PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[N]PERCOCET®-DEMI

(oxycodone hydrochloride 2.5 mg / acetaminophen 325 mg)

Tablets, USP

Opioid Analgesic

Bristol-Myers Squibb Canada Montreal, Canada

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[N]PERCOCET®-DEMI
(oxycodone hydrochloride 2.5 mg / acetaminophen 325 mg Tablets, USP)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Oral	Tablets and oxycodone hydrochloride 2.5 mg / acetaminophen 325 mg	Corn Starch, FD&C Blue #2 Lake, microcrystalline cellulose, povidone, pregelatinized starch, silicon dioxide, and stearic acid. Lactose-, sodium- and tratrazine free.

INDICATIONS AND CLINICAL USE

PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) is indicated for the relief of moderate to moderately severe pain, including conditions accompanied by fever.

PERCOCET-DEMI is not indicated as an as-needed (prn) analgesic.

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 **ACTION AND CLINICAL PHARMACOLOGY**, **Special Populations and Conditions**, **Geriatrics**).

Pediatrics (> 6 years of age)

PERCOCET®-DEMI can be considered for children of six years of age or older.

CONTRAINDICATIONS

- Patients who are hypersensitive to the active substances oxycodone hydrochloride and acetaminophenor other opioid analgesics or to any ingredient in the formulation. For a complete listing, see the **DOSAGE FORMS, COMPOSITION AND PACKAGING** section of the Product Monograph.
- Patients with severe hepatic insufficiency or active liver disease.
- In 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).

WARNINGS AND PRECAUTIONS

SERIOUS WARNINGS AND PRECAUTIONS

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the risks of overdose and death with immediate release opioid formulations, PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen tablets) should only be used in patients for whom alternative treatment options (e.g., non-opioid analgesics) are ineffective, not tolerated, or would be otherwise inadequate to provide appropriate management of pain (see DOSAGE AND ADMINISTRATION).

Addiction, Abuse, and Misuse

PERCOCET-DEMI poses risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Each patient's risk should be assessed prior to prescribing PERCOCET-DEMI, and all patients should be monitored regularly for the development of these behaviours or conditions (see WARNINGS AND PRECAUTIONS). PERCOCET-DEMI should be stored securely to avoid theft or misuse.

Life-threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of PERCOCET-DEMI. Patients should be monitored for respiratory depression, especially during initiation of PERCOCET-DEMI or following a dose increase.
PERCOCET-DEMI must be swallowed whole. Cutting, breaking, crushing, chewing, or dissolving PERCOCET-DEMI can lead to dangerous adverse events including death (see WARNINGS AND PRECAUTIONS).

Accidental Exposure

Accidental ingestion of even one dose of PERCOCET-DEMI, especially by children, can

SERIOUS WARNINGS AND PRECAUTIONS

result in a fatal overdose of PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) (see DOSAGE AND ADMINISTRATION, Disposal, for instructions on proper disposal).

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

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

- **Reserve concomitant prescribing of PERCOCET-DEMI 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.**

General

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

PERCOCET-DEMI 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.

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

Hyperalgesia that will not respond to a further dose increase of PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) can occur at particularly high doses. A PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) dose reduction or change in opioid may be required.

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.

Abuse and Misuse

Like all opioids, PERCOCET-DEMI is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, PERCOCET-DEMI 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 PERCOCET-DEMI, should be used with particular care in patients with a history of alcohol and illicit/prescription drug abuse. However, concerns about abuse, addiction, and diversion should not prevent the proper management of pain.

PERCOCET-DEMI 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

Oxycodone hydrochloride and acetaminophen 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 PERCOCET-DEMI.

The use of PERCOCET-DEMI 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 PERCOCET-DEMI 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 **ADVERSE REACTIONS and DOSAGE AND ADMINISTRATION, Adjustment or Reduction of Dosage).**

Use in Drug and Alcohol Addiction

PERCOCET-DEMI 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.

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 Effects

PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) and other morphine-like opioids have been shown to decrease bowel motility. PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) may obscure the diagnosis or clinical course of patients with acute abdominal conditions (see **CONTRAINDICATIONS**).

