

# Physiotherapy Beats Talk Therapy for Neck Pain

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**S**tandard physiotherapy appears more effective than a brief, cognitive behavioral-type intervention for neck pain, although patient preference for the brief intervention can enhance its effectiveness, according to a randomized trial.

However, because confidence intervals overlapped in the trial results, "some may argue that there is a role for the brief in-

tervention for all patients," noted Jennifer A. Klaber Moffett, Ph.D., of the University of Hull (England), and her colleagues (BMJ 2005;330:75). "It seems that the brief intervention should in any case be available for those who prefer it."

According to the researchers, previous studies have suggested that patients' expectations or preferences for a particular treatment may influence the outcome of that treatment.

A total of 268 adult patients with suba-

cute or chronic neck pain were randomized to receive either standard physiotherapy or the brief intervention. Prior to randomization, all patients were asked to complete a questionnaire, which included the Northwick Park neck pain questionnaire (NPQ), a measure of the level of neck pain and resulting disability; the short form 36 questionnaire (SF-36), a generic health and quality of life questionnaire that includes physical and psychological factors; and the Tampa scale for kineso-

phobia (a measure of fear and avoidance of movement). Distress was also measured on a scale of 0-10, with 10 representing extreme distress.

Patients were then asked if they had a preference for standard physiotherapy or brief intervention and were then randomized to a treatment independent of their preference.

The 139 patients in the brief intervention arm received between one and three hands-off sessions with a physiotherapist, during which time cognitive behavioral therapy strategies were emphasized and patients were encouraged to return to normal daily activities as soon as possible through self-management.

The 129 standard physiotherapy patients received any combination of electrotherapy, manual therapy or mobilization, ad-

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vice, home exercises, and other approaches according to therapists' judgments.

Follow-up questionnaires at 3 and 12 months post intervention showed that for the NPQ, the main outcome, the standard physiotherapy group showed more improvement than the brief intervention group—although this difference did not reach significance.

The SF-36 results showed a similar trend. And although the Tampa scores on fear of movement were in favor of brief intervention initially at 3 months, this trend was reversed at 12 months.

When patients' treatment preferences were factored in, those who wanted the brief intervention and got it had the biggest improvement on the NPQ score, although the difference was not statistically significant. Among patients who were indifferent about which treatment they wanted, there was an advantage to being assigned to standard physiotherapy. Among patients who stated a preference for standard physiotherapy and then received it, the overall treatment effect did not seem to be enhanced. However, if these patients were randomized to the brief intervention, their pain scores at 12 months were increased from baseline.

"Usual physiotherapy produced marginally better treatment outcomes at 12 months than the shorter, hands-off intervention," reported the authors. ■

## Exercise Guide for Older Adults

The National Institute on Aging offers a free exercise guide for older Americans. "Exercise: A Guide From the National Institute on Aging," is available in English or Spanish. To order, call 800-222-2225 or visit [www.niapublications.org/exercisebook/index.asp](http://www.niapublications.org/exercisebook/index.asp).

### OXYCONTIN® (OXYCODONE HCl CONTROLLED-RELEASE) TABLETS

10 mg 20 mg 40 mg 80 mg\* 160 mg\*

\*80 mg and 160 mg for use in opioid-tolerant patients only.

**BRIEF SUMMARY OF PRESCRIBING INFORMATION** (For complete prescribing information please see package insert.)

**WARNING:** Oxycodone is an opioid agonist and a Schedule II controlled substance with an abuse liability similar to morphine.

Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing Oxycodone in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

Oxycodone should be used with extreme caution in patients with significant chronic obstructive pulmonary disease or cor pulmonale, and in patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression. In such patients, even usual therapeutic doses of oxycodone may decrease respiratory drive to the point of apnea. In these patients alternative non-opioid analgesics should be considered, and opioids should be employed only under careful medical supervision at the lowest effective dose.

