PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

TEVA-OXYCODAN[N]

Oxycodone hydrochloride and acetylsalicylic acid tablets
Tablet, 5 mg /325 mg, Oral

Opioid Analgesic

Teva Canada Limited
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Toronto, Ontario
Canada M1B 2K9

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RECENT MAJOR LABEL CHANGES

3 Serious Warnings and Precautions Box	05/2024
7 WARNINGS AND PRECAUTIONS, Skin, Opioid induced hyperalgesia, Sleep related breathing disorder, 7.1.1 Pregnant Women	05/2024
Patient Medication Information	05/2024

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Adults

TEVA-OXYCODAN (oxycodone hydrochloride and acetylsalicylic acid (ASA)) is indicated for:

- the relief of mild to moderately severe pain, including conditions accompanied by fever and/or inflammation.

TEVA-OXYCODAN is not indicated as an as-needed (prn) analgesic.

1.1 Pediatrics (< 18 years of age)

The safety and efficacy of TEVA-OXYCODAN has not been studied in the pediatric population. Therefore Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics (> 65 years of age)

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, concomitant disease or other drug therapy (see 10 CLINICAL, Special Populations and Conditions, Geriatrics).

2 CONTRAINDICATIONS

TEVA-OXYCODAN is contraindicated in:

- Patients who are hypersensitive to the active substance or other opioid analgesics or to any ingredient in the formulation. For a complete listing, see the 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING section of the Product Monograph.
- Patients with known or suspected mechanical gastrointestinal obstruction (e.g., bowel obstruction or strictures), or any diseases/conditions that affect bowel transit (e.g., ileus of any type).
- Patients with suspected surgical abdomen (e.g., acute appendicitis or pancreatitis).
- Patients with mild pain that can be managed with other pain medications.
- Patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus.
- Patients with acute respiratory depression, elevated carbon dioxide levels in the blood and cor pulmonale.
- Patients with acute alcoholism, delirium tremens, and convulsive disorders.
- Patients with severe CNS depression, increased cerebrospinal or intracranial pressure,

and head injury.

- Patients taking monoamine oxidase (MAO) inhibitors (or within 14 days of such therapy).
- Patients with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to ASA or other nonsteroidal anti-inflammatory drugs. Anaphylactoid reactions have occurred in such patients.
- Peptic ulcer or other serious gastrointestinal lesions.
- Patients with a hemorrhagic diathesis (e.g., hemophilia, hypoprothrombinemia, von Willebrand's disease, thrombocytopenia, thrombasthenia and other ill-defined hereditary platelet dysfunctions, severe vitamin K deficiency and severe liver damage)
- Women who are breast-feeding, and during pregnancy, or during labour and delivery (see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, and 7 WARNINGS AND PRECAUTIONS).

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

TEVA-OXYCODAN must be swallowed whole. Cutting, breaking, crushing, chewing, or dissolving TEVA-OXYCODAN can lead to dangerous adverse events including death (see 7 WARNINGS AND PRECAUTIONS). Further, instruct patients of the hazards related to taking opioids including fatal overdose.

Accidental Exposure
Accidental ingestion of even one dose of TEVA-OXYCODAN, especially by children, can result in a fatal overdose of TEVA-OXYCODAN (see 4 DOSAGE AND ADMINISTRATION, Disposal).

Risk in Pregnancy: TEVA-OXYCODAN is contraindicated for use during pregnancy
Use of NSAIDS at approximately 20 weeks of gestation or later may cause fetal renal dysfunction leading to oligohydramnios and neonatal renal impairment or failure (see 7 WARNINGS AND PRECAUTIONS). During the third trimester, there is risk of premature closure of the ductus arteriosus and uterine inertia (prolonged parturition) (see also 7 WARNINGS AND PRECAUTIONS, Neonatal Opioid Withdrawal Syndrome (NOWS), and Special Populations, Pregnant Women).

Neonatal Opioid Withdrawal Syndrome
Prolonged maternal use of TEVA-OXYCODAN during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening (see 7 WARNINGS AND PRECAUTIONS).

Interaction with Alcohol
The co-ingestion of alcohol with TEVA-OXYCODAN should be avoided as it may result in dangerous additive effects, causing serious injury or death (see 7 WARNINGS AND PRECAUTIONS and 9 DRUG INTERACTIONS).

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 7 WARNINGS AND PRECAUTIONS, Neurologic and 9 DRUG INTERACTIONS).

- Reserve concomitant prescribing of TEVA-OXYCODAN 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.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

For acute pain, it is recommended that TEVA-OXYCODAN be used for a maximum of 7 days at the lowest dose that provides adequate pain relief.

All doses of opioids carry an inherent risk of fatal or non-fatal adverse events. This risk is increased with higher doses. For the management of chronic non-cancer, non-palliative pain, it is recommended that 60 mg (90 morphine milligram equivalent) of TEVA-OXYCODAN not be exceeded. Each patient should be assessed for their risk prior to prescribing TEVA-OXYCODAN, as the likelihood of experiencing serious adverse events can depend upon the type of opioid, duration of treatment, level of pain as well as the patient's own level of tolerance. In addition, the level of pain should be assessed routinely to confirm the most appropriate dose and the need for further use of TEVA-OXYCODAN (see 6 DOSAGE AND ADMINISTRATION, Adjustment or Reduction of Dosage).

TEVA-OXYCODAN should only be used in patients for whom alternative treatment options are ineffective or not tolerated (e.g., non-opioid analgesics).

TEVA-OXYCODAN must be swallowed whole. Cutting, breaking, crushing, chewing, or dissolving TEVA-OXYCODAN can lead to dangerous adverse events including death (see 7 WARNINGS AND PRECAUTIONS).

TEVA-OXYCODAN should be used with caution within 12 hours pre-operatively and within the first 12-24 hours post-operatively (see 7 WARNINGS AND PRECAUTIONS, Peri-operative Considerations).

TEVA-OXYCODAN is not indicated for rectal administration.

4.2 Recommended Dose and Dosage Adjustment

Adults (≥18 years of age):

Dosage should be adjusted according to the severity of the pain and the patient's response. It may occasionally be necessary to exceed the usual dosage recommended in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of opioids. The usual adult dose is one tablet every six hours as needed for pain or as directed by a physician.

Patients Not Receiving Opioids at the Time of Initiation of Oxycodone Hydrochloride and ASA Treatment: The usual initial adult dose of TEVA-OXYCODAN for patients who have not previously received opioid analgesics is one tablet every six hours as needed for pain.

Patients Currently Receiving Opioids: For patients who are receiving an alternate opioid, the "oral oxycodone equivalent" of the analgesic presently being used, should be determined. Having determined the total daily dosage of the present analgesic, Table 1 can be used to calculate the approximate daily oral oxycodone dosage that should provide equivalent analgesia. It is usually appropriate to treat a patient with only one opioid at a time. Further dose reductions should be considered due to incomplete cross-tolerance between opioids.

Table 1: Opioid Conversion Table			
Opioids	**To convert to oral morphine equivalent**	**To convert from oral morphine multiply by**	**90 MED equivalent dose**
Morphine	1	1	90 mg/d
Codeine	0.15	6.67	600 mg/d
Hydromorphone	5	0.2	18 mg/d
Oxycodone	1.5	0.667	60 mg/d
Tapentadol	0.3-0.4	2.5-3.33	300 mg/d
Tramadol	0.1-0.2	6	***
Methadone	Morphine dose equivalence is not reliably established		

*** The maximum recommended daily dose of tramadol is 300 mg - 400 mg depending on the formulation.

Busse J. The 2017 Canadian guideline for opioids for chronic non-cancer pain. Hamilton (ON): McMaster University; 2017

Geriatrics:

Respiratory depression has occurred in the elderly following administration of large initial doses of opioids to patients who were not opioid-tolerant or when opioids were co-administered with other agents that can depress respiration. TEVA-OXYCODAN should be initiated at a low dose and slowly titrated to effect (see 7 WARNINGS AND PRECAUTIONS and 10 CLINICAL PHARMACOLOGY).

Pediatrics (>18 years of age):
Health Canada has not authorized an indication for pediatric use (see 1.1Pediatrics)

Patients with Hepatic and Renal Impairment:
Caution should be exercised when prescribing TEVA-OXYCODAN to patients with any degree of hepatic or renal impairment.

Dose Titration:

Dose titration is the key to success with opioid analgesic therapy. Proper optimization of doses scaled to the relief of the individual's pain should aim at administration of the lowest dose which will achieve the overall treatment goal of satisfactory pain relief with acceptable side effects.

