

PRESCRIBING INFORMATION
INCLUDING PATIENT MEDICATION INFORMATION

[®]TALWIN[®]

pentazocine hydrochloride

Tablets, 50 mg

Narcotic Analgesic

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Date of Revision:
May 22, 2018

Submission Control No: 213122

s-a Version 4.0 dated May 22, 2018

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® TALWIN®

pentazocine hydrochloride tablets

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Oral	Tablets, 50 mg	Aerosil, avicel, cornstarch, dibasic calcium phosphate, magnesium stearate, kolliphor, sodium metabisulphite. <i>For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section.</i>

INDICATIONS AND CLINICAL USE

Adults

TALWIN is indicated for the relief of chronic or acute pain of moderate to severe degree.

TALWIN 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.

Pediatrics (< 18 years of age)

The safety and efficacy of TALWIN has not been studied in the pediatric population. Therefore the use of TALWIN is not recommended in patients under 18 years of age.

CONTRAINDICATIONS

- Patients who are hypersensitive to the active substance pentazocine hydrochloride or other opioid analgesics or to any ingredient in the formulation. For a complete listing, see the **DOSAGE FORMS, COMPOSITION AND PACKAGING** section of the Prescribing Information.
- 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).
- Women who are breast-feeding or pregnant (see **SERIOUS WARNINGS AND PRECAUTIONS** and **WARNINGS AND PRECAUTIONS**).

WARNINGS AND PRECAUTIONS

SERIOUS WARNINGS AND PRECAUTIONS
<p><u>Limitations of Use</u> 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, TALWIN (pentazocine hydrochloride) 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).</p>
<p><u>Addiction, Abuse, and Misuse</u> TALWIN 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 TALWIN, and all patients should be monitored regularly for the development of these behaviours or conditions (see WARNINGS AND PRECAUTIONS). TALWIN should be stored securely to avoid theft or misuse.</p>
<p><u>Life-threatening Respiratory Depression: OVERDOSE</u> Serious, life-threatening, or fatal respiratory depression may occur with use of TALWIN. Infants exposed <i>in-utero</i> or through breast milk are at risk of life-threatening respiratory depression upon delivery or when nursed. Patients should be monitored for respiratory depression, especially during initiation of TALWIN or following a dose increase. Further, instruct patients of the hazards related to taking opioids including fatal overdose.</p> <p>TALWIN must be swallowed whole. Cutting, breaking, crushing, chewing, or dissolving TALWIN can lead to dangerous adverse events including death (see WARNINGS AND PRECAUTIONS).</p>

SERIOUS WARNINGS AND PRECAUTIONS

Accidental Exposure

Accidental ingestion of even one dose of TALWIN, especially by children, can result in a fatal overdose of pentazocine hydrochloride (see DOSAGE AND ADMINISTRATION, Disposal, for instructions on proper disposal).

Neonatal Opioid Withdrawal Syndrome

Prolonged maternal use of TALWIN 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 TALWIN 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 sedation, respiratory depression, coma, and death (see WARNINGS AND PRECAUTIONS, Neurologic and DRUG INTERACTIONS).

- **Reserve concomitant prescribing of TALWIN 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 closely for signs and symptoms of sedation and respiratory depression.**

General

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

TALWIN 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 TALWIN as it may increase the chance of experiencing serious adverse events, including death.

Hyperalgesia that will not respond to a further dose increase of pentazocine hydrochloride can occur at particularly high doses. A pentazocine hydrochloride dose reduction or change in opioid may be required.

Abuse and Misuse

Like all opioids, TALWIN is a potential drug of abuse and misuse, which can lead to overdose and death. Therefore, TALWIN 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 TALWIN, 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.

TALWIN 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

Pentazocine hydrochloride 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 TALWIN.

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

Patients with Cardiovascular disease: TALWIN can elevate blood pressure, possibly through the release of endogenous catecholamines. Particular caution should be observed in conditions where alterations in vascular resistance and blood pressure might be particularly undesirable such as in the acute phase of myocardial infarction.

Dependence/Tolerance

As with other opioids, tolerance and physical dependence may develop upon repeated administration of TALWIN 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.

In chronic usage, care should be exercised to avoid any unnecessary increase in dosage since prolonged use of high doses of TALWIN may produce dependence. Patients with a history of drug abuse should be under close supervision when receiving TALWIN.

Patients Dependent on Narcotics: Because TALWIN is a **weak narcotic** antagonist, patients who are addicted to narcotics may experience withdrawal symptoms and therefore it should be given with special caution to such persons. In non-addicted patients receiving narcotics for a short period, symptoms believed to be related to antagonism may be observed. Intolerance or untoward reactions are usually not observed following administration of TALWIN to patients who have received single doses of or who have had limited exposure to narcotics.