**Oxycodone Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.**

**Oxycodone Tablets are NOT intended for use as a prn analgesic.**

**Oxycodone 80 mg and 160 mg Tablets ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY.** These tablet strengths may cause fatal respiratory depression when administered to patients not previously exposed to opioids.

**Oxycodone TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED Oxycodone TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.**

**INDICATIONS AND USAGE**

Oxycodone Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.

Oxycodone is NOT intended for use as a prn analgesic.

Physicians should individualize treatment in every case, initiating therapy at the appropriate point along a progression from non-opioid analgesics, such as non-steroidal anti-inflammatory drugs and acetaminophen to opioids in a plan of pain management such as outlined by the World Health Organization, the Agency for Healthcare Research and Quality (formerly known as the Agency for Health Care Policy and Research), the Federation of State Medical Boards Model Guidelines, or the American Pain Society.

Oxycodone is not indicated for pain in the immediate postoperative period (the first 12-24 hours following surgery), or if the patient is mild or not expected to persist for an extended period of time. Oxycodone is only indicated for postoperative use if the patient is already receiving the drug prior to surgery or if the post-operative pain is expected to be moderate to severe and persist for an extended period of time. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. (See American Pain Society guidelines.)

**CONTRAINDICATIONS**

Oxycodone is contraindicated in patients with known hypersensitivity to oxycodone, or in any situation where opioids are contraindicated. This includes patients with significant respiratory depression (in unmonitored settings or the absence of resuscitative equipment), and patients with acute or severe bronchial asthma or hypercarbia. Oxycodone is contraindicated in any patient who has or is suspected of having paralytic ileus.

**WARNINGS**

**OXYCODONE TABLETS ARE TO BE SWALLOWED WHOLE AND ARE NOT TO BE BROKEN, CHEWED, OR CRUSHED. TAKING BROKEN, CHEWED, OR CRUSHED OXYCODONE TABLETS LEADS TO RAPID RELEASE AND ABSORPTION OF A POTENTIALLY FATAL DOSE OF OXYCODONE.**

Oxycodone 80 mg and 160 mg Tablets ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. These tablet strengths may cause fatal respiratory depression when administered to patients not previously exposed to opioids.

Oxycodone 80 mg and 160 mg Tablets are for use only in opioid-tolerant patients requiring daily oxycodone equivalent doses of 160 mg or more for the 80 mg tablet and 320 mg or more for the 160 mg tablet. Care should be taken in the prescribing of these tablet strengths. Patients should be instructed against use by individuals other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death.

**Misuse, Abuse and Diversion of Opioids**

Oxycodone is an opioid agonist of the morphine-type. Such drugs are sought by drug abusers and people with addiction disorders and are subject to criminal diversion.

Oxycodone can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing Oxycodone in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion.

Oxycodone has been reported as being abused by crushing, snorting, or injecting the dissolved product. These practices will result in the uncontrolled delivery of the opioid and pose a significant risk to the abuser that could result in overdose and death (see WARNINGS and DRUG ABUSE AND ADDICTION). Concerns about abuse, addiction, and diversion should not prevent the proper management of pain. The development of addiction to opioid analgesics in properly managed patients with pain has been reported to be rare. However, data are not available to establish the true incidence of addiction in chronic pain patients.

Healthcare professionals should contact their State Professional Licensing Board, or State Controlled Substances Authority for information on how to prevent and detect abuse or diversion of this product.

**Interactions with Alcohol and Drugs of Abuse**

Oxycodone may be expected to have additive effects when used in conjunction with alcohol, other opioids, or illicit drugs that cause central nervous system depression.

**DRUG ABUSE AND ADDICTION**

Oxycodone is a mu-agonist opioid with an abuse liability similar to morphine and is a Schedule II controlled substance. Oxycodone, like morphine and other opioids used in analgesia, can be abused and is subject to criminal diversion.

Drug addiction is characterized by compulsive use, use for non-medical purposes, and continued use despite harm or risk of harm. Drug addiction is a treatable disease, utilizing a multi-disciplinary approach, but relapse is common.