Hepatic

Administration of acetaminophen in doses higher than recommended may result in hepatic injury, including the risk of severe hepatotoxicity and death. The maximum daily dose of acetaminophen includes all routes of administration (intravenous, oral, and rectal) and all products containing acetaminophen (oral solution/drops, syrup, pills, capsules, suppositories, etc.). Do not exceed the maximum recommended daily dose of acetaminophen. (see DRUG

INTERACTION

Administration of acetaminophen doses higher than recommended entails the risk for very serious liver damage. Clinical symptoms of liver damage are usually first seen after one to two days following acetaminophen overdose. Maximum liver damage symptoms are usually observed after 3-4 days (see OVERDOSE). Acetaminophen should be used with caution in cases of hepatic insufficiency

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.

PERCOCET-DEMI should not be given to pregnant women unless, in the judgement of the physician, the potential benefits outweigh the possible hazards.

Neurologic

Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol): PERCOCET-DEMI should be used with caution and in a reduced dosage during concomitant administration of other opioid analgesics, general anesthetics, phenothiazines and other tranquilizers, sedative-hypnotics, tricyclic antidepressants, antipsychotics, antihistamines, benzodiazepines, centrally-active anti-emetics and other CNS depressants. 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 **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 PERCOCET-DEMI 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 **DRUG INTERACTIONS**).

PERCOCET-DEMI should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects, including death (see **CONTRAINDICATIONS** and **ADVERSE REACTIONS**, **Sedation**, and **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 Syndrome: PERCOCET-DEMI could cause a rare but potentially life-threatening condition resulting from concomitant administration of serotonergic drugs (e.g. anti-depressants, migraine medications). Treatment with the serotoninergic drug should be discontinued if such events (characterized by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated. PERCOCET-DEMI should not be used in combination with MAO inhibitors or serotonin-precursors (such as L-tryptophan, oxitriptan) and should be used with caution in combination with other serotonergic drugs (triptans, certain tricyclic antidepressants, lithium, tramadol, St. John's Wort) due to the risk of serotonergic syndrome (see **DRUG INTERACTIONS).**

Head Injury:

The respiratory depressant effects of PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen), 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, PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) may produce confusion, miosis, vomiting and other side effects which obscure the clinical course of patients with head injury. In such patients, PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) must be used with extreme caution and only if it is judged essential (see **CONTRAINDICATIONS).**

Peri-operative Considerations

PERCOCET-DEMI 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 PERCOCET-DEMI for at least 24 hours before the operation and PERCOCET-DEMI should not be used in the immediate post-operative period.

Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. Thereafter, if PERCOCET-DEMI 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 acetaminophen 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 decreased bowel motility in post-operative patients receiving opioids. Standard supportive therapy should be implemented.

PERCOCET-DEMI 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.

Psychomotor Impairment

PERCOCET-DEMI 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 ofPERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) with other CNS depressants, including other opioids, phenothiazine, sedative/hypnotics and alcohol.

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. PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) should be used with extreme caution in patients with substantially decreased respiratory reserve, pre-existing respiratory depression, hypoxia or hypercapnia (see **CONTRAINDICATIONS)**.

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of PERCOCET-DEMI, 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 PERCOCET-DEMI 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 PERCOCET-DEMI are essential. Overestimating the PERCOCET-DEMI 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 **WARNINGS AND**

PRECAUTIONS, **Special Populations**, **Special Risk Groups**, and **DOSAGE AND ADMINISTRATION**).

Use in 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 PERCOCET-DEMI, as in these patients, even usual therapeutic doses of PERCOCET-DEMI 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 PERCOCET-DEMI is contraindicated in Patients with acute or severe bronchial asthma, chronic obstructive airway, or status asthmaticus (see **CONTRAINDICATIONS**).

Sexual Function/Reproduction

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

Skin

Hypersensitivity Reactions: Serious skin reactions

Rarely, acetaminophen can cause serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens – Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. It is important to recognize and react quickly to the initial symptoms of these reactions which may occur without warning but may be manifested by any serious skin reactions. Patients should be informed about the signs of serious skin reactions, and use of the drug should be discontinued at their first appearance.