Dosage adjustments should be based on the patient's clinical response.

Adjustment or Reduction of Dosage:

Physical dependence with or without psychological dependence tends to occur with chronic administration of opioids, including TEVA-OXYCODAN. Withdrawal (abstinence) symptoms may occur following abrupt discontinuation of therapy. These symptoms may include body aches, diarrhea, gooseflesh, loss of appetite, nausea, nervousness or restlessness, runny nose, sneezing, tremors or shivering, stomach cramps, tachycardia, trouble with sleeping, unusual increase in sweating, palpitations, unexplained fever, weakness and yawning.

Following successful relief of moderate to severe pain, periodic attempts to reduce the opioid dose should be made. Smaller doses or complete discontinuation may become feasible due to a change in the patient's condition or mental state. Patients on prolonged therapy should be withdrawn gradually from the drug if it is no longer required for pain control. In patients who are appropriately treated with opioid analgesics and who undergo gradual withdrawal for the drug, these symptoms are usually mild (see 7 WARNINGS AND PRECAUTIONS). Tapering should be individualised and carried out under medical supervision.

Patient should be informed that reducing and/or discontinuing opioids decreases their tolerance to these drugs. If treatment needs to be re-initiated, the patient must start at the lowest dose and titrate up to avoid overdose.

Opioid analgesics may only be partially effective in relieving dysesthetic pain, postherpetic neuralgia, stabbing pains, activity-related pain and some forms of headache. That is not to say that patients with advanced cancer suffering from some of these forms of pain should not be given an adequate trial of opioid analgesics, but it may be necessary to refer such patients at an early time to other forms of pain therapy.

4.5 Missed Dose

If the patient forgets to take one or more doses, they should take their next dose at the next scheduled time and in the normal amount.

5 OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Symptoms:

TEVA-OXYCODAN (oxycodone hydrochloride and ASA) is a combination product. The clinical presentation of overdose may include the signs and symptoms of oxycodone toxicity, ASA toxicity or both.

Oxycodone

Serious overdosage with oxycodone may be characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, miosis, hypotonia, cold and clammy skin, toxic leukoencephalopathy, delayed post-hypoxic leukoencephalopathy and sometimes bradycardia and hypotension. Severe overdose may result in apnea, circulatory collapse, cardiac arrest pulmonary edema and death.

ASA

The ingestion of very large amounts of this medication may, in addition, result in acute salicylate intoxication.

Acute ASA poisoning is characterized by hyperpnea; hypercapnia; acid-base disturbances with the development of metabolic acidosis, especially in children; and gastrointestinal irritation with vomiting and abdominal pain. In addition, acetone odour in breath, tinnitus, sweating, hyperthermia, dehydration, hypoprothrombinemia with spontaneous bleeding, restlessness, delirium, convulsions and coma may occur.

Treatment:

Primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The opioid antagonist naloxone is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to opioids, including oxycodone. Therefore, an appropriate dose of this antagonist should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Since the duration of action of

oxycodone may exceed that of the antagonist, the patient should be kept under continued surveillance and repeat doses of the antagonist should be administered as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression.

Oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Gastric emptying by emesis or lavage may be useful in removing unabsorbed drug.

Special features due to salicylate (ASA) overdosage:

1) The prominent features of salicylate intoxication are metabolic acidosis and electrolyte disturbance, and these require evaluation and correction. Sodium bicarbonate 400 mg (5 mEq)/kg as a 1% solution in 5% dextrose water is not only effective in correcting acidosis, but effectively and rapidly accelerates salicylate excretion by the kidneys. The administration of sodium bicarbonate must be carefully monitored with frequent blood pH and plasma CO_2 content determinations, as large amounts of sodium bicarbonate may result in severe alkalosis, particularly in children. THAM, an osmotic alkalinizing diuretic, also greatly increases the excretion of salicylate. This is given as a 0.3 molar solution at a rate not exceeding 5 mL/kg/hour. Potassium deficiency may occur and should be corrected.
2) Treat hyperthermia and dehydration with ice packs and i.v. fluids.
3) Treat hypoprothrombinemia with vitamin K_1 50 mg given daily i.v.
4) Hemodialysis, peritoneal dialysis or exchange transfusion are indicated in very severe salicylate intoxication.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Oral	Tablets, oxycodone hydrochloride 5 mg and acetylsalicylic acid 325 mg	Colloidal silicon dioxide, FD&C yellow #5 aluminum lake, lactose, microcrystalline cellulose, sodium starch glycolate and stearic acid.

TEVA-OXYCODAN is supplied as yellow, scored tablet and available in bottles of 100 and 500 tablets

7 WARNINGS AND PRECAUTIONS

General

Patients should be instructed not to give TEVA-OXYCODAN (oxycodone hydrochloride and ASA) tablets to anyone other than the patient for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death. TEVA-OXYCODAN should be stored securely to avoid theft or misuse.

TEVA-OXYCODAN should only be prescribed by persons knowledgeable in the continuous administration of potent opioids, in the management of patients receiving potent opioids for the treatment of pain, and in the detection and management of respiratory depression, including the use of opioid antagonists.

This medication should not be administered to infants or children.

Patients should be cautioned not to consume alcohol while taking TEVA-OXYCODAN as it may increase the chance of experiencing serious adverse events, including death.

Reye's syndrome: A possible association between Reye's syndrome and the use of salicylates has been suggested but not established. Reye's syndrome has also occurred in many patients not exposed to salicylates. However, caution is advised when prescribing salicylate-containing medications for young adults with influenza or chickenpox.

Abuse and Misuse

Like all opioids, TEVA-OXYCODAN is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, TEVA-OXYCODAN should be prescribed and handled with caution.

Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids. All patients receiving opioids should be routinely monitored for signs of misuse and abuse.
Opioids, such as TEVA-OXYCODAN, should be used with particular care in patients with a history of alcohol and illicit/prescription drug abuse and other mental health disorders including, but not limited to, major depression and anxiety. However, concerns about abuse, addiction, and diversion should not prevent the proper management of pain.

TEVA-OXYCODAN is intended for oral use only. The tablets should be swallowed whole, and not chewed or crushed. Abuse of oral dosage forms can be expected to result in serious adverse events, including death.

Cardiovascular

TEVA-OXYCODAN (Oxycodone hydrochloride and ASA) administration may result in severe hypotension in patients whose ability to maintain adequate blood pressure is compromised by reduced blood volume, or concurrent administration of drugs such as phenothiazines and other tranquilizers, sedative/hypnotics, tricyclic antidepressants or general anesthetics. These patients should be monitored for signs of hypotension after initiating or titrating the dose of TEVA-OXYCODAN.

The use of TEVA-OXYCODAN in patients with circulatory shock should be avoided as it may cause vasodilation that can further reduce cardiac output and blood pressure.

Dependence/Tolerance

As with other opioids, tolerance and physical dependence may develop upon repeated administration of TEVA-OXYCODAN and there is a potential for development of psychological dependence.

Physical dependence and tolerance reflect the neuroadaptation of the opioid receptors to chronic exposure to an opioid, and are separate and distinct from abuse and addiction. Tolerance, as well as physical dependence, may develop upon repeated administration of opioids, and are not by themselves evidence of an addictive disorder or abuse.

Patients on prolonged therapy should be tapered gradually from the drug if it is no longer required for pain control. Withdrawal symptoms may occur following abrupt discontinuation of therapy or upon administration of an opioid antagonist. Some of the symptoms that may be associated with abrupt withdrawal of an opioid analgesic include body aches, diarrhea, gooseflesh, loss of appetite, nausea, nervousness or restlessness, anxiety, runny nose, sneezing, tremors or shivering, stomach cramps, tachycardia, trouble with sleeping, unusual increase in sweating, palpitations, unexplained fever, weakness and yawning (see 8 ADVERSE REACTIONS and 6 DOSAGE AND ADMINISTRATION, Adjustment or Reduction of Dosage**).**

Neonatal Opioid Withdrawal Syndrome (NOWS): Prolonged maternal use of opioids during pregnancy can result in withdrawal signs in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening.

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.

Use of TEVA-OXYCODAN is contraindicated in pregnant women (see 2 CONTRAINDICATIONS).

Use in Drug and Alcohol Addiction

TEVA-OXYCODAN 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. Patients with a history of addiction to drugs or alcohol may be at higher risk of becoming addicted to TEVA-OXYCODAN; extreme caution and awareness is warranted to mitigate the risk.