"Drug-seeking" behavior is very common in addicts and drug abusers. 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 physicians. "Doctor shopping" to obtain additional prescriptions is common among drug abusers and people suffering from untreated addiction.

Abuse and addiction are separate and distinct from physical dependence and tolerance. Physicians 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 and is characterized by misuse for non-medical purposes, often in combination with other psychoactive substances. Oxycodone, like other opioids, has been diverted for non-medical use. Careful record-keeping of prescribing information, including quantity, frequency, and renewal requests 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 limit abuse of opioid drugs.

**Oxycodone consists of a dual-polymer matrix, intended for oral use only. Abuse of the crushed tablet poses a hazard of overdose and death. This risk is increased with concurrent abuse of alcohol and other substances. With parenteral abuse, the tablet excipients, especially talc, can be expected to result in local tissue necrosis, infection, pulmonary granulomas, and increased risk of endocarditis and valvular heart injury. Parenteral drug abuse is commonly associated with transmission of infectious diseases such as hepatitis and HIV.**

**Respiratory Depression**

Respiratory depression is the chief hazard from oxycodone. The active ingredient in Oxycodone, as with all opioid agonists, respiratory depression is a particular problem in elderly or debilitated patients, usually following large initial doses in non-tolerant patients, or when opioids are given in conjunction with other agents that depress respiration.

Oxycodone should be used with extreme caution in patients with significant chronic obstructive pulmonary disease or cor pulmonale, and in patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression. In such patients, even usual therapeutic doses of oxycodone may decrease respiratory drive to the point of apnea. In these patients alternative non-opioid analgesics should be considered, and opioids should be employed only under careful medical supervision at the lowest effective dose.

**Head Injury**

The respiratory depressant effects of opioids include carbon dioxide retention and secondary elevation of cerebrospinal fluid pressure, and may be markedly exaggerated in the presence of head injury, intracranial lesions, or other sources of pre-existing increased intracranial pressure. Oxycodone produces effects on pupillary response and consciousness which may obscure neurological signs of further increases in intracranial pressure in patients with head injuries.

**Hypotensive Effect**

Oxycodone may cause severe hypotension. There is an added risk to individuals whose ability to maintain blood pressure has been compromised by a depleted blood volume, or after concurrent administration with drugs such as phenothiazines or other agents which compromise vasomotor tone. Oxycodone may produce orthostatic hypotension in ambulatory patients. Oxycodone, like all opioid agonists of the morphine-type, should be administered with caution to patients in circulatory shock, since vasodilation produced by the drug may further reduce cardiac output and blood pressure.

**PRECAUTIONS**

**General**

Opioid analgesics have a narrow therapeutic index in certain patient populations, especially when combined with CNS depressant drugs, and should be reserved for cases where the benefits of opioid analgesia outweigh the known risks of respiratory depression, altered mental state, and postural hypotension.

Use of Oxycodone is associated with increased potential risks and should be used only with caution in the following conditions: acute alcoholism; adrenocortical insufficiency (e.g., Addison's disease); CNS depression or coma; delirium tremens; debilitated patients; kyphoscoliosis associated with respiratory depression; myxedema or hypothyroidism; prostatic hypertrophy or urethral stricture; severe impairment of hepatic, pulmonary or renal function; and toxic psychosis.

The administration of oxycodone may obscure the diagnosis or clinical course in patients with acute abdominal conditions. Oxycodone may aggravate convulsions in patients with convulsive disorders, and all opioids may induce or aggravate seizures in some clinical settings.

**Interactions with other CNS Depressants**

Oxycodone should be used with caution and started in a reduced dosage (1/2 to 1/3 of the usual dosage) in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothiazines, tranquilizers, and alcohol. Inhibitive effects resulting in respiratory depression, hypotension, profound sedation, or coma may result if these drugs are taken in combination with the usual doses of Oxycodone.

