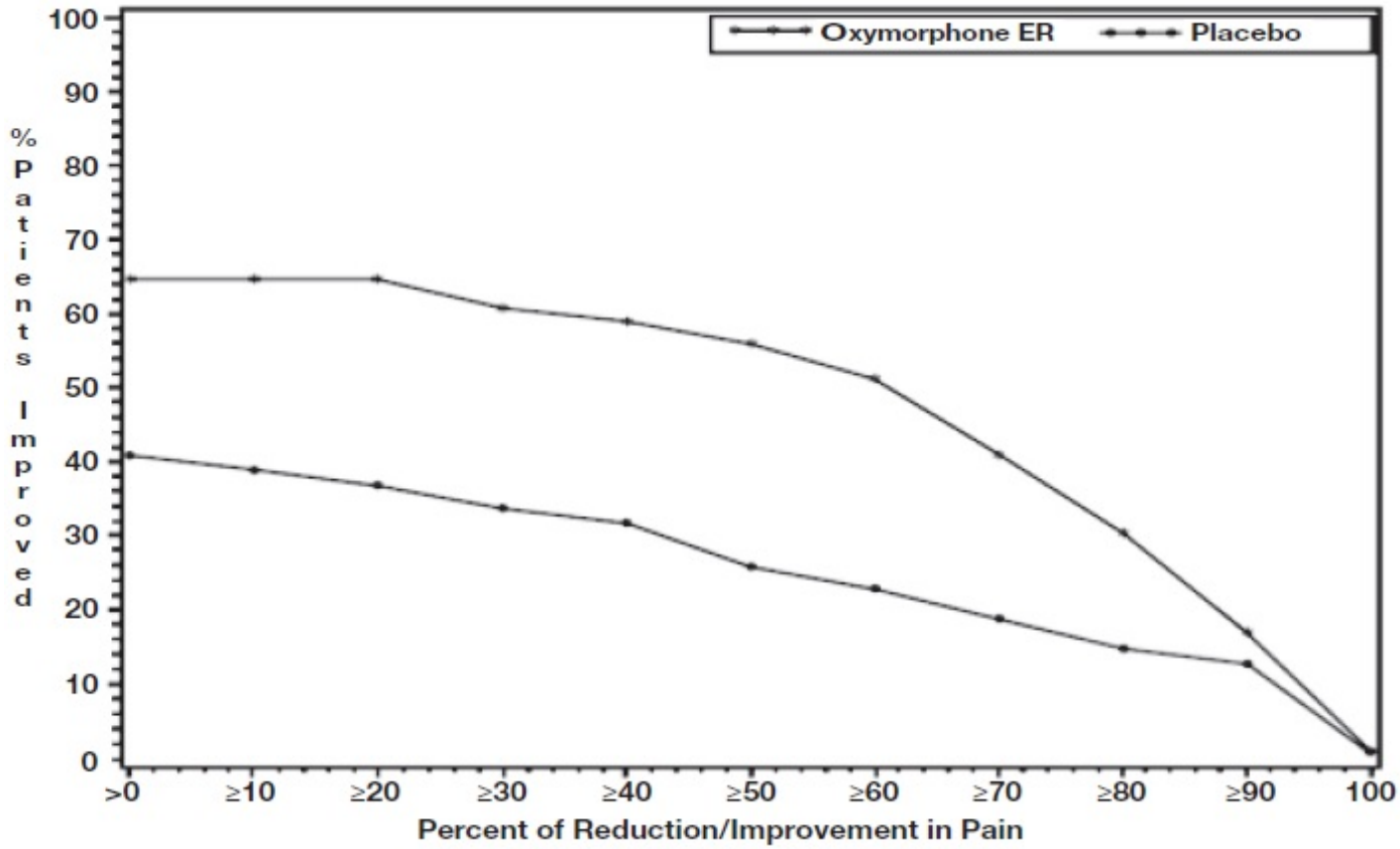
12-Week Study in Opioid-Naïve Patients with Low Back Pain