Special Populations

Special Risk Groups:

PERCOCET-DEMI **(oxycodone hydrochloride and acetaminophen)** should be administered with caution to patients with a history of alcohol and drug abuse and in a reduced dosage to debilitated patients, and in patients with severely impaired pulmonary function, or renal impairment (creatinine clearance ≤30 mL/min) Addison's disease, hypothyroidism, myxedema, toxic psychosis, prostatic hypertrophy or urethral stricture.

Pregnant Women:

Studies in humans have not been conducted. While animal reproduction studies have revealed no evidence of harm to the fetus due to oxycodone hydrochloride and acetaminophen. PERCOCET-DEMI does cross the placental barrier. Thus, PERCOCET-DEMI should not be administered to pregnant women unless in the judgment of the physician, potential benefits outweigh the risks.

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 **WARNINGS AND PRECAUTIONS, Neonatal Opioid Withdrawal Syndrome, ADVERSE REACTIONS, Post-Marketing Experience**).

Labour, Delivery and Nursing Women:

Since opioids can cross the placental barrier and are excreted in breast milk, PERCOCET-DEMI should not be used unless, in the judgement of the physician, the potential benefits outweigh the risks. Respiratory depression can occur in the infant if opioids are administered during labour. Naloxone, a drug that counters the effects of opiates, should be readily available

Pediatrics (>6 years of age):

PERCOCET-DEMI can be considered for children of six years of age or older

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 **DOSAGE AND ADMINISTRATION** and **ACTION AND CLINICAL PHARMACOLOGY**, **Special Populations and Conditions**, **Geriatrics**).

Patients with Hepatic Impairment:

PERCOCET-DEMI is contraindicated in patients with severe hepatic insufficiency or active liver disease (see CONTRAINDICATION).

Acetaminophen should be used with caution in cases of hepatic insufficiency. (See DOSAGE AND ADMINISTRATION and ACTION AND CLINICAL PHARMACOLOGY).

Patients with Renal Impairment:

Acetaminophen should be used with caution in cases of severe renal insufficiency (creatinine clearance ≤30 mL/min)

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Adverse effects of PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) 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 PERCOCET-DEMI 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.

Post-Marketing Experience

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.

DRUG INTERACTIONS

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/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 **WARNINGS AND PRECAUTIONS**, **Neurologic**, **Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol) and Psychomotor Impairment**). PERCOCET-DEMI **(**oxycodone hydrochloride and acetaminophen) should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects.

Drug-Drug Interactions

Table 1 - Established or Potential Drug-Drug Interactions

Class (Proper name)	Ref	Effect	Clinical comment
Azole-antifungal agents (e.g., ketoconazole, voriconazole)	CT	↑ C_{max} (1.7 fold) ↑ AUC (3.6 fold)	If co-administration with PERCOCET-DEMI 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.
Macrolide antibiotics (e.g., erythromycin)	T	↓ clearance ↑ plasma concentrations	
Protease inhibitors (e.g., ritonavir)	T	↓ clearance ↑ plasma concentrations	

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

Use with Other Acetaminophen-Containing Products

Due to the potential for acetaminophen hepatotoxicity at doses higher than the maximum daily dose (4000 mg of acetaminophen per day for adults), PERCOCET-DEMI should not be used concomitantly with other acetaminophen-containing products (See WARNINGS AND PRECAUTIONS).

Drug-Lifestyle Interactions

The concomitant use of alcohol should be avoided (see **WARNINGS AND PRECAUTIONS, General**).

DOSAGE AND ADMINISTRATION

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

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

PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) should be used with caution within 12 hours pre-operatively and within the first 12-24 hours post-operatively **(see WARNINGS AND PRECAUTIONS, Peri-operative Considerations).**

PERCOCET-DEMI is not indicated for rectal administration

Patients Not Receiving Opioids at the Time of Initiation of Oxycodone Hydrochloride and Acetaminophen Treatment: The usual initial adult dose of **PERCOCET-DEMI** for patients who have not previously received opioid analgesics is one or two tablets every 6 hours. **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 2** 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 2: OPIOID ANALGESICS: APPROXIMATE ANALGESIC EQUIVALENCES[1]