**Interactions with Mixed Agonist/Antagonist Opioid Analgesics**

Agonist/antagonist analgesics (i.e., pentazocine, nalbuphine, and butorphanol) should be administered with caution to a patient who has received or is receiving a course of therapy with a pure opioid agonist analgesic such as oxycodone. In this situation, mixed agonist/antagonist analgesics may reduce the analgesic effect of oxycodone and/or may precipitate withdrawal symptoms in these patients.

**Ambulatory Surgery and Postoperative Use**

Oxycodone is not indicated for pre-emptive analgesia (administration pre-operatively for the management of postoperative pain).

Oxycodone is not indicated for pain in the immediate postoperative period (the first 12 to 24 hours following surgery) for patients not previously taking the drug, because its safety in this setting has not been established.

Oxycodone is not indicated for pain in the postoperative use if the patient is mild or not expected to persist for an extended period of time.

Oxycodone is only indicated for postoperative use if the patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. (See American Pain Society guidelines.)

Patients who are already receiving Oxycodone Tablets as part of ongoing analgesic therapy may be safely continued on the drug if appropriate dosage adjustments are made considering the procedure, other drugs given, and the temporary changes in physiology caused by the surgical intervention (see DOSAGE AND ADMINISTRATION).

Oxycodone and other morphine-like opioids have been shown to decrease bowel motility. Ileus is a common postoperative complication, especially after intra-abdominal surgery with opioid analgesia. Caution should be taken to monitor for ileus in postoperative patients receiving opioids. Standard supportive therapy should be implemented.

**Use in Pancreatic/Biliary Tract Disease**

Oxycodone may cause spasm of the sphincter of Oddi and should be used with caution in patients with biliary tract disease, including acute pancreatitis. Opioids like oxycodone may cause increases in the serum amylase level.

**Tolerance and Physical Dependence**

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). Physical dependence is manifested by withdrawal symptoms after abrupt discontinuation of a drug or upon administration of an antagonist. Physical dependence and tolerance are not unusual during chronic opioid therapy.

The opioid abstinence or withdrawal syndrome is characterized by some or all of the following: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia, and mydriasis. Other 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.

In general, opioids should not be abruptly discontinued.

**Information for Patients/Caregivers**

If clinically advisable, patients receiving Oxycodone Tablets or their caregivers should be given the following information by the physician, nurse, pharmacist, or caregiver:

1. Patients should be aware that Oxycodone Tablets contain oxycodone, which is a morphine-like substance.
2. Patients should be advised that Oxycodone Tablets were designed to work properly only if swallowed whole. Oxycodone Tablets will release all their contents at once if broken, chewed, or crushed, resulting in a risk of fatal overdose.
3. Patients should be advised to report episodes of breakthrough pain and adverse experiences occurring during therapy. Individualization of dosage is essential to make optimal use of this medication.
4. Patients should be advised not to adjust the dose of Oxycodone without consulting the prescribing professional.
5. Patients should be advised that Oxycodone may impair mental and/or physical ability required for the performance of potentially hazardous tasks (e.g., driving, operating heavy machinery).
6. Patients should not combine Oxycodone with alcohol or other central nervous system depressants (sleep aids, tranquilizers) except by the directions of the prescribing physician, because dangerous additive effects may occur, resulting in serious injury or death.
7. Women of childbearing potential who become, or are planning to become, pregnant should be advised to consult their physician regarding the effects of analgesics and other drug use during pregnancy on themselves and their unborn child.
8. Patients should be advised that Oxycodone is a potential drug of abuse. They should protect it from theft, and it should never be given to anyone other than the individual for whom it was prescribed.
9. Patients should be advised that they may pass empty matrix "ghosts" (tablets) via colostomy or in the stool, and that this is of no concern since the active medication has already been absorbed.
10. Patients should be advised that if they have been receiving treatment with Oxycodone for more than a few weeks and cessation of therapy is indicated, it may be appropriate to taper the Oxycodone dose, rather than abruptly discontinue it, due to the risk of precipitating withdrawal symptoms. Their physician can provide a dose schedule to accomplish a gradual discontinuation of the medication.
11. Patients should be instructed to keep Oxycodone in a secure place out of the reach of children. When Oxycodone is no longer needed, the unused tablets should be destroyed by flushing down the toilet.