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, vomiting, nervousness or restlessness, anxiety, runny nose, sneezing, lacrimation, tremors or shivering, stomach cramps, tachycardia, trouble with sleeping, unusual increase in sweating, palpitations, unexplained fever, weakness and yawning (see **ADVERSE REACTIONS, DOSAGE AND ADMINISTRATION, Adjustment or Reduction of Dosage**).

However, even when these symptoms have occurred, discontinuance has been accomplished with minimal difficulty. In the rare patient in whom more than minor difficulty has been encountered, reinstatement of TALWIN with gradual withdrawal has ameliorated the patient's symptoms.

Use in Drug and Alcohol Addiction

TALWIN 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 TALWIN; extreme caution and awareness is warranted to mitigate the risk.

Endocrine and Metabolism

Patients with Porphyria: Particular caution should be exercised in administering TALWIN to patients with porphyria, since it may provoke an acute attack in susceptible individuals.

Caution should also be observed when administering TALWIN in patients with adrenocortical insufficiency.

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

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

Genitourinary

Obstructive Uropathy: Because urinary retention has been observed in a few patients receiving TALWIN, caution is advised in administration of the drug to patients with obstructive uropathy.

Caution should also be observed when administering TALWIN in patients with prostate hypertrophy.

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 TALWIN is contraindicated in pregnant women (see **CONTRAINDICATIONS**).

There have been rare reports of a withdrawal syndrome in newborns after prolonged use of TALWIN by the mother during pregnancy.

Neurologic

Interactions with Central Nervous System Depressants (including alcohol): Pentazocine hydrochloride 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. Sedation, respiratory depression, hypotension, 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 sedation and respiratory depression.

Advise both patients and caregivers about the risks of sedation and respiratory depression when TALWIN 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**).

TALWIN 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.

Acute CNS Manifestations: There have been reported instances of the acute onset of hallucinations (usually visual), disorientation, and confusion in patients receiving therapeutic doses of TALWIN. These manifestations have cleared spontaneously within hours upon discontinuation of the drug. The mechanism responsible for this reaction is not known. Patients demonstrating this reaction should be closely observed and if therapy with TALWIN is to be restarted, administration should proceed cautiously since the acute CNS manifestations may recur.

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

Seizure-Prone Patients: Caution should be observed in patients who are prone to convulsions; convulsions have occurred in a few such patients in association with the use of TALWIN, although no cause and effect relationship has been established.

Serotonin Syndrome: TALWIN 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 serotonergic 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. TALWIN 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**).

Peri-Operative Considerations

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

Physicians should individualize treatment, moving from parenteral to oral analgesics as appropriate. Thereafter, if TALWIN 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).

Pentazocine hydrochloride 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.

TALWIN 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

TALWIN 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 pentazocine hydrochloride 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. Pentazocine hydrochloride should be used with extreme caution in patients with substantially decreased respiratory reserve, bronchial asthma established respiratory depression, obstructive respiratory conditions, 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 TALWIN, 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 TALWIN 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 TALWIN are essential. Overestimating the TALWIN 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**).

TALWIN tablets contain sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

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 TALWIN, as in these patients, even usual therapeutic doses of TALWIN 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 TALWIN 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**).

Special Populations

Special Risk Groups: Pentazocine hydrochloride 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, Addison's disease, hypothyroidism, myxedema, toxic psychosis, prostatic hypertrophy or urethral stricture.

Pregnant Women: Studies in humans have not been conducted. TALWIN crosses the placental barrier and is contraindicated in pregnant women. Animal reproduction studies have revealed no evidence of harm to the fetus due to pentazocine hydrochloride, teratogenic effects were reported only at doses high enough to cause maternal toxicity.

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, may be life-threatening (see **WARNINGS AND PRECAUTIONS, Neonatal Opioid Withdrawal Syndrome (NOWS), ADVERSE REACTIONS**).

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.

There have been rare reports of a withdrawal syndrome in newborns after prolonged use of TALWIN by the mother during pregnancy.

The safe use of TALWIN in pregnant women (other than during labor) has not been established.

Patients receiving TALWIN during labor have experienced no adverse effects other than those that occur with commonly used narcotic analgesics. Pentazocine can cross the placental barrier and can cause central nervous system depression in the newborn and, if used regularly throughout pregnancy, may lead to symptoms of withdrawal in the newborn. TALWIN should be used with caution in women delivering premature infants.

In case of pentazocine abuse during pregnancy, there is a risk of intrauterine growth retardation.