Drug	Equivalent Dose (mg)[2] (compared to morphine 10 mg IM)		Duration of Action (hours)
	Parenteral	**Oral**	
Strong Opioid Agonists:			
Morphine	10	60[3]	3-4
Oxycodone	15	30[4]	2-4
Hydromorphone	1.5	7.5	2-4
Anileridine	25	75	2-3
Levorphanol	2	4	4-8
Meperidine[6]	75	300	1-3
Oxymorphone	1.5	5 (rectal)	3-4
Methadone[5]	-	-	-
Heroin	5-8	10-15	3-4
Weak Opioid Agonists:			
Codeine	120	200	3-4
Propoxyphene	50	100	2-4
Mixed Agonist-Antagonists[7]:			
Pentazocine[6]	60	180	3-4
Nalbuphine	10	-	3-6
Butorphanol	2	-	3-4

Footnotes:

[1]References:

Expert Advisory Committee on the Management of Severe Chronic Pain in Cancer Patients, Health and Welfare Canada. Cancer pain: A monograph on the management of cancer pain. Ministry of Supplies and Services Canada, 1987. Cat. No. H42-2/5-1984E.

Foley KM. The treatment of cancer pain. N Engl J Med 1985;313(2):84-95.

Aronoff GM, Evans WO. Pharmacological management of chronic pain: A review. In: Aronoff GM, editor. Evaluation and treatment of chronic pain. 2nd ed. Baltimore (MD): Williams and Wilkins; 1992. p. 359-68.

Cherny NI, Portenoy RK. Practical issues in the management of cancer pain. In: Wall PD, Melzack R, editors. Textbook of pain. 3rd ed. New York: Churchill Livingstone; 1994. p. 1437-67.

[2] **Most of the data were derived from single-dose, acute pain studies and should be considered an approximation for selection of doses when treating chronic pain. As analgesic conversion factors are approximate and patient response may vary, dosing should be individualized according to relief of pain and side effects. Because of incomplete cross-tolerance, dose reductions of 25% to 50% of the equianalgesic dose may be appropriate in some patients when converting from one opioid to another, particularly at high doses.[†] Upward titration may be required to reach appropriate maintenance doses.**

[†]Levy MH. Pharmacologic treatment of cancer pain. N Engl J Med 1996;335:1124-1132.

[3] **For acute pain, the oral or rectal dose of morphine is six times the injectable dose. However, for chronic dosing, clinical experience indicates that this ratio is 2-3:1 (i.e., 20-30 mg of oral or rectal morphine is equivalent to 10 mg of parenteral morphine).**

[4] Based on single entity oral oxycodone in acute pain.

[5] Extremely variable equianalgesic dose. Patients should undergo individualized titration starting at an equivalent to 1/10 of the morphine dose.

[6] Not recommended for the management of chronic pain.

[7] Mixed agonist-antagonists can precipitate withdrawal in patients on pure opioid agonists.

Recommended Dose and Dosage Adjustment

Adults:

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 below in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of opioids.

Usual Adult Dose

One or two tablets every six hours.

Usual Children's Dose

12 years and older: 1/2 tablet every 6 hours

6-12 years: 1/4 of a tablet every 6 hours

PERCOCET-DEMI is not indicated for children under 6 years of age.

Patients with Hepatic Impairment:

PERCOCET-DEMI is contraindicated in patients with severe hepatic insufficiency or active liver disease (see **CONTRAINDICATIONS**).

Acetaminophen should be used with caution in cases of hepatic insufficiency (see **WARNINGS AND PRECAUTIONS, Hepatic).**

Patients with Renal Impairment:

PERCOCET-DEMI should be given with caution to patients with renal insufficiency (creatinine clearance ≤30 mL/min), (see WARNINGS AND PRECAUTIONS).

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. PERCOCET-DEMI should be initiated at a low dose

and slowly titrated to effect (see **WARNINGS AND PRECAUTIONS** and **ACTION AND CLINICAL PHARMACOLOGY**).

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 PERCOCET-DEMI. 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.

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 **WARNINGS AND PRECAUTIONS**).

Disposal

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

PERCOCET-DEMI **should never be disposed of in household trash.** Disposal via a pharmacy take back program is recommended. Unused or expired PERCOCET-DEMI 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.

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.

OVERDOSAGE

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

Symptoms:

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

Oxycodone

Serious overdose with PERCOCET-DEMI is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdose, apnea, circulatory collapse, cardiac arrest and death may occur.