Patients with chronic low back pain who were suboptimally responsive to their non-opioid therapy entered a 4-week, open-label dose titration phase. Patients initiated therapy with two days of treatment with oxymorphone hydrochloride extended-release tablets 5 mg, every 12 hours. Thereafter, patients were titrated to a stabilized dose, at increments of 5 mg to 10 mg every 12 hours every 3 to 7 days. Of the patients who were able to stabilize within the Open-Label Titration Period, the mean±SD VAS score at Screening was 69.4±11.8 mm and at Baseline (beginning of Double-Blind Period) were 18.5±11.2 mm and 19.3±11.3 mm for the oxymorphone ER and placebo groups, respectively. Sixty-three percent of the patients enrolled were able to titrate to a tolerable dose and were randomized into a 12-week double-blind treatment phase with placebo or their stabilized dose of oxymorphone hydrochloride extended-release tablets. The mean±SD stabilized doses were 39.2±26.4 mg and 40.9±25.3 mg for the oxymorphone hydrochloride extended-release tablets and placebo groups, respectively; total daily doses ranged from 10 mg to 140 mg.

During the first 4 days of double-blind treatment patients were allowed an unlimited number of oxymorphone hydrochloride tablets, an immediate-release (IR) formulation of oxymorphone, 5 mg tablets, every 4 to 6 hours as supplemental analgesia; thereafter the number of oxymorphone hydrochloride tablets was limited to two tablets per day. This served as a tapering method to minimize opioid withdrawal symptoms in placebo patients. Sixty-eight percent of patients treated with oxymorphone hydrochloride extended-release tablets completed the 12-week treatment compared to 47% of patients treated with placebo. Oxymorphone hydrochloride extended-release tablets provided superior analgesia compared to placebo. The analgesic effect of oxymorphone hydrochloride extended-release tablets was maintained throughout the double-blind treatment period in 89% of patients who completed the study. These patients reported a decrease, no change, or a ≤ 10 mm increase in VAS score from Day 7 until the end of the study.

The proportion of patients with various degrees of improvement from screening to study endpoint is shown in Figure 1. The figure is cumulative, so that patients whose change from baseline is, for example, 30%, are also included at every level of improvement below 30%. Patients who did not complete the study were assigned 0% improvement.

Figure 1: Percent Reduction in Average Pain Intensity from Screening to Final Visit