Labour, Delivery and Nursing Women: Since opioids can cross the placental barrier and are excreted in breast milk, TALWIN is contraindicated in nursing women and during labor 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 opioids, should be readily available if TALWIN is used in this population.

Pediatrics (< 18 years of age): The safety and efficacy of TALWIN have not been studied in the pediatric population. Therefore, use of TALWIN is not recommended in patients under 18 years of age.

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:

Although laboratory tests have not indicated that TALWIN causes or increases hepatic impairment, the drug should be administered with caution to patients with such impairment. Extensive liver disease appears to predispose to a higher incidence of side effects (e.g. marked apprehension, anxiety, dizziness, sleepiness) with the usual clinical dose, and may be the result of decreased metabolism of the drug by the liver (see **DOSAGE AND ADMINISTRATION** and **ACTION AND CLINICAL PHARMACOLOGY**).

Patients with Renal Impairment:

Although laboratory tests have not indicated that TALWIN causes or increases renal impairment, the drug should be administered with caution to patients with such impairment (see **DOSAGE AND ADMINISTRATION**).

ADVERSE REACTIONS**Adverse Drug Reaction Overview**

Adverse effects of TALWIN (pentazocine hydrochloride) 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 reactions of TALWIN are sedation or somnolence, vertigo, nausea, vomiting, dizziness, lightheadedness and sweating. Sedation may be more marked in the elderly.

The following adverse effects occur less frequently with opioid analgesics and include those reported in TALWIN clinical trials, whether related or not to pentazocine hydrochloride:

Cardiovascular: infrequently hypotension, tachycardia, hypertension, and circulatory depression.

Dermatologic/Allergic: allergic reactions sometimes severe have been reported including edema of the face or anaphylactic shock, flushed skin including plethora, dermatitis including pruritus. Erythema multiforme, toxic epidermal necrolysis have been reported.

Gastrointestinal: constipation, abdominal distress, anorexia, diarrhoea, dry mouth, biliary tract spasm.

Central and Peripheral Nervous System: euphoria, lightheadedness, headache, dizziness, weakness, disturbed dreams, hallucinations, visual disturbances, insomnia, tinnitus, irritability, excitement, sweating, infrequently flushing or chills, disorientation, paresthesia, syncope, grand mal convulsions, increased intracranial pressure, confusion, tremor.

Hallucinations were noted to occur more frequently when doses exceeding that recommended were employed.

Genitourinary: urinary retention

Hematologic: depression of white blood cell count, with rare cases of agranulocytosis, which is usually reversible, moderate transient eosinophilia.

Hepatobiliary: Scattered reports of abnormal liver function of questionable significance were noted during the clinical trials.

Musculoskeletal and connective tissue: muscle tremor

Ophthalmic: miosis

Pregnancy, puerperium and perinatal conditions: alterations in rate of strength of uterine contractions during labor, alterations in maturation.

Respiratory: respiratory depression

Other: chills

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.

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

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/hypnotics, tricyclic antidepressants, tranquilizers, general anesthetics, antipsychotics, phenothiazines, antihistamines, antiemetics, and alcohol) and beta-blockers, increases the risk of sedation, respiratory depression, 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 sedation and respiratory depression (see **WARNINGS AND PRECAUTIONS, Neurologic, Interactions with Central Nervous System Depressants (including benzodiazepines and alcohol) and Psychomotor Impairment**). TALWIN should not be consumed with alcohol as it may increase the chance of experiencing dangerous side effects.

Drug-Drug Interactions

TALWIN can antagonize the effects of opiate agonists such as diamorphine, morphine, and heroin and is itself antagonized by naloxone.

Because pentazocine has narcotic antagonist activity, it may provoke withdrawal symptoms if given to narcotic addicts, and it should be given with caution to patients recently being treated with large doses of narcotics.

Concomitant use of monoamine oxidase inhibitors (MAOIs) with TALWIN may cause CNS excitation and hypertension through their respective effects on catecholamines. Caution should, therefore, be observed in administering TALWIN to patients who are currently receiving MAOIs or who have received them within the preceding 14 days.

Coadministration of pentazocine hydrochloride 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 **WARNINGS AND PRECAUTIONS**).

Drug-Lifestyle Interactions

Tobacco smoking could enhance the metabolic clearance rate of TALWIN reducing the clinical effectiveness of a standard dose of TALWIN.

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

DOSAGE AND ADMINISTRATION

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

For acute pain, it is recommended that TALWIN 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 243 mg (90 morphine milligram equivalent) daily of TALWIN not be exceeded. Each patient should be assessed for their risk prior to prescribing TALWIN, 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 TALWIN (see **DOSAGE AND ADMINISTRATION, Adjustment or Reduction of Dosage).**

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

Dosing Considerations

TALWIN (pentazocine hydrochloride tablets) 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**).