Acetaminophen

The ingestion of very large amounts of PERCOCET-DEMI may, in addition, result in acute acetaminophen intoxication, characterized by anorexia, nausea, vomiting and sweating within two or three hours of ingestion, and possibly cyanosis with methemoglobinemia. Within 48 hours, liver function tests rise abnormally, and the liver becomes enlarged and tender. Within three to five days, jaundice, coagulation defects, myocardiopathy, encephalopathy, and renal failure occur, followed by death due to hepatic necrosis. The ingestion of 10 g of acetaminophen is considered to result in intoxication, with the possibility of a fatal outcome if the amount exceeds 15 g. Hepatotoxicity occurs when plasma levels of 300 mcg /ml are observed within four hours of ingestion.

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. The instructions contained in the package insert provided by the manufacturer should be carefully observed.

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, and should be carried out at an early stage of treatment. Plasma levels of acetaminophen should be determined. If hemodialysis is carried out within ten hours of ingestion, it may be of some value.

Overdose treatment includes administration of the antidote, N-acetylcysteine (NAC) by intravenous or oral route, if possible, within 8 hours of ingestion. NAC can give some degree of protection even after 16 hours.

ACTION AND CLINICAL PHARMACOLOGY

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 PERCOCET-DEMI are analgesia and sedation.

PERCOCET-DEMI also contains the non-opioid antipyretic analgesic, acetaminophen; the latter exerts its effects by a mechanism similar to that of the salicylates but, unlike the salicylates, does not have anti-inflammatory or uricosuric properties.

Pharmacodynamics

Central Nervous System:

PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) 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.

PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) 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.

PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) 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:

PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) 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 pancreatic secretions, spasm of the sphincter of Oddi, and transient elevations in serum amylase.

Cardiovascular System:

PERCOCET-DEMI (oxycodone hydrochloride and acetaminophen) 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.**

Pharmacokinetics

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. Acetaminophen is rapidly and almost completely absorbed from the gastrointestinal tract, peak plasma levels being obtained within ten minutes to one hour.

Special Populations and Conditions

Pediatrics:
PERCOCET-DEMI can be considered for children of six years of age or older.

Individuals under 6 years of age should not take PERCOCET-DEMI.

Geriatrics: See WARNINGS and PRECAUTIONS.

Hepatic Impairment: See WARNINGS and PRECAUTIONS.

Renal Impairment: See WARNINGS and PRECAUTIONS.

STORAGE AND STABILITY

Store at room temperature (15 to 30°C).Patients should be instructed to store PERCOCET-DEMI, as any medication, safely out of the sight and reach of children.

SPECIAL HANDLING INSTRUCTIONS

Not applicable.

DOSAGE FORMS, COMPOSITION AND PACKAGING

PERCOCET-DEMI, supplied as blue, biconvex, quadrisected tablets in bottles of 100 tablets.

Composition:

Each tablet contains: oxycodone HCl 2.5 mg and acetaminophen 325 mg. Non-medicinal ingredients: corn starch, FD&C Blue #2 Lake, microcrystalline cellulose, povidone, pregelatinized starch, silicon dioxide, and stearic acid. Lactose-, sodium- and tratrazine free. The tablet is quadrisected and embossed on one side with PERCOCET-DEMI and the other side blank.

Packaging: PERCOCET-DEMI is available in bottles of 100 tablets.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:

Oxycodone hydrochloride

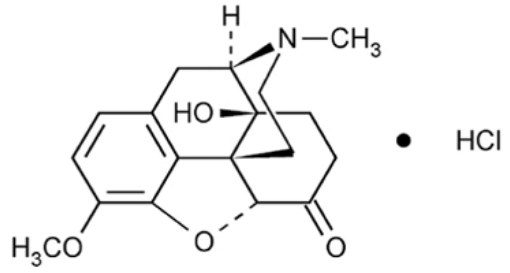
Chemical name:

14-hydroxydihydrocodeinone

Molecular formula and molecular mass:

Oxycodone - $C_{18}H_{21}NO_4$.HCl and 351.82

Structural formula:



Physicochemical Properties:

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

Drug Substance

Proper name:

Acetaminophen

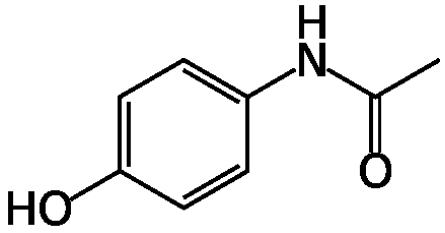
Chemical name:

Acetaminophen is paracetamol, APAP, N-acetyl p-aminobenzoic acid, 4'-hydroxyacetanilide

Molecular formula and molecular mass:

Acetaminophen - $C_8H_9NO_2$ and 151.16

Structural formula:



Physicochemical Properties:

Acetaminophen is a white, crystalline powder and is soluble in alcohols and most polar organicsolvents, and slightly soluble in water and nonpolar and chlorinated hydrocarbons. Acetaminophen is a major metabolite of phenacetin.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

[N]PERCOCET®-DEMI

Oxycodone hydrochloride 2.5 mg and acetaminophen 325 mg Tablets, USP

Read this carefully before you start taking **PERCOCET-DEMI** 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 **PERCOCET-DEMI.**

Serious Warnings and Precautions

- **Even if you take PERCOCET-DEMI as prescribed you are at a risk for opioid addiction, abuse and misuse. This can lead to overdose and death.**
- **When you take PERCOCET-DEMI 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.**
- **You may get life-threatening breathing problems while taking PERCOCET-DEMI. This is less likely to happen if you take it as prescribed by your doctor.**
- **You should never give anyone your PERCOCET-DEMI. They could die from taking it. If a person has not been prescribed PERCOCET-DEMI, taking even one dose can cause a fatal overdose. This is especially true for children.**
- **If you took PERCOCET-DEMI 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 PERCOCET-DEMI 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 PERCOCET-DEMI used for?

[N]PERCOCET®-DEMI is a combination product that contains two medications: oxycodone hydrochloride and acetaminophen. Oxycodone - acetaminophen is used to relieve moderate to moderately severe pain, including conditions associated with fever.

How does PERCOCET-DEMI work?

PERCOCET-DEMI is a painkiller belonging to the class of drugs known as opioids. It relieves pain by acting on specific nerve cells of the spinal cord and brain. Acetaminophen belongs to the group of medications called analgesics (pain relievers) and antipyretics (fever reducers). Oxycodone belongs to the group of medications called narcotic analgesics.

What are the ingredients in PERCOCET-DEMI?

Medicinal ingredients: Oxycodone hydrochloride and acetaminophen

Non-medicinal ingredients: Corn starch, FD&C Blue #2 Lake, microcrystalline cellulose, povidone, pregelatinized starch, silicon dioxide, and stearic acid.

PERCOCET-DEMI comes in the following dosage forms:

Each PERCOCET-DEMI tablet contains 2.5 mg oxycodone hydrochloride, and 325 mg acetaminophen.

Do not use PERCOCET-DEMI if:

- Your doctor did not prescribe it for you
- Your pain is mild
- you are allergic to oxycodone hydrochloride, acetaminophen or any of the other ingredients in PERCOCET-DEMI
- you can control your pain by the occasional use of other pain medications. This includes those available without a prescription
- you have severe asthma, trouble breathing, or other breathing problems
- you have any heart problems
- You have severe liver disease
- you have bowel blockage or narrowing of the stomach or intestines
- you have severe pain in your abdomen
- you have a head injury
- you are at risk for seizures
- you suffer from alcoholism

- 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 a planned surgery

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

- suffer from migraines
- have a history of illicit or prescription drug or alcohol abuse. You must not consume alcohol while taking PERCOCET-DEMI, as it may increase the chance of experiencing dangerous side effects
- if you 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 disease
- are taking other products containing acetaminophen. Acetaminophen can cause decreased liver function. Taking more than the maximum daily dose of acetaminophen may cause severe or possibly fatal liver damage People with liver disease or reduced liver function should discuss with their doctor how this medication may affect their medical condition, how their medical condition may affect the dosing and effectiveness of this medication, and whether any special monitoring is needed.
- have low blood pressure
- have or had depression
- suffer from chronic or severe constipation
- have problems with your thyroid, adrenal or prostate gland
- have, or had in the past hallucinations or other severe mental problems
- are pregnant or planning to become pregnant or you are in labour. This medication should not be used during pregnancy unless the benefits outweigh the risks. If you become pregnant while taking this medication, contact your doctor immediately.
- are breastfeeding. This medication passes into breast milk. If you are a breast-feeding mother and are taking oxycodone and acetaminophen, it may affect your baby. Talk to your doctor about whether you should continue breast-feeding.
- adrenal gland problems, such as Addison's disease
- hallucinations or other severe mental problems