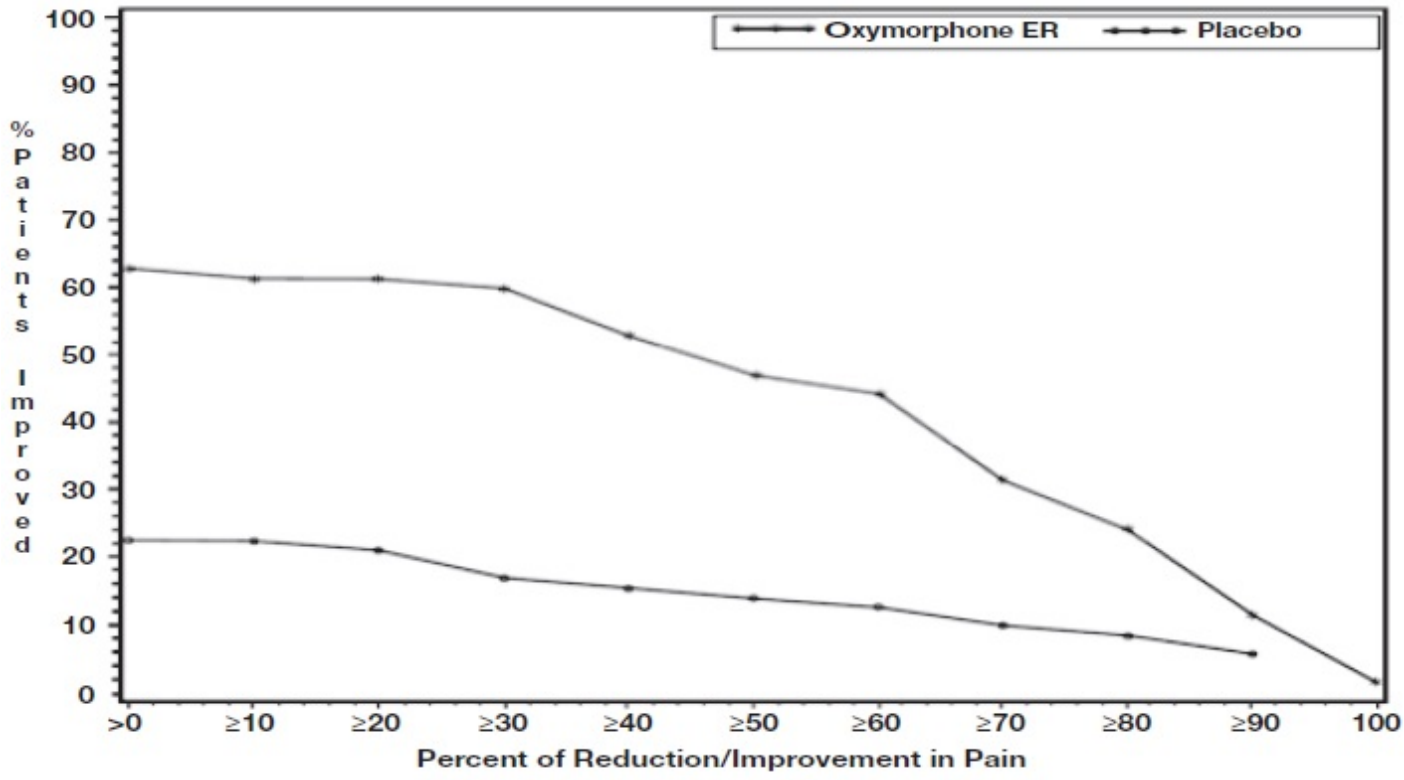


12-Week Study in Opioid-Experienced Patients with Low Back Pain

Patients on chronic opioid therapy entered a 4-week, open-label titration phase with oxymorphone hydrochloride extended-release tablets dosed every 12 hours at an approximated equianalgesic dose of their pre-study opioid medication. Of the patients who were able to stabilize within the Open-Label Titration Period, the mean±SD VAS score at Screening was 69.5±17.0 mm and at Baseline (beginning of Double-Blind Period) were 23.9±12.1 mm and 22.2±10.8 mm for the oxymorphone ER and placebo groups, respectively. Stabilized patients entered a 12-week double-blind treatment phase with placebo or their stabilized dose of oxymorphone hydrochloride extended-release tablets. The mean±SD stabilized doses were 80.9±59.3 mg and 93.3±61.3 mg for the oxymorphone hydrochloride extended-release tablets and placebo groups, respectively; total daily doses ranged from 20 mg to 260 mg. During the first 4 days of double-blind treatment, patients were allowed an unlimited number of oxymorphone hydrochloride 5 mg tablets, every 4 to 6 hours as supplemental analgesia; thereafter the number of oxymorphone hydrochloride tablets was limited to two tablets per day. This served as a tapering method to minimize opioid withdrawal symptoms in placebo patients. Fifty-seven percent of patients were titrated to a stabilized dose within approximately 4 weeks of oxymorphone hydrochloride extended-release tablets dose titration. Seventy percent of patients treated with oxymorphone hydrochloride extended-release tablets and 26% of patients treated with placebo completed the 12-week treatment. Oxymorphone hydrochloride extended-release tablets provided superior analgesia compared to placebo. The analgesic effect of oxymorphone hydrochloride extended-release tablets was maintained throughout the double-blind treatment period in 80% of patients who completed the study. These patients reported a decrease, no change, or a ≤ 10 mm increase in VAS score from Day 7 until the end of the study.

The proportion of patients with various degrees of improvement from screening to study endpoint is shown in Figure 2. The figure is cumulative, so that patients whose change from baseline is, for example, 30%, are also included at every level of improvement below 30%. Patients who did not complete the study were assigned 0% improvement.

Figure 2: Percent Reduction in Average Pain Intensity from Screening to Final Visit



16 HOW SUPPLIED/STORAGE AND HANDLING

Oxymorphone hydrochloride extended-release tablets, USP are supplied as the following strengths:

Oxymorphone Hydrochloride Extended-release Tablets USP, **5 mg are** purple, round, film-coated extended-release tablets debossed with “G71” on one side and blank on the other side.
They are available as follows:

Oxymorphone Hydrochloride Extended-release Tablets USP, **7.5 mg are** gray, round, film-coated extended-release tablets debossed with “G75” on one side and blank on the other side.
They are available as follows:

Oxymorphone Hydrochloride Extended-release Tablets USP, **10 mg are** orange, round, film-coated extended-release tablets debossed with “G72” on one side and blank on the other side.