Driving and Operating Machinery

TEVA-OXYCODAN may impair the mental and/or physical abilities needed for certain potentially hazardous activities such as driving a car or operating machinery. Patients should be cautioned accordingly. Patients should also be cautioned about the combined effects of TEVA-OXYCODAN (oxycodone hydrochloride and ASA) with other CNS depressants, including other opioids, phenothiazine, sedative/hypnotics and alcohol.

Endocrine

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.

Gastrointestinal

TEVA-OXYCODAN (Oxycodone hydrochloride and ASA) and other morphine-like opioids have been shown to decrease bowel motility. TEVA-OXYCODAN (Oxycodone hydrochloride and ASA) may obscure the diagnosis or clinical course of patients with acute abdominal conditions (see 2 CONTRAINDICATIONS).

Hematologic

Because of its ASA content, TEVA-OXYCODAN should be used with caution in patients with a history of bleeding tendencies, in patients on anticoagulant therapy and in patients with underlying hemostatic defects and with extreme caution in patients with peptic ulceration.

Thrombocytopenia has been reported in association with the use of ASA, and may be the underlying cause of the increased risk of bleeding, intracerebral hemorrhage and hemorrhagic

stroke observed in patients treated with ASA as an antiplatelet therapy.

ASA administered pre-operatively may prolong the bleeding time.

Hepatic/Biliary/Pancreatic

Caution should be exercised when prescribing TEVA-OXYCODAN to patients with any degree of hepatic impairment.

Immune

Therapeutic doses of ASA can cause anaphylactic shock and other severe allergic reactions. It should be ascertained if the patient is allergic to ASA, although a specific history of allergy may be lacking.

Precautions should be taken when administering salicylates to persons with known allergies. Hypersensitivity to ASA is particularly likely in patients with nasal polyps and relatively common in those with asthma.

Neurologic

Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol): TEVA-OXYCODAN should be used with caution and in a reduced dosage during concomitant administration of other opioid analgesics, general anesthetics, phenothiazines and other tranquilizers, sedatives, hypnotics, tricyclic antidepressants, antipsychotics, antihistamines, benzodiazepines, gabapentinoids, baclofen, centrally active anti-emetics, and other CNS depressants. Respiratory depression, hypotension and profound sedation, coma or death may result. Respiratory depression, hypotension and profound sedation, coma or death may result.

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 9 DRUG INTERACTIONS). 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 TEVA-OXYCODAN is 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 9 DRUG INTERACTIONS).

TEVA-OXYCODAN should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects, including death (see 2 CONTRAINDICATIONS and 8 ADVERSE REACTIONS, Sedation, and 9 DRUG INTERACTIONS**).**

Severe pain antagonizes the subjective and respiratory depressant actions of opioid analgesics. Should pain suddenly subside, these effects may rapidly become manifest.

Serotonin Toxicity / Serotonin Syndrome:
Serotonin toxicity, also known as serotonin syndrome, is a potentially life-threatening condition and has been reported with oxycodone, including TEVA-OXYCODAN, particularly during combined use with other serotonergic drugs (See 9 DRUG INTERACTIONS). Serotonin toxicity is characterised by neuromuscular excitation, autonomic stimulation (e.g.,tachycardia, flushing) and altered mental state (e.g., anxiety, agitation, hypomania). In accordance with the Hunter Criteria, serotonin toxicity diagnosis is likely when, in the presence of at least one serotonergic agent, one of the following is observed:

- Spontaneous clonus
- Inducible clonus or ocular clonus with agitation or diaphoresis
- Tremor and hyperreflexia
- Hypertonia and body temperature >38°C and ocular clonus or inducible clonus.

If concomitant treatment with TEVA-OXYCODAN and other serotonergic agents is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases (see 9 DRUG INTERACTIONS). If serotonin toxicity is suspected, discontinuation of the serotonergic agents should be considered.

Opioid induced hyperalgesia: Opioid induced hyperalgesia (OIH) is a paradoxical response to an opioid in which there is an increase in pain perception despite stable or increased opioid exposure. It differs from tolerance, in which higher opioid doses are required to achieve the same analgesic effect or treat recurring pain. Clinically, OIH may be associated with high opioid doses, long term opioid treatment, and intra-operative opioid use. OIH may manifest as an unexplained increase in pain, more diffuse pain than pre-existing, or as pain from ordinary (i.e. non-painful stimuli (allodynia), in the absence of disease progression. When OIH is suspected, the dose of opioid should be reduced or tapered off, if possible. It is reasonable to consider opioid rotation, or the use of a non-opioid strategy for pain control. There is currently no well-established treatment for OIH.

Head Injury: The respiratory depressant effects of TEVA-OXYCODAN (oxycodone hydrochloride and ASA), and the capacity to elevate cerebrospinal fluid pressure, may be greatly increased in the presence of an already elevated intracranial pressure produced by trauma. Also, TEVA-OXYCODAN (oxycodone hydrochloride and ASA) may produce confusion, miosis, vomiting and other side effects which obscure the clinical course of patients with head injury. In such patients, TEVA-OXYCODAN (oxycodone hydrochloride and ASA) must be used with extreme caution and only if it is judged essential (see 2 CONTRAINDICATIONS).

Headache: Because headache often involves a significant psychological component, an opioid analgesic should only be employed for the treatment of headache when no other treatment is effective, in order to minimize the risk of psychological and physical dependence.

Peri-operative Considerations

TEVA-OXYCODAN is not indicated for pre-emptive analgesia (administration pre-operatively for the management of post-operative pain).

In the case of planned chordotomy or other pain-relieving operations, patients should not be treated with TEVA-OXYCODAN for at least 24 hours before the operation and TEVA-OXYCODAN should not be used in the immediate post-operative period.

Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. Thereafter, if TEVA-OXYCODAN is to be continued after the patient recovers from the post-operative period, a new dosage should be administered in accordance with the changed need for pain relief. The risk of withdrawal in opioid-tolerant patients should be addressed as clinically indicated.

The administration of analgesics in the peri-operative period should be managed by healthcare providers with adequate training and experience (e.g., by an anesthesiologist).

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

TEVA-OXYCODAN should not be used in the early post-operative period (12 to 24 hours post-surgery) unless the patient is ambulatory and gastrointestinal function is normal.

Renal

Caution should be exercised when prescribing TEVA-OXYCODAN to patients with any degree of renal impairment.

Reproductive Health: Female and Male Potential

Long-term use of opioids may be associated with decreased sex hormone levels and symptoms such as low libido, erectile dysfunction, or infertility (**see** 8 ADVERSE REACTIONS, Post- Marketing Experience).

Respiratory

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. TEVA-OXYCODAN (oxycodone hydrochloride and ASA) should be used with extreme caution in patients with substantially decreased respiratory reserve, pre-existing respiratory depression, hypoxia or hypercapnia (see 2 CONTRAINDICATIONS).

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of TEVA-OXYCODAN, the risk is greatest during the initiation of therapy or following a dose increase. Patients should be closely monitored for respiratory depression when initiating therapy with TEVA-OXYCODAN and following dose increases.

Life-threatening respiratory depression is more likely to occur in the elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients.

To reduce the risk of respiratory depression, proper dosing and titration of TEVA-OXYCODAN are essential. Over estimating the TEVA-OXYCODAN dose when converting patients from another opioid product can result in a fatal overdose with the first dose. In these patients, the use of non-opioid analgesics should be considered, if feasible (see 7 WARNINGS AND PRECAUTIONS, Special Populations, Special Risk Groups, and 6 DOSAGE AND ADMINISTRATION).

Patients with Chronic Pulmonary Disease: Monitor patients with significant chronic obstructive pulmonary disease or cor pulmonale, and patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or preexisting respiratory depression for respiratory depression, particularly when initiating therapy and titrating with TEVA-OXYCODAN, as in these patients, even usual therapeutic doses of TEVA-OXYCODAN may decrease respiratory drive to the point of apnea. In these patients, use of alternative non-opioid analgesics should be considered, if possible. The use of TEVA-OXYCODAN is contraindicated in Patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus (see 2 CONTRAINDICATIONS).

Sleep related breathing disorder: Opioids can cause sleep-related breathing disorders such as

sleep apnea syndromes (including central sleep apnea [CSA]) and hypoxemia (including sleep related hypoxemia). Opioid use increases the risk of CSA in a dose-dependent fashion. Evaluate patients on an ongoing basis for the onset of a new sleep apnea, or a worsening of an existing sleep apnea. In patients who present with CSA, consider decreasing the total opioid dosage or stopping the opioid treatment if appropriate, using best practices for tapering of opioids (see 7 WARNINGS AND PRECAUTIONS, Dependence/Tolerance and 4.2 Recommended Dose and Dosage Adjustment, Adjustment or Reduction of Dosage).