**Use in Drug and Alcohol Addiction**

Oxycodone is an opioid with no approved use in the management of addictive disorders. Its proper usage in individuals with drug or alcohol dependence, either active or in remission, is for the management of pain requiring opioid analgesia.

**Drug-Drug Interactions**

Oxycodone, including Oxycodone Tablets, may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce respiratory depression. Oxycodone is metabolized in part to oxycodone via cytochrome P450 2D6. While this pathway may be blocked by a variety of drugs (e.g., certain cardiovascular drugs including amiodarone and quinidine as well as polycyclic antidepressants), such blockade has not yet been shown to be of clinical significance with this agent. Clinicians should be aware of this possible interaction, however.

**Use with CNS Depressants**

Oxycodone, like all opioid analgesics, should be started at 1/2 to 1/3 of the usual dosage in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothiazines, centrally acting anti-emetics, tranquilizers, and alcohol because respiratory depression, hypotension, and profound sedation or coma may result. No specific interaction between oxycodone and monoamine oxidase inhibitors has been observed, but caution in the use of any opioid in patients taking this class of drugs is appropriate.

**Carcinogenicity, Mutagenesis, Impairment of Fertility**

Studies of oxycodone to evaluate its carcinogenic potential have not been conducted.

Oxycodone was not mutagenic in the following assays: Ames Salmonella and E. coli test with and without metabolic activation at doses of up to 5000 µg; chromosomal aberration test in human lymphocytes in the absence of metabolic activation at doses of up to 1500 µg/mL and with activation 48 hours after exposure at doses of up to 5000 µg/mL and in the in vivo bone marrow micronucleus test in mice (at plasma levels of up to 40 µg/mL). Oxycodone was clastogenic in the human lymphocyte chromosomal assay in the presence of metabolic activation in the human chromosomal aberration test (at greater than or equal to 1250 µg/mL) at 24 but not 48 hours of exposure and in the mouse lymphoma assay at doses of 50 µg/mL or greater with metabolic activation and at 400 µg/mL or greater without metabolic activation.

**Pregnancy**

**Teratogenic Effects—Category B:** Reproduction studies have been performed in rats and rabbits by oral administration at doses up to 8 mg/kg and 125 mg/kg, respectively. These doses are 3 and 46 times a human dose of 160 mg/day, based on mg/kg basis. The results did not reveal evidence of harm to the fetus due to oxycodone. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**Labor and Delivery**

Oxycodone is not recommended for use in women during and immediately prior to labor and delivery because oral opioids may cause respiratory depression in the newborn. Neonates whose mothers have been taking oxycodone chronically may exhibit respiratory depression and/or withdrawal symptoms, either at birth and/or in the nursery.

**Nursing Mothers**

Low concentrations of oxycodone have been detected in breast milk. Withdrawal symptoms can occur in breast-feeding infants when maternal administration of the opioid is stopped. Ordinarily, nursing should not be undertaken while a patient is receiving Oxycodone because of the possibility of sedation and/or respiratory depression in the infant.

**Pediatric Use**

Safety and effectiveness of Oxycodone have not been established in pediatric patients below the age of 18. It must be remembered that Oxycodone Tablets cannot be crushed or divided for administration.