They are available as follows:

Bottles of 60: NDC 55700-788-60

Oxymorphone Hydrochloride Extended-release Tablets USP, **15 mg are** white, round, film-coated extended-release tablets debossed with “G76” on one side and blank on the other side.
They are available as follows:

Oxymorphone Hydrochloride Extended-release Tablets USP, **20 mg are** green, round, film-coated extended-release tablets debossed with “G73” on one side and blank on the other side.
They are available as follows:

Oxymorphone Hydrochloride Extended-release Tablets USP, **30 mg are** brown, round, film-coated extended-release tablets debossed with “G77” on one side and blank on the other side.
They are available as follows:

Oxymorphone Hydrochloride Extended-release Tablets USP, **40 mg are** orange, round, film-coated extended-release tablets debossed with “G74” on one side and blank on the other side.
They are available as follows:

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Dispense in tight container as defined in the USP, with a child-resistant closure (as required).

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Addiction, Abuse, and Misuse

Inform patients that the use of oxymorphone hydrochloride extended-release tablets, even when taken as recommended, can result in addiction, abuse, and misuse, which can lead to overdose or death *[see Warnings and Precautions (5.1)]*. Instruct patients not to share oxymorphone hydrochloride extended-release tablets with others and to take steps to protect oxymorphone hydrochloride extended-release tablets from theft or misuse.

Life-Threatening Respiratory Depression

Inform patients of the risk of life-threatening respiratory depression, including information that the risk is greatest when starting oxymorphone hydrochloride

extended-release tablets or when the dosage is increased, and that it can occur even at recommended doses *[see Warnings and Precautions (5.3)]*. Advise patients how to recognize respiratory depression and to seek medical attention if breathing difficulties develop.

Accidental Ingestion

Inform patients that accidental ingestion, especially by children, may result in respiratory depression or death *[see Warnings and Precautions (5.3)]*. Instruct patients to take steps to store oxymorphone hydrochloride extended-release tablets securely and to dispose of unused oxymorphone hydrochloride extended-release tablets by flushing the tablets down the toilet.

Interactions with Benzodiazepines and other CNS Depressants

Inform patients and caregivers that potentially fatal additive effects may occur if oxymorphone hydrochloride extended-release tablets are used with benzodiazepines or other CNS depressants, including alcohol, and not to use these concomitantly unless supervised by a health care provider *[see Warnings and Precautions (5.5), Drug Interactions (7)].*

Instruct patients not to consume alcoholic beverages, as well as prescription and over-the-counter products that contain alcohol, during treatment with oxymorphone hydrochloride extended-release tablets. The co-ingestion of alcohol with oxymorphone hydrochloride extended-release tablets may result in increased plasma levels and a potentially fatal overdose of oxymorphone *[see Warnings and Precautions (5.5)]*.

Anaphylaxis, Angioedema, and Other Hypersensitivity Reactions

Inform patients that anaphylaxis and other hypersensitivity reactions have been reported with ingredients contained in oxymorphone hydrochloride extended-release tablets. Advise patients how to recognize such a reaction and when to seek medical attention *[see Contraindications (4), Warnings and Precautions (5.7), Adverse Reactions (6)].*

Serotonin Syndrome

Inform patients that opioids could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs. Warn patients of the symptoms of serotonin syndrome and to seek medical attention right away if symptoms develop. Instruct patients to inform their physicians if they are taking, or plan to take serotonergic medications *[see Drug Interactions (7)]*.

MAOI Interaction

Inform patients to avoid taking oxymorphone hydrochloride extended-release tablets while using any drugs that inhibit monoamine oxidase. Patients should not start MAOIs while taking oxymorphone hydrochloride extended-release tablets *[see Drug Interactions (7)]*.

Adrenal Insufficiency

Inform patients that opioids could cause adrenal insufficiency, a potentially life-threatening condition. Adrenal insufficiency may present with non-specific symptoms

and signs such as nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. Advise patients to seek medical attention if they experience a constellation of these symptoms *[see Warnings and Precautions (5.8)].*

Important Administration Instructions

Instruct patients how to properly take oxymorphone hydrochloride extended-release tablets, including the following:

- Oxymorphone hydrochloride extended-release tablets are designed to work properly only if swallowed intact. Taking cut, broken, chewed, crushed, or dissolved oxymorphone hydrochloride extended-release tablets can result in a fatal overdose *[see Dosage and Administration (2.1)].*
- Use oxymorphone hydrochloride extended-release tablets exactly as prescribed to reduce the risk of life-threatening adverse reactions (e.g., respiratory depression) *[see Dosage and Administration (2), Warnings and Precautions (5.3)].*
- Do not discontinue oxymorphone hydrochloride extended-release tablets without first discussing the need for a tapering regimen with the prescriber *[see Dosage and Administration (2.4), Warnings and Precautions (5.14)].*

Hypotension

Inform patients that oxymorphone hydrochloride extended-release tablets may cause orthostatic hypotension and syncope. Instruct patients how to recognize symptoms of low blood pressure and how to reduce the risk of serious consequences should hypotension occur (e.g., sit or lie down, carefully rise from a sitting or lying position).