Skin

Serious Skin Reactions: Use of some NSAIDs, such as TEVA-OXYCODAN, have been associated with rare post-market cases of serious, fatal or otherwise life-threatening skin reactions, including:

- drug reaction with eosinophilia and systemic symptoms (DRESS)
- Stevens-Johnson syndrome,
- toxic epidermal necrolysis,
- exfoliative dermatitis and
- erythema multiforme.

Patients appear to be at higher risk for these events early in the course of therapy, with the onset of cases usually occurring within the first month of treatment. These reactions may be reversible if the causative agent is discontinued and appropriate treatment instituted. Patients should be advised that they should discontinue their NSAID at the first appearance of a skin rash, mucosal lesions or any other sign of hypersensitivity, and contact their physician immediately for assessment and advice, including which therapies to discontinue.

DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection, and eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident.

7.1 Special Populations

7.1.1 Pregnant Women

Studies in pregnant women have not been conducted for oxycodone. TEVA-OXYCODAN crosses the placental barrier and is contraindicated in pregnant women (see 2 CONTRAINDICATIONS).

Prolonged maternal use of opioids during pregnancy can result in withdrawal signs in the neonate. Neonatal opioid withdrawal syndrome (NOWS), unlike opioid withdrawal syndrome in

adults, can be life-threatening (see 7 WARNINGS AND PRECAUTIONS, Neonatal Opioid Withdrawal Syndrome (NOWS), 8 ADVERSE REACTIONS, Post-Marketing Experience).

Pregnant women using opioids should not discontinue their medication abruptly as this can cause pregnancy complication such as miscarriage or still-birth. Tapering should be slow and under medical supervision to avoid serious adverse events to the fetus.

Due to the NSAID component of TEVA-OXYCODAN, during the third trimester of pregnancy there are also risks of premature closure of the ductus arteriosus and the potential to prolong parturition. During the first and second trimesters of pregnancy, particularly from the middle to end of the second trimester of pregnancy (onset at approximately 20 weeks) there is a risk of possible fetal renal dysfunction leading to oligohydramnios and, in some cases. neonatal renal impairment or failure.

Published studies and postmarketing reports describe maternal NSAID use at approximately 20 weeks gestation or later in pregnancy associated with fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment or failure. NSAIDs were shown to cause significant reduction in fetal urine production prior to reduction of amniotic fluid volume. There have also been a limited number of case reports of maternal NSAID use and neonatal renal dysfunction and renal impairment without oligohydramnios, some of which were irreversible, even after treatment discontinuation.

These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Complications of prolonged oligohydramnios may for example, include limb contractures and delayed lung maturation. In some postmarketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If after careful consideration of the benefit-risk, TEVA-OXYCODAN treatment is considered necessary to be administered anywhere from the middle (onset at approximately 20 weeks) to the end of the second trimester of pregnancy, the use should be limited to the lowest effective dose and shortest duration possible. It is also recommended that ultrasound monitoring of amniotic fluid be considered if TEVA-OXYCODAN treatment extends beyond 48 hours and that TEVA-OXYCODAN treatment be discontinued if oligohydramnios occurs, followed by appropriate medical follow up.

Inhibition of prostaglandin synthesis may adversely affect pregnancy and/or embryo-fetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation after use of a prostaglandin synthesis inhibitor in early pregnancy.

In animals, administration of a prostaglandin synthesis inhibitor has been shown to result in increased pre- and post-implantation loss and embryo-fetal lethality. In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenesis period.

Therapeutic doses of ASA in pregnant women close to term may cause bleeding in mother, fetus, or neonate. During the last 6 months of pregnancy, regular use of ASA in high doses may prolong pregnancy and delivery.

7.1.2 Breast-feeding

Since opioids can cross the placental barrier and are excreted in breast milk, TEVA-OXYCODAN is contraindicated in nursing women and during labour and delivery. Life-threatening respiratory depression can occur in the infant if opioids are administered to the mother. Naloxone, a drug that counters the effects of opiates, should be readily available if TEVA-OXYCODAN is used in this population.

7.1.3 Pediatrics (< 18 years of age):

The safety and efficacy of TEVA-OXYCODAN have not been studied in the pediatric population. Therefore, use of TEVA-OXYCODAN is not recommended in patients under 18 years of age.

7.1.4 Geriatrics (> 65 years of age):

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range and titrate slowly, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy (see 4 DOSAGE AND ADMINISTRATION and 10 CLINICAL PHARMACOLOGY, Special Populations and Conditions, Geriatrics).

8 ADVERSE REACTIONS

8.1 Adverse Drug Reaction Overview

Adverse effects of TEVA-OXYCODAN (oxycodone hydrochloride and ASA) tablets are similar to those of other opioid analgesics, and represent an extension of pharmacological effects of the drug class. The major hazards of opioids include respiratory and central nervous system depression and to a lesser degree, circulatory depression, respiratory arrest, shock and cardiac arrest.

The most frequently observed adverse effects of TEVA-OXYCODAN are light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in non-ambulatory patients, and some of these adverse reactions may be alleviated if the patient lies down.

Other adverse reactions include euphoria, dysphoria, constipation and pruritus.

Sedation:

Sedation is a common side effect of opioid analgesics, especially in opioid naïve individuals. Sedation may also occur partly because patients often recuperate from prolonged fatigue after the relief of persistent pain. Most patients develop tolerance to the sedative effects of opioids within three to five days and, if the sedation is not severe, will not require any treatment except reassurance. If excessive sedation persists beyond a few days, the dose of the opioid should be reduced and alternate causes investigated. Some of these are: concurrent CNS depressant medication, hepatic or renal dysfunction, brain metastases, hypercalcemia and respiratory failure. If it is necessary to reduce the dose, it can be carefully increased again after three or four days if it is obvious that the pain is not being well controlled. Dizziness and unsteadiness may be caused by postural hypotension, particularly in elderly or debilitated patients, and may be alleviated if the patient lies down.

Nausea and Vomiting:

Nausea is a common side effect on initiation of therapy with opioid analgesics and is thought to occur by activation of the chemoreceptor trigger zone, stimulation of the vestibular apparatus and through delayed gastric emptying. The prevalence of nausea declines following continued treatment with opioid analgesics. When instituting therapy with an opioid for chronic pain, the routine prescription of an antiemetic should be considered. In the cancer patient, investigation of nausea should include such causes as constipation, bowel obstruction, uremia, hypercalcemia, hepatomegaly, tumor invasion of celiac plexus and concurrent use of drugs with emetogenic properties. Persistent nausea which does not respond to dosage reduction may be caused by opioid-induced gastric stasis and may be accompanied by other symptoms including anorexia, early satiety, vomiting and abdominal fullness. These symptoms respond to chronic treatment with gastrointestinal prokinetic agents.

Constipation:

Practically all patients become constipated while taking opioids on a persistent basis. In some patients, particularly the elderly or bedridden, fecal impaction may result. It is essential to caution the patients in this regard and to institute an appropriate regimen of bowel management at the start of prolonged opioid therapy. Stimulant laxatives, stool softeners, and other appropriate measures should be used as required. As fecal impaction may present as overflow diarrhea, the presence of constipation should be excluded in patients on opioid therapy prior to initiating treatment for diarrhea.

8.5 Post-Market Adverse Reactions

Androgen deficiency: 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. Patients presenting with symptoms of androgen deficiency should undergo laboratory evaluation.

There have also been reported post-marketing cases of Neonatal Opioid Withdrawal Syndrome (NOWS) in patients treated with oxycodone (see 7 WARNINGS AND PRECAUTIONS).