**Geriatric Use**

In controlled pharmacokinetic studies in elderly subjects (greater than 65 years) the clearance of oxycodone appeared to be slightly reduced. Care should be taken when Oxycodone is administered to elderly patients who have increased approximately 15%. Of the total number of subjects (445) in clinical studies of Oxycodone, 148 (33.3%) were age 65 and older (including those age 75 and older) while 40 (9.0%) were age 75 and older. In clinical trials with appropriate initiation of therapy and dose titration, no untoward or unexpected side effects were seen in the elderly patients who received Oxycodone. Thus, the usual doses and dosing intervals are appropriate for these patients. As with all opioids, the starting dose should be reduced to 1/2 to 1/3 of the usual dosage in debilitated, non-tolerant patients. Respiratory depression is the chief hazard in elderly or debilitated patients, usually following large initial doses in non-tolerant patients, or when opioids are given in conjunction with other agents that depress respiration.

**Laboratory Monitoring**

Due to the broad range of plasma concentrations seen in clinical populations, the varying degrees of pain, and the development of tolerance, plasma oxycodone measurements are usually not helpful in clinical management. Plasma concentrations of the active drug substance may be of value in selected, unusual or complex cases.

**Hepatic Impairment**

A study of Oxycodone in patients with hepatic impairment indicates greater plasma concentrations than those with normal function. The initiation of therapy at 1/2 to 1/3 the usual doses and careful dose titration is warranted.

**Renal Impairment**

In patients with renal impairment, as evidenced by decreased creatinine clearance (<60 mL/min), the concentrations of oxycodone in the plasma are approximately 50% higher than in subjects with normal renal function. Dose initiation should follow a conservative approach. Dosages should be adjusted according to the clinical situation.

**Gender Differences**

In pharmacokinetic studies, opioid-naïve females demonstrate up to 25% higher average plasma concentrations and greater frequency of typical opioid adverse events than males, even after adjustment for body weight. The clinical relevance of a difference of this magnitude is low for a drug intended for chronic use at individualized dosages, and there was no male/female difference detected for efficacy or adverse events in clinical trials.

**ADVERSE REACTIONS**

The safety of Oxycodone was evaluated in double-blind clinical trials involving 713 patients with moderate to severe pain of various etiologies. In open-label studies of cancer pain, 187 patients received Oxycodone in total daily doses ranging from 20 mg to 640 mg per day. The average total daily dose was approximately 105 mg per day.

Serious adverse reactions which may be associated with Oxycodone Tablet therapy in clinical use are those observed with other opioid analgesics, including respiratory depression, apnea, respiratory arrest, and (to an even lesser degree) circulatory depression, hypotension, or shock (see OVERDOSAGE).

The non-serious adverse events seen on initiation of therapy with Oxycodone are typical opioid side effects. These events are dose-dependent, and their frequency depends upon the dose, the clinical setting, the patient's level of opioid tolerance, and host factors specific to the individual. They should be expected and managed as a part of opioid analgesia. The most frequent (>5%) include: constipation, nausea, somnolence, dizziness, vomiting, pruritus, headache, dry mouth, sweating, and asthenia.

In many cases the frequency of these events during initiation of therapy may be minimized by careful individualization of starting dosage, slow titration, and the avoidance of large swings in the plasma concentrations of the opioid. Many of these adverse events will cease or decrease in intensity as Oxycodone therapy is continued and some degree of tolerance is developed.

Clinical trials comparing Oxycodone with immediate-release oxycodone and placebo revealed a similar adverse event profile between Oxycodone and immediate-release oxycodone. The most common adverse events (>5%) reported by patients at least once during therapy were:

Oxycodone (n=227)	Immediate-Release (n=225)	Placebo (n=45)
Constipation (23)	(26)	(7)
Nausea (23)	(27)	(11)
Somnolence (23)	(24)	(4)
Dizziness (13)	(16)	(9)
Pruritus (13)	(12)	(2)
Vomiting (12)	(14)	(7)
Headache (7)	(9)	(7)
Dry Mouth (6)	(7)	(2)
Asthenia (6)	(7)	(—)
Sweating (5)	(6)	(2)

The following adverse experiences were reported in Oxycodone-treated patients with an incidence between 1% and 5%, in descending order of frequency: they were anorexia, nervousness, insomnia, fever, constipation, diarrhea, abnormal pain, dyspepsia, rash, anxiety, euphoria, dyspnea, postural hypotension, chills, twitching, gastritis, abnormal dreams, thought abnormalities, and hiccups.