DO NOT take with other products containing acetaminophen. Taking more than the maximum daily dose of acetaminophen may cause severe or possibly fatal liver damage

Serious Skin Reactions (Acute Generalized Exanthematous Pustulosis, Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis):

Acetaminophen can cause serious skin reactions that can spread to your mouth, lips, face, hands, trunk, arms and legs. This condition is life-threatening.

Other warnings you should know about:

Driving and using machines: Before you do tasks which may require special attention, you should wait until you know how you react to PERCOCET-DEMI. PERCOCET-DEMI can cause:

- drowsiness
- dizziness or
- lightheadedness

This can usually occur after you take your first dose and when your dose is increased.

Children:

The safety and effectiveness of ^{N}PERCOCET®-DEMI has not been established for children under 6 years old.

Dependence and withdrawal: This medication contains oxycodone. Physical dependence, psychological dependence, and abuse have occurred with the use of oxycodone. People with a history of past or current substance use problems may be at greater risk of developing abuse or addiction while taking this medication. Abuse is not a problem with people who require this medication for pain relief. If this medication is stopped suddenly, you may experience withdrawal symptoms such as anxiety, sweating, trouble sleeping, shaking, pain, nausea, tremors, diarrhea, and hallucinations. If you have been taking this medication for a while, it should be stopped gradually as directed by your doctor.

Liver Injury: Liver injury can occur when more than the maximum daily dose of acetaminophen is taken. Follow your doctor's instructions to know how much acetaminophen you can take in a day. Acetaminophen can be in oral solutions/drops, syrup, pills, capsules, suppositories, intravenous solutions etc. To calculate how much acetaminophen you have had in a day, read the labels on all products to see if they contain acetaminophen. Keep track of how much acetaminophen is in each dose and how much you have taken in a 24 hour period.

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

The following may interact with PERCOCET-DEMI:

- Alcohol. This includes prescription and non-prescription medications that contain alcohol.**Do not** drink alcohol while you are taking PERCOCET-DEMI. It can lead to:
    - drowsiness
    - unusually slow or weak breathing

    - serious side effects or
    - a fatal overdose
- drugs used to treat migraines (e.g. triptans)
- other opioid analgesics (drugs used to treat pain)
- other medications that contain acetaminophen (including over-the-counter preparations containing acetaminophen), or oxycodone
- general anesthetics (drugs used during surgery)
- benzodiazepines (drugs used to help you sleep or that help reduce anxiety)
- antidepressants (for depression and mood disorders). **Do not** take PERCOCET-DEMI with MAO inhibitors (MAOi) or if you have taken MAOi's in the last 14 days.
- drugs used to treat serious mental or emotional disorders (such as schizophrenia)
- antihistamines (drugs used to treat allergies)
- anti-emetics (drugs used for the prevention of vomiting)
- drugs used to treat muscle spasms and back pain
- warfarin (such as Coumadin) and other anticoagulants (used for prevention or treatment of blood clots)
- anti-retroviral drugs (used to treat viral infections)
- anti-fungal drugs (used to treat fungal infections)
- antibiotic drugs (used to treat bacterial infections)
- some heart medication (such as beta blockers)
- grapefruit juice
- nonprescription, (over- the-counter) medications
- herbal remedies

How to take PERCOCET-DEMI:

Swallow whole. Do not cut, break, crush, chew or dissolve the tablet. This can be dangerous and can lead to death or seriously harm you.

The dosage varies according to each individual and can be affected by the severity of the pain as well as each person's response to the medication.

The usual recommended dose of PERCOCET-DEMI (each tablet contains 2.5 mg oxycodone and 325 mg acetaminophen) is the following:

Adults:

- **one or two tablets every 6 hours as needed for pain**

Children:

- **12 years and older: 1/2 tablet every 6 hours**
- **6-12 years: 1/4 tablet every 6 hours**

Do not give this medication to anyone else, even if they have the same symptoms as you do. It can be harmful for people to take this medication if their doctor has not prescribed it.