Pregnancy

Neonatal Opioid Withdrawal Syndrome

Inform female patients of reproductive potential that prolonged use of oxymorphone hydrochloride extended-release tablets during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated *[see Warnings and Precautions (5.4), Use in Specific Populations (8.1)]*.

Embryo-Fetal Toxicity

Inform female patients of reproductive potential that oxymorphone hydrochloride extended-release tablets can cause fetal harm and to inform their healthcare provider of a known or suspected pregnancy *[see Use in Specific Populations (8.1)]*.

Lactation

Advise patients that breastfeeding is not recommended during treatment with oxymorphone hydrochloride extended-release tablets *[see Use in Specific Populations (8.2)].*

Infertility

Inform patients that chronic use of opioids may cause reduced fertility. It is not known whether these effects on fertility are reversible *[see Adverse Reactions (6.2), Use in Specific Populations (8.3)].*

Driving or Operating Heavy Machinery

Inform patients that oxymorphone hydrochloride extended-release tablets may impair

the ability to perform potentially hazardous activities such as driving a car or operating heavy machinery. Advise patients not to perform such tasks until they know how they will react to the medication *[see Warnings and Precautions (5.15)].*

Constipation

Advise patients of the potential for severe constipation, including management instructions and when to seek medical attention *[see Adverse Reactions (6), Clinical Pharmacology (12.2)].*

Disposal of Unused Oxymorphone Hydrochloride Extended-Release Tablets

Advise patients to flush the unused tablets down the toilet when oxymorphone hydrochloride extended-release tablets are no longer needed.

Manufactured by:
Amneal Pharmaceuticals of NY, LLC
Brookhaven, NY 11719

Distributed by:
Amneal Specialty, a division of Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807

Rev. 06-2019-01

Medication Guide

Oxymorphone Hydrochloride (ox" i mor' fone hye" droe klor' ide) **Extended-Release Tablets, USP, CII**

Oxymorphone hydrochloride extended-release tablets are:

- A strong prescription pain medicine that contains an opioid (narcotic) that is used to manage pain severe enough to require daily around-the-clock, long-term treatment with an opioid, when other pain treatments such as non-opioid pain medicines or immediate-release opioid medicines do not treat your pain well enough or you cannot tolerate them.
- A long-acting (extended-release) opioid pain medicine that can put you at risk for overdose and death. Even if you take your dose correctly as prescribed you are at risk for opioid addiction, abuse, and misuse that can lead to death.
- Not for use to treat pain that is not around-the-clock.

Important information about oxymorphone hydrochloride extended-release tablets:

- **Get emergency help right away if you take too much oxymorphone hydrochloride extended-release tablets (overdose).** When you first start taking oxymorphone hydrochloride extended-release tablets, when your dose is changed, or if you take too much (overdose), serious or life-threatening breathing problems that can lead to death may occur.
- Taking oxymorphone hydrochloride extended-release tablets with other opioid medicines, benzodiazepines, alcohol, or other central nervous system depressants

(including street drugs) can cause severe drowsiness, decreased awareness, breathing problems, coma, and death.
- Never give anyone your oxymorphone hydrochloride extended-release tablets. They could die from taking it. Store oxymorphone hydrochloride extended-release tablets away from children and in a safe place to prevent stealing or abuse. Selling or giving away oxymorphone hydrochloride extended-release tablets is against the law.

Do not take oxymorphone hydrochloride extended-release tablets if you have:
- severe asthma, trouble breathing, or other lung problems.
- a bowel blockage or have a narrowing of the stomach or intestines.