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions

Serious Drug Interactions

- Risks from concomitant use of opioids and benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma and death (see 7 WARNINGS AND PRECAUTIONS, Neurologic)
- Reserve concomitant prescribing of TEVA-OXYCODAN and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate
- Consider dose reduction of CNS depressants in situations of concomitant prescribing
- Follow patients for signs and symptoms of respiratory depression and sedation
- MAO inhibitors intensify the effects of opioid drugs which can cause anxiety, confusion and decreased respiration. TEVA-OXYCODAN is contraindicated in patients receiving MAO inhibitors or who have used them within the previous 14 days

9.2 Drug Interactions Overview

Interaction with Benzodiazepines and Other Central Nervous System (CNS) Depressants:

Due to additive pharmacologic effect, the concomitant use of benzodiazepines or other CNS depressants (e.g. other opioids, sedatives, gabapentinoids such as pregabalin, baclofen, hypNotics, antidepressants, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, phenothiazines, neuroleptics, antihistamines, antiemetics and alcohol) and beta-blockers, increases the risk of respiratory depression, profound sedation, coma, and death. 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 7 WARNINGS AND PRECAUTIONS, Neurologic, Interactions with CNS Depressants (including benzodiazepines and alcohol)). TEVA-OXYCODAN should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects.

9.3 Drug-Behavioural Interactions

Alcohol: Increased damage to gastrointestinal mucosa and prolonged bleeding time due to additive effects of acetylsalicylic acid and alcohol. The concomitant use of alcohol should be avoided and patients having 3 or more alcoholic drinks per day should consult their physician before use. (see 7 WARNINGS AND PRECAUTIONS, General).

9.4 Drug-Drug Interactions

Drugs Metabolized by Cytochrome P450 Isozymes
Oxycodone is metabolized in part by cytochrome P450 2D6 and cytochrome P450 3A4 pathways. The activities of these metabolic pathways may be inhibited or induced by various co- administered drugs or dietary elements. Oxycodone doses may need to be adjusted.

Inhibitors of CYP3A4: Since the CYP3A4 isoenzyme plays a major role in the metabolism of TEVA-OXYCODAN, drugs that inhibit CYP3A4 activity, such as macrolide antibiotics (e.g., clarithromycin), azole-antifungal agents (e.g., ketoconazole), and protease inhibitors (e.g., ritonavir) and grapefruit juice may cause decreased clearance of oxycodone which could lead to an increase in oxycodone plasma concentrations. A published study showed that the co-administration of the antifungal drug, voriconazole, increased oxycodone AUC and C_{max} by 3.6- and 1.7-fold, respectively. Although clinical studies have not been conducted with other CYP3A4 inhibitors, the expected clinical results would be increased or prolonged opioid effects. If co-administration with TEVA-OXYCODAN is necessary, caution is advised when initiating therapy with, currently taking, or discontinuing CYP450 inhibitors. Evaluate these patients at frequent intervals and consider dose adjustments until stable drug effects are achieved.

Inducers of CYP3A4: CYP450 inducers, such as rifampin, carbamazepine, phenytoin, and St. John's wort, may induce the metabolism of oxycodone and, therefore, may cause increased clearance of the drug which could lead to a decrease in oxycodone plasma concentrations, lack of efficacy or possibly the development of an abstinence syndrome in a patient who had developed physical dependence to oxycodone. A published study showed that the co-administration of rifampin, a drug metabolizing enzyme inducer, decreased oxycodone (oral) AUC and C_{max} by 86% and 63% respectively. If co-administration with TEVA-OXYCODAN is necessary, caution is advised when initiating therapy with, currently taking or discontinuing CYP3A4 inducers. Evaluate these patients at frequent intervals and consider dose adjustments until stable drug effects are achieved.

Inhibitors of CYP2D6: Oxycodone is metabolized in part to oxymorphone via cytochrome CYP2D6. 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 been shown to be of clinical significance during oxycodone treatment.

Administration with Mixed Activity Agonist/Antagonist Opioids: Mixed agonist/antagonist opioid analgesics (i.e., pentazocine, nalbuphine, butorphanol, and buprenorphine) 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.

Anticholinergics: Concomitant administration of oxycodone with anticholinergics or medications with anticholinergic activity (e.g., tricyclic antidepressants, antihistamines, antipsychotics, muscle relaxants, anti-Parkinson drugs) may result in increased anticholinergic adverse effects.

MAO Inhibitors: MAO Inhibitors intensify the effects of opioid drugs which can cause anxiety, confusion and decreased respiration. TEVA-OXYCODAN is contraindicated in patients receiving MAO Inhibitors or who have used them within the previous 14 days (see CONTRAINDICATIONS).

Serotonergic Agents: Coadministration of oxycodone with a serotonergic agent, such as a Selective Serotonin Re-uptake Inhibitor or a Serotonin Norepinephrine Re-uptake Inhibitor, may increase the risk of serotonin syndrome, a potentially life-threatening condition (see 7. WARNINGS AND PRECAUTIONS, Neurologic).

Interaction with anticoagulants and thrombolytics/ other antiplatelet drugs:
ASA should be used with caution with other products that have anticoagulation or antiplatelet effects, as these effects may be potentiated. Bleeding may result from inhibition of prothrombin formation in the liver and displacement of anticoagulants from plasma protein binding sites.

Interaction with corticosteroids:
In patients receiving concomitant corticosteroids and chronic use of ASA, withdrawal of corticosteroids may result in salicylism because corticosteroids enhance renal clearance of salicylates and their withdrawal is followed by return to normal rates of renal clearance.

Interaction with hypoglycemic (antidiabetic) agents and insulin: Large doses of salicylates have a hypoglycemic action and may enhance the effect of oral hypoglycemic agents. Diabetics receiving concurrent salicylate and hypoglycemic therapy should be monitored closely, in certain cases, dose reduction may be necessary.

Interaction with Methotrexate: Salicylates may retard the elimination of methotrexate by decreasing renal clearance of methotrexate, displacing methotrexate from protein binding sites, and thereby increasing its hematological toxicity.

Interaction with Uricosuric Agents: ASA competes with these agents for protein binding sites thereby reducing their effectiveness in the treatment of conditions such as gout.

Interaction with other NSAIDs:
May increase the risk of peptic ulceration and gastrointestinal bleeding due to a synergistic

effect.

9.6 Drug-Laboratory Test Interactions

ASA may interfere with the following laboratory determinations in blood: serum amylase, fasting blood glucose, cholesterol, protein, aspartate aminotransferase (AST), uric acid, triiodothyronine , prothrombin time and bleeding time. ASA may interfere with the following laboratory determinations in urine: glucose, 5-hydroxyindoleactic acid, Gerhardt ketone, vanillylmandelic acid (VMA), uric acid and diacetic acid.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

The principal ingredient, oxycodone, is a semisynthetic opioid analgesic with multiple actions qualitatively similar to those of morphine; the most prominent of these involve the central nervous system and organs composed of smooth muscle. The principal actions of therapeutic value of the oxycodone in TEVA-OXYCODAN are analgesia and sedation.

Oxycodone is similar to codeine and methadone in that it retains at least one half of its analgesic activity when administered orally. It has been suggested that less rapid biotransformation in the liver may be due to the protective effect of a methoxy group in the 3-position, the site of glucuronide conjugation in morphine.

TEVA-OXYCODAN also contains the non-opioid, anti-inflammatory and antipyretic analgesic, ASA.

ASA is a salicylate that binds to the cyclooxygenase enzyme leading to a reduction in prostaglandin activity.

10.2 Pharmacodynamics

Central Nervous System:

TEVA-OXYCODAN (oxycodone hydrochloride and ASA) produces respiratory depression by direct action on brain stem respiratory centres. The respiratory depression involves both a reduction in the responsiveness of the brain stem centres to increases in CO_2 tension and to electrical stimulation.

TEVA-OXYCODAN (oxycodone hydrochloride and ASA) depresses the cough reflex by direct effect on the cough centre in the medulla. Antitussive effects may occur with doses lower than those usually required for analgesia.

TEVA-OXYCODAN (oxycodone hydrochloride and ASA) 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 the setting of oxycodone overdose.

Gastrointestinal Tract and Other Smooth Muscle:

TEVA-OXYCODAN (oxycodone hydrochloride and ASA) 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 may be increased to the point of spasm resulting in constipation. Other opioid-induced effects may include a reduction in gastric, biliary and poancreatic secretions, spasm of the sphincter of Oddi, and transient elevations in serum amylase.

Cardiovascular System:

TEVA-OXYCODAN (oxycodone hydrochloride and ASA) may produce release of histamine with or without associated peripheral vasodilation. Manifestations of histamine release and/or peripheral vasodilatation may include pruritus, flushing, red eyes, hyperhidrosis and/or orthostatic hypotension.

Endocrine System:

Opioids may influence the hypothalamic-pituitary-adrenal or -gonadal axes. Some changes that can be seen include an increase in serum prolactin, and decreases in plasma cortisol and testosterone. Clinical signs and symptoms may be manifest from these hormonal changes.