Your dose is tailored/personalized just for you. Be sure to follow your doctor's dosing instructions exactly. Do not increase or decrease your dose without consulting your doctor.

Review your pain regularly with your doctor to determine if you still need PERCOCET-DEMI. Be sure to use PERCOCET-DEMI only for the condition for which it was prescribed.

If your pain increases or you develop any side effect as a result of taking PERCOCET-DEMI, tell your doctor immediately.

Stopping your Medication

This medication may be habit-forming if taken for long periods of time. If you have been taking PERCOCET-DEMI for more than a few days you should not stop taking it all of a sudden. You should check with your doctor for directions on how to slowly stop taking it. You should do it slowly to avoid uncomfortable symptoms such as having:

- body aches
- diarrhea
- gooseflesh
- 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
- an unexplained fever
- weakness
- yawning
- hallucinations
- anxiety

Refilling your Prescription for PERCOCET-DEMI:

A new written prescription is required from your doctor each time you need more PERCOCET-DEMI. Therefore, it is important that you contact your doctor before your current supply runs out.

Overdose:

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

Exceeding the recommendations by your doctor can result in respiratory depression (shallow, slow breathing), seizures, liver damage, coma, heart stoppage and death. Taking a significant overdose can result in hepatic toxicity.

Signs of overdose may include:

- unusually slow or weak breathing
- dizziness
- confusion
- extreme drowsiness
- increased sweating
- nausea
- vomiting
- stomach pain
- loss of appetite

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 succession, talk to your doctor before restarting your medication.

What are possible side effects from using PERCOCET-DEMI?

These are not all the possible side effects you may feel when taking PERCOCET-DEMI. If you experience any side effects not listed here, contact 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
- Sweating
- Constipation
- Mood changes
- Sleepiness
- Low sex drive, impotence (erectile dysfunction), infertility

Talk with your doctor or pharmacist about ways to prevent constipation when you start using PERCOCET-DEMI.

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 **Overdose:** hallucinations, confusion, inability to walk normally, slow or weak breathing, extreme sleepiness, sedation, or dizziness, floppy muscles/low muscle tone cold and clammy skin.			√
Respiratory Depression: Slow, shallow or weak breathing.			√
Allergic Reaction: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug
Bowel Blockage (impaction): abdominal pain, severe constipation, nausea			√
Withdrawal: nausea, vomiting, diarrhea, anxiety, shivering, cold and clammy skin, body aches, loss of appetite, sweating.		√	
Fast, Slow or Irregular Heartbeat: heart palpitations.		√	
Low Blood Pressure: dizziness, fainting, light-headedness.	√		
Serotonin Syndrome: agitation or restlessness, loss of muscle control or muscle twitching tremor, diarrhea			√
VERY RARE **Serious Skin Reactions (Acute Generalized Exanthematous Pustulosis, Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis)**: any combination of itchy skin rash, redness, blistering and peeling of the skin and/or of the lips, eyes, mouth, nasal passages or genitals, accompanied by fever, chills, headache, cough, body aches or joint pain, yellowing of the skin or eyes, dark urine			√
Liver Injury: yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite		√	
UNKNOWN **Convulsions (seizures)**			√

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

Reporting Side Effects
We encourage you to report serious or unexpected side effects to Health Canada. The information is used to check for new safety concerns about health products. As a consumer, your report contributes to the safe use of health products for everyone.
3 ways to report:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada, Postal Locator 0701E
    Ottawa, ON
    K1A 0K9

    Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

Storage:

PERCOCET-DEMI tablets should be stored at room temperature (15°C to 30°C).

Keep unused or expired PERCOCET-DEMI in a secure place to prevent theft, misuse or accidental exposure.

Keep PERCOCET-DEMI out of sight and reach of children and pets.

Disposal:
PERCOCET-DEMI 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 PERCOCET-DEMI:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this consumer medication information by visiting the Health Canada website; the manufacturer's website http://www.bmscanada.ca, or by calling 1-800-463-6267.

This leaflet was prepared by Bristol-Myers Squibb Canada

Last Revised October 17, 2016