The following adverse reactions occurred in less than 1% of patients involved in clinical trials or were reported in postmarketing experience:

**General:** accidental injury, chest pain, facial edema, malaise, neck pain, pain, and symptoms associated with either an anaphylactoid or anaphylactoid reaction.

**Cardiovascular:** migraine, syncope, vasodilation, ST depression.

**Digestive:** dysphagia, eructation, flatulence, gastrointestinal disorder, increased appetite, nausea and vomiting, stomatitis, ileus.

**Hemic and Lymphatic:** lymphadenopathy.

**Metabolic and Nutritional:** dehydration, edema, hyponatremia, peripheral edema, syndrome of inappropriate antidiuretic hormone secretion, thirst.

**Nervous:** abnormal gait, agitation, amnesia, depersonalization, depression, emotional lability, hallucination, hyperkinesia, hyposthesia, hypotonia, malaise, paresthesia, seizures, speech disorder, stupor, tremor, tetraplegia, withdrawal syndrome with or without seizures.

**Respiratory:** cough increased, pharyngitis, voice alteration.

**Skin:** dry skin, exfoliative dermatitis, urticaria.

**Special Senses:** abnormal vision, taste perversion.

**Urogenital:** amenorrhea, decreased libido, dysuria, hematuria, impotence, polyuria, urinary retention, uterine impaired.

**OVERDOSAGE**

Acute overdose with oxycodone can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, bradycardia, hypotension, and death.

Deaths due to overdose have been reported with abuse and misuse of Oxycodone, by ingesting, inhaling, or injecting the crushed tablets. Review of case reports has indicated that the risk of fatal overdose is further increased when Oxycodone is abused concurrently with alcohol or other CNS depressants, including other opioids.

In the treatment of oxycodone overdose, primary attention should be given to the re-establishment of a patent airway and institution of assisted or controlled ventilation. Supportive measures (including oxygen and vasopressors) should be employed in the management of circulatory shock and pulmonary edema accompanying overdose as indicated. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation.

The pure opioid antagonists such as naloxone or nalmefene are specific antidotes against respiratory depression from opioid overdose. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdose. In patients who are physically dependent on any opioid agonist including Oxycodone, an abrupt or complete reversal of opioid effects may precipitate an acute abstinence syndrome. The severity of the withdrawal syndrome produced will depend on the degree of physical dependence and the dose of the antagonist administered. Please see the prescribing information for the specific opioid antagonist for details of their proper use.

**Managing Expected Opioid Adverse Experiences**

Most patients receiving opioids, especially those who are opioid-naïve, will experience side effects. Frequently the side effects from Oxycodone are transient, but may require evaluation and management. Adverse events such as constipation should be anticipated and treated aggressively and prophylactically with a stimulant laxative and/or stool softener. Patients do not usually become tolerant to the constipating effects of opioids.

Other opioid-related side effects such as sedation and nausea are usually self-limited and often do not persist beyond the first few days. If nausea persists and is unacceptable to the patient, treatment with antiemetics or other modalities may relieve these symptoms and should be considered.

Patients receiving Oxycodone may pass an intact matrix "ghost" in the stool or via colostomy. These ghosts contain little or no residual oxycodone and are of no clinical consequence.

**SAFETY AND HANDLING**

Oxycodone Tablets are solid dosage forms that contain oxycodone which is a controlled substance. Like morphine, oxycodone is controlled under Schedule II of the Controlled Substances Act.

Oxycodone has been targeted for theft and diversion by criminals. Healthcare professionals should contact their State Professional Licensing Board or State Controlled Substances Authority for information on how to prevent and detect abuse or diversion of this product.

Store at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F).  
Healthcare professionals can telephone Purdue Pharma's Medical Services Department (1-888-726-7538) for information on this product.

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