Immune System:

In vitro and animal studies indicate that opioids have a variety of effects on immune functions, depending on the context in which they are used. The clinical significance of these findings is unknown.

10.3 Pharmacokinetics

Oxycodone:

Absorption:
About 60% to 87% of an oral dose of oxycodone reaches the central compartment in comparison to a parenteral dose. The high oral bioavailability is due to low pre-systemic and/or first-pass metabolism.

Distribution:
Following intravenous administration, the steady-state volume of distribution (V_{SS}) for oxycodone was 2.6 L/kg. Oxycodone binding to plasma protein at 37°C and a pH of 7.4 was about 45%. Once absorbed, oxycodone is distributed to skeletal muscle, liver, intestinal tract, lungs, spleen, and brain. Oxycodone has been found in breast milk.

Metabolism:
Oxycodone is extensively metabolized by multiple metabolic pathways to produce noroxycodone, oxymorphone and noroxymorphone, which are subsequently glucuronidated. Noroxycodone and noroxymorphone are the major circulating metabolites. CYP3A mediated N- demethylation to noroxycodone is the primary metabolic pathway of oxycodone with a lower contribution from CYP2D6 mediated O-demethylation to oxymorphone. Therefore, the formation of these and related metabolites can, in theory, be affected by other drugs (see 9 DRUG INTERACTIONS, Drug-Drug Interactions).

Noroxycodone exhibits very weak anti-nociceptive potency compared to oxycodone, however, it undergoes further oxidation to produce noroxymorphone, which is active at opioid receptors.
Although noroxymorphone is an active metabolite and is present at relatively high concentrations in circulation, it does not appear to cross the blood-brain barrier to a significant extent.

Oxymorphone has been shown to be active and possessing analgesic activity but its contribution to analgesia following oxycodone administration is thought to be clinically insignificant. Other metabolites (α- and β-oxycodol, noroxycodol and oxymorphol) may be present at very low concentrations and demonstrate limited penetration in to the brain as compared to oxycodone.
The enzymes responsible for keto-reduction and glucuronidation pathways in oxycodone metabolism have not been established.

Oxycodone has an elimination half-life of approximately 3 hours.

Excretion:
Oxycodone and its metabolites are excreted in both urine and feces. The amounts measured in the urine have been reported as follows: free and conjugated oxycodone 8.9%, free noroxycodone 23%, free oxymorphone less than 1%, conjugated oxymorphone 10%, free and conjugated noroxymorphone 14%, reduced free and conjugated metabolites up to 18%. The total plasma clearance was approximately 1.4 L/min in adults.

Acetylsalicylic acid (ASA)

The systemic availability of ASA after an oral dose is highly dependent on the dosage form, the presence of food, the gastric emptying time, gastric pH, antacids, buffering agents, and particle size. These factors affect not necessarily the extent of absorption of total salicylates but more the stability of ASA prior to absorption.

During the absorption process and after absorption, ASA is mainly hydrolyzed to salicylic acid and distributed to all body tissues and fluids, including fetal tissues, breast milk, and the central

nervous system (CNS). Highest concentrations are found in plasma, liver, renal cortex, heart, and lung. In plasma, about 50% - 80% of the salicylic acid and its metabolites are loosely bound to plasma proteins.

The clearance of total salicylates is subject to saturable kinetics; however, first-order elimination kinetics are still a good approximation for doses up to 650 mg. The plasma half-life for ASA is about 12 minutes and for salicylic acid and/or total salicylates is about 3 hours.

The elimination of therapeutic doses is through the kidneys either as salicylic acid or other biotransformation products. The renal clearance is greatly augmented by an alkaline urine as is produced by concurrent administration of sodium bicarbonate or potassium citrate.

The biotransformation of ASA occurs primarily in the hepatocytes. The major metabolites are salicyluric acid (75%), the phenolic and acyl glucuronides of salicylate (15%), and gentisic and gentisuric acid (1%).

Special Populations and Conditions

- **Pediatrics:** Individuals under 18 years of age should not take TEVA-OXYCODAN tablets.
- **Geriatrics:** See 7 WARNINGS AND PRECAUTIONS.
- **Hepatic Insufficiency:** See 7 WARNINGS AND PRECAUTIONS.
- **Renal Insufficiency:** See 7 WARNINGS AND PRECAUTIONS.

11 STORAGE, STABILITY AND DISPOSAL

Store at room temperature (15 to 30°C).

TEVA-OXYCODAN should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended. Unused or expired TEVA-OXYCODAN should be properly disposed of as soon as it is no longer needed to prevent accidental exposure to others, including children or pets. If temporary storage is required before disposal, a sealed child-proof container, such as a biohazard waste container or a lockable medication box could be obtained from a pharmacy.

TEVA-OXYCODAN should be kept in a safe place, out of the sight and reach of children before, during and after use. TEVA-OXYCODAN should not be used in front of children, since they may copy these actions.

12 SPECIAL HANDLING INSTRUCTIONS

Not applicable.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

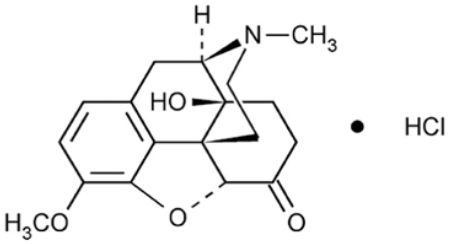
Drug Substance

Proper name: Oxycodone hydrochloride

Chemical name: Oxycodone is 14-hydroxydihydrocodeinone

Molecular formula and molecular mass: $C_{18}H_{21}NO_4$ HCl and 351.82

Structural formula:



Physicochemical Properties:

Oxycodone is a white odorless crystalline powder which is derived from the opium alkaloid, thebaine.

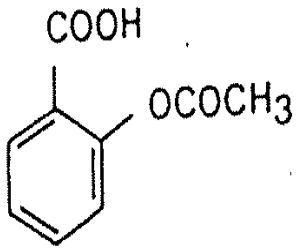
Drug Substance Reference: Novasen PM dated Oct. 9, 2012

Proper name: Acetylsalicylic Acid

Chemical name: 2-(Acetyloxy) benzoic acid; salicylic acid acetate

Molecular formula and molecular mass: $C_9H_8O_4$ and 180.16

Structural formula:



Physicochemical Properties:

Aspirin occurs as white crystals, which are usually tubular or needle-like or as a white, crystalline powder. The drug may have a faint odour, has a pka of 3.5 and is slightly soluble in water and freely soluble in alcohol. Each gram of aspirin contains approximately 760 mg of salicylate.

14 CLINICAL TRIALS

Clinical trial information for this product is not available.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

Non-clinical information for this product is not available.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[N] TEVA-OXYCODAN

oxycodone hydrocholoride and acetylsalicylic acid tablets

Read this carefully before you start taking **TEVA-OXYCODAN** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **TEVA-OXYCODAN**.

Serious Warnings and Precautions

- Even if you take TEVA-OXYCODAN as prescribed you are at a risk for opioid addiction, abuse and misuse. This can lead to overdose and death. To understand your risk of opioid addition, abuse, and misuse you should speak to your healthcare professional.
- When you take TEVA-OXYCODAN it must be swallowed whole. Do not cut, break, crush, chew, dissolve the tablet. This can be dangerous and can lead to death or seriously harm you.
- Life threatening breathing problems can happen while taking TEVA-OXYCODAN, especially if not taken as directed. This is less likely to happen if you take it as prescribed by your healthcare professional. Babies are at risk of life-threatening breathing problems if their mothers take opioids while pregnant or nursing.
- Never give anyone your TEVA-OXYCODAN. They could die from taking it. If a person has not been prescribed TEVA-OXYCODAN, taking even one dose can cause a fatal overdose. This is especially true for children.
- **DO NOT** take TEVA-OXYCODAN if you are pregnant. Medicines like TEVA-OXYCODAN may cause harm to you and your baby. If your healthcare professional feels it is necessary for you to take TEVA-OXYCODAN during pregnancy, your healthcare professional will need to closely monitor your health and that of your baby (including your amniotic fluid levels) if they prescribe TEVA-OXYCODAN during this time.
- If you took TEVA-OXYCODAN while you were pregnant, whether for short or long periods of time or in small or large doses, your baby can suffer life-threatening withdrawal symptoms after birth. This can occur in the days after birth and for up to 4 weeks after delivery. If your baby has any of the following symptoms:
    - has changes in their breathing (such as weak, difficult or fast breathing)

- is unusually difficult to comfort
- has tremors (shakiness)
- has increased stools, sneezing, yawning, vomiting, or fever

Seek immediate medical help for your baby.