Before taking oxymorphone hydrochloride extended-release tablets, tell your healthcare provider if you have a history of:
- head injury, seizures
- problems urinating
- abuse of street or prescription drugs, alcohol addiction, or mental health problems
- liver, kidney, thyroid problems
- pancreas or gallbladder problems

Tell your healthcare provider if you are:
- **pregnant or planning to become pregnant.** Prolonged use of oxymorphone hydrochloride extended-release tablets during pregnancy can cause withdrawal symptoms in your newborn baby that could be life-threatening if not recognized and treated.
- **breast-feeding.** Not recommended during treatment with oxymorphone hydrochloride extended-release tablets. It may harm your baby.
- taking prescription or over-the-counter medicines, vitamins, or herbal supplements. Taking oxymorphone hydrochloride extended-release tablets with certain other medicines can cause serious side effects that could lead to death.

When taking oxymorphone hydrochloride extended-release tablets:
- Do not change your dose. Take oxymorphone hydrochloride extended-release tablets exactly as prescribed by your healthcare provider. Use the lowest dose possible for the shortest time needed.
- Take your prescribed dose every 12 hours at the same time every day on an empty stomach, at least 1 hour before or 2 hours after meals. Do not take more than your prescribed dose in 24 hours. If you miss a dose, take your next dose at your usual time.
- Swallow oxymorphone hydrochloride extended-release tablets whole. Do not cut, break, chew, crush, dissolve, snort, or inject oxymorphone hydrochloride extended-release tablets because this may cause you to overdose and die.
- **Call your healthcare provider if the dose you are taking does not control your pain.**
- **Do not stop taking oxymorphone hydrochloride extended-release tablets without talking to your healthcare provider.**
- After you stop taking oxymorphone hydrochloride extended-release tablets, flush any unused tablets down the toilet.

While taking oxymorphone hydrochloride extended-release tablets DO NOT:

- Drive or operate heavy machinery, until you know how oxymorphone hydrochloride extended-release tablets affect you. Oxymorphone hydrochloride extended-release tablets can make you sleepy, dizzy, or lightheaded.
- Drink alcohol or use prescription or over-the-counter medicines that contain alcohol. Using products containing alcohol during treatment with oxymorphone hydrochloride extended-release tablets may cause you to overdose and die.

The possible side effects of oxymorphone hydrochloride extended-release tablets:

- constipation, nausea, sleepiness, vomiting, tiredness, headache, dizziness, abdominal pain.
  Call your healthcare provider if you have any of these symptoms and they are severe.

Get emergency medical help if you have:

- trouble breathing, shortness of breath, fast heartbeat, chest pain, swelling of your face, tongue, throat, or hands, hives, itching, rash, extreme drowsiness, light-headedness when changing positions, feeling faint, agitation, high body temperature, trouble walking, stiff muscles, or mental changes such as confusion.

These are not all the possible side effects of oxymorphone hydrochloride extended-release tablets. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

For more information go to dailymed.nlm.nih.gov.

For more information about oxymorphone hydrochloride extended-release tablets, call Amneal Pharmaceuticals at 1-877-835-5472.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by:
Amneal Pharmaceuticals of NY, LLC
Brookhaven, NY 11719

Distributed by:
Amneal Specialty, a division of Amneal Pharmaceuticals LLC
Bridgewater, NJ 08807

Rev. 04-2019-00

OXYMORPHONE HYDROCHLORIDE

oxymorphone hydrochloride tablet, film coated, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:55700-788(NDC:64896-697)
Route of Administration	ORAL	**DEA Schedule**	CII

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
OXYMORPHONE HYDROCHLORIDE (UNII: 5Y2EI94NBC) (OXYMORPHONE - UNII:9VXA968E0C)	OXYMORPHONE HYDROCHLORIDE	10 mg

Inactive Ingredients	
Ingredient Name	**Strength**
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
HYPROMELLOSES (UNII: 3NXW29V3WO)	
XANTHAN GUM (UNII: TTV12P4NEE)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYVINYL ALCOHOL, UNSPECIFIED (UNII: 532B59J990)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
TALC (UNII: 7SEV7J4R1U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
ALUMINUM OXIDE (UNII: LMI26O6933)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	

Product Characteristics			
Color	ORANGE	**Score**	no score

Shape	ROUND	**Size**	5mm
Flavor		**Imprint Code**	G72
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:55700-788-60	60 in 1 BOTTLE; Type 0: Not a Combination Product	02/11/2021	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA079087	08/30/2019	

Labeler - Quality Care Products, LLC (831276758)

Establishment

Name	Address	ID/FEI	Business Operations
Quality Care Products, LLC		831276758	relabel(55700-788)

Revised: 9/2022 Quality Care Products, LLC