- Taking TEVA-OXYCODAN 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.

What is TEVA-OXYCODAN used for?

TEVA-OXYCODAN is used in adults to relieve mild to moderately severe pain, including conditions associated with fever and/or inflammation.

It is NOT used "as-needed" to treat pain that you only have once in a while.

How does TEVA-OXYCODAN work?

TEVA-OXYCODAN contains 2 drugs that work together.

- Oxycodone is a painkiller belonging to the class of medicines known as opioids. It relieves pain by acting on specific nerve cells of the spinal cord and brain.
- Acetylsalicylic acid (ASA) belongs to the group of medications called analgesics (pain relievers), antipyretics (fever reducers), and antiinflammatories (inflammation reducers) It reduces the amount of prostaglandin made in the body and this lowers pain, fever and swelling.

What are the ingredients in TEVA-OXYCODAN?

Medicinal ingredients: oxycodone hydrochloride and acetylsalicylic acid (ASA)

Non-medicinal ingredients: colloidal silicon dioxide, FD&C yellow #5 aluminum lake, lactose, microcrystalline cellulose, sodium starch glycolate and stearic acid.

TEVA-OXYCODAN comes in the following dosage forms:

Tablets; 5 mg oxycodone hydrochloride and 325 mg ASA.

Do not use TEVA-OXYCODAN if:

- your healthcare professional did not prescribe it for you
- you are allergic to oxycodone hydrochloride, ASA or any of the other ingredients in TEVA-OXYCODAN
- you have mild pain that can be controlled by the occasional use of painkillers, including those available without a prescription
- you have severe asthma, trouble breathing, or other breathing problems

- you have any heart problems
- you have bowel blockage or narrowing of the stomach or intestines
- you have appendicitis or a problem with your pancreas called pancreatitis
- you have a condition where the bowel does not work properly (ileus) or you have severe pain in your abdomen
- you have increased pressure in your skull or a head injury
- you have severe CNS depression (nervous system slows down)
- you have or have a history of epilepsy
- you suffer from alcoholism or alcohol withdrawal
- you are taking or have taken within the past 2 weeks a Monoamine Oxidase inhibitor (MAOi) (such as phenelzine sulphate, tranylcypromine sulphate, moclobemide or selegiline)
- you are going to have, or recently had, a planned surgery
- you are pregnant or planning to become pregnant or you are in labour and delivery
- you are breastfeeding
- you have a condition such as hemophilia, hypoprothrombinemia, von Willebrand's disease, thrombocytopenia, thrombasthenia and other ill-defined hereditary platelet dysfunctions, severe vitamin K deficiency and severe liver damage that makes you more likely to have bleeding problems
- you have nasal polyps, allergic reaction or breathing problems to ASA or other nonsteroidal anti-inflammatory drugs (NSAIDs)
- you have stomach ulcers or other serious stomach or bowel sores

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take TEVA-OXYCODAN. Talk about any health conditions or problems you may have, including if you:

- have a history of illicit or prescription drug or alcohol abuse.
- are taking any other medications, including natural health products, salicylates or other pain and fever relief medications (nonsteroidal anti-inflammatory drugs (NSAIDS)), or prescription medications
- have severe kidney, liver or lung problems
- have low blood pressure
- have or have had problems with your mood (such as depression or anxiety), hallucinations, or other mental health problems
- suffer from chronic or severe constipation
- have problems with your adrenal or prostate gland
- suffer from migraines
- have nasal polyps or asthma
- have a history of bleeding problems
- have a blood clotting disorder or are taking blood thinners

- are planning on drinking alcohol. Drinking alcohol while taking TEVA-OXYCODAN may cause dangerous side effects. Do not drink alcohol while taking TEVA-OXYCODAN.
- are planning to breastfeed
- have circulatory problems (body does not get enough oxygen and nutrients to function properly due to lack of blood flow)
- have a fever, the flu or chickenpox
- are 65 years of age or older

Other warnings you should know about:

Taking TEVA-OXYCODAN can cause the following serious side effects:

- **Disorder of the adrenal gland:** You may develop a disorder of the adrenal gland called adrenal insufficiency. This means that your adrenal gland is not making enough of certain hormones. You may experience symptoms such as:
  - nausea, vomiting
  - feeling tired, weak or dizzy
  - decreased appetite

  You may be more likely to have problems with your adrenal gland if you have been taking opioids for longer than one month. Your healthcare professional may do tests, give you another medication, and slowly take you off TEVA-OXYCODAN.

- **Serious Skin Reactions:** Use of some NSAIDs, such as TEVA-OXYCODAN, have been associated with rare post-market cases of serious, fatal or otherwise life-threatening skin reactions, including:
  - Drug reaction with eosinophilia and systemic symptoms (DRESS)
  - Stevens-Johnson syndrome,
  - toxic epidermal necrolysis (TEN),
  - exfoliative dermatitis and
  - erythema multiforme**.**

  You may be at a greater risk of experiencing a serious skin reaction usually during the first month of treatment. See the Serious side effects and what to do about them table, below, for more information on these and other serious side effects.

- **Serotonin Toxicity (also known as serotonin syndrome):** TEVA-OXYCODAN can cause Serotonin Toxicity, a rare but potentially life-threatening condition. It can cause serious changes in how your brain, muscles and digestive system work. You may develop Serotonin Toxicity if you take TEVA-OXYCODAN with certain anti-depressants or migraine medications.

  Serotonin Toxicity symptoms include:
  - fever, sweating, shivering, diarrhea, nausea, vomiting;
  - muscle shakes, jerks, twitches or stiffness, overactive reflexes, loss of

coordination;
- fast heartbeat, changes in blood pressure;
- confusion, agitation, restlessness, hallucinations, mood changes, unconsciousness, and coma.

- **Sleep apnea:** Opioids can cause a problem called sleep apnea (stopping breathing from time to time while sleeping). Tell your healthcare professional if you have a history of sleep apnea or if anyone notices you stop breathing from time to time while sleeping.

See the Serious side effects and what to do about them table below for more information on these and other serious side effects.

Pregnancy, nursing, labour and delivery: Do not use TEVA-OXYCODAN while pregnant, nursing, during labour or delivery. Opioids can be transferred to your baby through breast milk, or while still in the womb. TEVA-OXYCODAN can then cause life-threatening breathing problems in your unborn baby or nursing infant. If you become pregnant while taking TEVA-OXYCODAN, tell your healthcare professional right away.

If you are pregnant and are taking TEVA-OXYCODAN, it is important that you don't stop taking your medication all of a sudden. If you do, it can cause a miscarriage or a still-birth. Your healthcare professional will monitor and guide you on how to slowly stop taking TEVA-OXYCODAN. This may help avoid serious harm to your unborn baby.

Driving and using machines: Before you do tasks which may require special attention, you should wait until you know how you react to TEVA-OXYCODAN. TEVA-OXYCODAN can cause:
- drowsiness
- dizziness or
- lightheadedness

This can usually occur after you take your first dose and when your dose is increased. Taking TEVA-OXYCODAN with other medicines that affect your nervous system can make these side effects worse. This includes:
- other opioids,
- phenothiazine (used to treat mental health problems and prevent vomiting during chemotherapy),
- sedatives and hypnotics (used to cause relaxation and help you sleep), and
- alcohol.

Sexual Function/Reproduction: Long term use of opioids may lead to a decrease in sex hormone levels. It may also lead to low libido (desire to have sex), erectile dysfunction or being infertile.

Drug addiction, dependence, and tolerance: Like any opioid, if you use TEVA-OXYCODAN for a

long time, it may cause mental and physical dependence. Oxycodone hydrochloride also has the potential to cause addiction. There are important differences between physical dependence and addiction. If you use opioids for a long time, you may develop tolerance. Tolerance means that, over time, a higher dose may be needed to get the same level of pain relief. It is important that you talk to your healthcare professional if you have questions or concerns about addiction, physical dependence, or tolerance. Your healthcare professional should prescribe and administer TEVA-OXYCODAN with the same degree of caution appropriate to the use of other oral opioid medications. It is not recommended to use these products for a long period of time.

Worsened pain: Taking opioids for pain can sometimes have the unintended effect of making your pain feel worse (opioid-induced hyperalgesia) even though your opioid dose has been unchanged or increased. This can also include feeling pain in new places in your body, or feeling pain from something that would not normally hurt, for example, feeling pain from clothing touching your skin. Tell your healthcare professional if you notice a change like this in your pain while you are taking TEVA-OXYCODAN.

Testing and check-ups: Tell any healthcare professional that you see that you are taking TEVA-OXYCODAN. TEVA-OXYCODAN can cause abnormal blood and urine test results. Your healthcare professional will decide when to perform these tests and will interpret the results.

Your healthcare professional will regularly monitor your health. This includes monitoring for signs of:

- misuse and abuse
- low blood pressure
- sleep apnea (a sleep disorder which causes pauses in breathing or shallow breathing while sleeping)
- respiratory depression and sedation (slow, shallow, or weak breathing)

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Serious Drug Interactions

Taking TEVA-OXYCODAN with the following medicines can cause serious side effects, including breathing problems that can lead to death:

- benzodiazepines used to help you sleep or that help reduce anxiety
- central nervous system (CNS) depressants used to slow down the nervous system. These can include:
    - opioids and mixed opioid agonists/antagonists used to relieve pain (such as pentazocine, nalbuphine, butorphanol, and buprenorphine)
    - sedatives which may enhance the drowsiness
    - pregabalin, used to treat nerve pain
    - hypnotics used to help with sleeping
    - antidepressants used for depression and mood disorders (such as tricyclic

antidepressants, serotonin norepinephrine re-uptake inhibitors (SNRIs) and selective serotonin re-uptake inhibitors (SSRIs) such as St. John's Wort)
    - anxiolytics, tranquilizers, and phenothiazines used to treat mental or emotional disorders
    - muscle relaxants used to treat muscle spasms and back pain (such as baclofen)
    - general anesthetics used during surgery
    - antipsychotics and neuroleptics used to treat mental health disorders
    - antihistamines used to treat allergies
    - antiemetics used to prevent nausea or vomiting
    - beta blockers used to lower blood pressure
    - alcohol, including prescription and non-prescription medicines that contain alcohol. **Do not** drink alcohol while you are taking TEVA-OXYCODAN. It can lead to drowsiness, unusually slow or weak breathing, serious side effects, or fatal overdose.
- monoamine oxidase inhibitors (MAOIs) used to treat depression. Do not take TEVA-OXYCODAN with MAOIs or if you have taken MAOIs in the last 14 days.

The following may interact with TEVA-OXYCODAN:

- medicines used to treat migraines (e.g. triptans)
- other medications that contain ASA (including over-the-counter preparations containing ASA), or oxycodone
- anticoagulants, used for prevention or treatment of blood clots
- antiretrovirals, used to treat viral infections
- antifungals, used to treat fungal infections
- antibiotics, used to treat bacterial infections
- grapefruit juice
- anticonvulsants, used to treat seizures
- corticosteroids, used to treat inflammation
- oral medicines to treat diabetes and/or insulin
- medicines used to suppress the immune system such as methotrexate
- NSAIDS (non-steroidal anti-inflammatory drugs) to treat pain such as ibuprofen and naproxen
- drugs medicines used to treat gout such as probenecid and sulfinpyrazone

How to take TEVA-OXYCODAN:

- Take TEVA-OXYCODAN exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- TEVA-OXYCODAN must be taken orally, by mouth. Do NOT take the TEVA-OXYCODAN tablets using any other route as this can cause serious harm, including death.
- **Swallow the tablet whole. Do not cut, break, crush, chew or dissolve the tablet. This can be dangerous and can lead to death or seriously harm you.**

- Review your pain regularly with your healthcare professional to determine if you still need TEVA-OXYCODAN. Be sure to take TEVA-OXYCODAN only for the condition for which is was prescribed.

Usual Dose:

Your dose is tailored/personalized just for you. Take it exactly as your healthcare professional has told you. Do not increase or decrease your dose without talking to your healthcare professional. Taking higher doses can lead to more side effects and a greater change of overdose.

Stopping your Medication

This medication may be habit-forming for long periods of time. If you have been taking TEVA-OXYCODAN for more than a few days you should not stop taking it all of a sudden. Your healthcare professional will monitor and guide you on how to slowly stop taking TEVA-OXYCODAN. You should do it slowly to avoid uncomfortable symptoms such as having:

- body aches
- diarrhea
- goosebumps
- loss of appetite
- nausea
- feeling nervous or restless
- runny nose
- sneezing
- tremors or shivering
- stomach cramps
- rapid heart rate (tachycardia)
- having trouble sleeping
- an unusual increase in sweating
- heart palpitations
- an unexplained fever
- weakness
- yawning

By reducing or stopping your opioid treatment, your body will become less used to opioids. If you start treatment again, you will need to start at the lowest dose. You may overdose if you restart at the last dose you took before you slowly stopped taking TEVA-OXYCODAN.

Refilling your Prescription for TEVA-OXYCODAN:

A new written prescription is required from your healthcare professional each time you need more TEVA-OXYCODAN. Therefore, it is important that you contact your healthcare professional before your current supply runs out.

Only obtain prescriptions for this medicine from the doctor healthcare professional in charge of your treatment. Do not seek prescriptions from other healthcare professionals unless you switch to another healthcare professional for your pain management.

Overdose:

Signs of an overdose may include:

- unusually slow or weak breathing
- dizziness
- confusion
- extreme drowsiness
- floppy muscles/low muscle tone
- cold and clammy skin
- slow heart rate
- low blood pressure
- sleep apnea (a disorder which pauses in breathing or shallow breathing while sleeping)
- heart attack
- vomiting and abdominal pain
- acetone odour in breath
- sweating, abnormally high body temperature
- dehydration
- restlessness
- seizures

If you think you have taken too much TEVA-OXYCODAN, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

If you miss one dose, take it as soon as possible. However, if it is almost time for your next dose, then skip the missed dose. Do not take two doses at once. If you miss several doses in a row, talk to your healthcare professional before restarting your medication.

What are possible side effects from using TEVA-OXYCODAN?

These are not all the possible side effects you may feel when taking TEVA-OXYCODAN. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- Drowsiness
- Insomnia
- Dizziness

- Fainting
- Nausea, vomiting, or a poor appetite
- Dry mouth
- Headache
- Problems with vision
- Weakness, uncoordinated muscle movement
- Itching
- Light headedness
- Sweating
- Constipation. Talk to your healthcare professional about ways to prevent constipation when you start using TEVA-OXYCODAN.
- Low sex drive, impotence (erectile dysfunction), infertility
- Feeling of pleasure or excitement
- Feeling unhappy, uneasy or dissatisfied

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
RARE			
Allergic Reaction: difficulty swallowing or breathing, hives, rash, swelling of the face, lips, tongue or throat,			**√**
Bowel Blockage (impaction)**:** abdominal pain, severe constipation, nausea			**√**
Disorder of the adrenal gland: anorexia, dizziness, or low blood pressure, fatigue, nausea, vomiting, weakness,			**√**
Fast, Slow or Irregular Heartbeat: heart palpitations		**√**	
Hypotension (low blood pressure): dizziness, fainting, light-headedness	**√**		
Overdose: cold and clammy skin, confusion, extreme sleepiness, hallucinations, , inability to walk			**√**

Respiratory Depression: shallow or weak breathing slow,			√
Serious Skin Reactions: blisters and peeling skin that may start in and around the mouth, nose, eyes and genitals and spread to other areas of the body, fever, flu-like feeling, severe rash, swelling of face and/or legs, swollen lymph glands, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinating less often, less urine or dark urine			√
Serotonin toxicity (also known as serotonin syndrome): a reaction which may cause feelings of agitation or restlessness, heavy sweating, high body temperature (> 38 °C) or rigid muscles, flushing, muscle twitching, involuntary eye movements			√
Sleep apnea: stop breathing for short periods during your normal nightly sleep.		√	
Withdrawal: anxiety, body aches, nausea, cold and clammy skin, diarrhea, shivering, vomiting, loss of appetite, sweating		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health
Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store tablets at room temperature (15°C to 30°C).
- Keep unused or expired TEVA-OXYCODAN in a secure place to prevent theft, misuse or accidental exposure. It should be kept under lock, out of sight and reach of children and pets.
- Never take medicine in front of small children as they will want to copy you. Accidental ingestion by a child is dangerous and may result in death. If a child accidentally takes TEVA-OXYCODAN, get emergency help right away.
- TEVA-OXYCODAN should never be thrown into household trash, where children and pets may find it. It should be returned to a pharmacy for proper disposal.

If you want more information about TEVA-OXYCODAN:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website http://www.tevacanada.com ; or by calling 1-800-268-4127 ext. 3; or email druginfo@tevacanada.com .

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