TALWIN is not indicated for rectal administration.

TALWIN should be taken after meals, with a glass of water.

Recommended Dose and Dosage Adjustment

Individual dosing requirements vary considerably based on each patient's age, weight, severity and cause of pain, and medical and analgesic history.

Adults:

Patients Not Receiving Opioids at the Time of Initiation of TALWIN Treatment:

The usual adult starting dose is 50 mg every 4 hours after meals. Dosage should be adjusted to individual requirements and tolerance within the range of 50-100 mg (1-2 tabs) every 3 to 4 hours. Total daily oral dose should not exceed 600 mg.

Patients Currently Receiving Opioids

For patients who are receiving an alternate opioid, the "oral pentazocine 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 pentazocine 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.

Opioid switching / rotation:

Conversion ratios for opioids are subject to variations in kinetics governed by genetics and other factors. Therefore, when switching from one opioid to another, **reduce calculated dose by 25-50%** to minimize the risk of overdose. Subsequently, up-titrate the dose as required to reach appropriate maintenance dose.

Table 1: Opioid Conversion Table^a

Opioids	To convert to oral morphine equivalent, multiply by	To convert from oral morphine, multiply by	Daily 90 mg MED^b
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
Pentazocine	0.37	2.7	243 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.

a. Adapted from the 2017 Canadian guideline for opioids for chronic non-cancer pain. McMaster University; 2017

b. MED: Morphine Equivalent Dose

Patients with Hepatic Impairment:

Although laboratory tests have not indicated that TALWIN causes or increases hepatic impairment, the drug should be administered with caution to patients with such impairment. (see **WARNINGS AND PRECAUTIONS**).

Patients with Renal Impairment:

Although laboratory tests have not indicated that TALWIN causes or increases renal impairment, the drug should be administered with caution to patients with such impairment. (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. TALWIN should be initiated at a low dose and slowly titrated to effect (see **WARNINGS AND PRECAUTIONS** and **ACTION AND CLINICAL PHARMACOLOGY**).

Use with Non-Opioid Medications:

If a non-opioid analgesic is being provided, it may be continued. If the non-opioid is discontinued, consideration should be given to increasing the opioid dose to compensate for the non-opioid analgesic. When anti-inflammatory or antipyretic effects are desired in addition to analgesia, acetyl salicylic acid (A.S.A.) can be administered concomitantly with TALWIN.

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 TALWIN. 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 **WARNINGS AND PRECAUTIONS**). Tapering should be individualized and carried out under medical supervision.

The 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.

Disposal

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

TALWIN should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended. Unused or expired TALWIN 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: The symptoms and clinical signs of TALWIN overdose may resemble those of morphine or other opioids. They may include somnolence, respiratory depression, hypotension, hypertension, tachycardia, hallucinations or seizures. Circulatory failure and deepening coma may occur in more severe cases, particularly in patients who have also ingested other CNS depressants such as alcohol, sedative/hypnotics or antihistamines.

Treatment: Adequate measures to maintain ventilation and general circulatory support should be employed and consideration given to gastric lavage and gastric aspiration. For respiratory depression due to overdose or unusual sensitivity to TALWIN, parenteral naloxone is a specific and effective antagonist. Initial doses of 0.4 to 2.0 mg of naloxone are recommended, repeated at 2-3 minute intervals if needed, up to a total of 10 mg. Anticonvulsant therapy may be necessary.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

TALWIN (pentazocine hydrochloride) is a member of the benzazocine series of synthetic benzomorphans. It produces both analgesic (agonist) and narcotic antagonist effects.

Opiate antagonism: Pentazocine weakly antagonizes the analgesic effects of morphine, meperidine and phenazocine. In addition, it produces incomplete reversal of cardiovascular, respiratory and behavioral depression produced by morphine and meperidine. Pentazocine has about 1/50 the antagonistic activity of nalorphine.

Pharmacodynamics

Central Nervous System:

Pentazocine hydrochloride 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 CO₂ tension and to electrical stimulation.

Pentazocine hydrochloride 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.

Pentazocine hydrochloride 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:

Pentazocine hydrochloride 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:

Pentazocine hydrochloride 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, hypertension 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 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.

Absorption:

TALWIN is well absorbed from the gastrointestinal tract. The onset of analgesia following oral administration of TALWIN can occur within 15 to 30 minutes and the duration of effect is usually 3 hours or longer. The onset and duration of analgesia are, in part, related to the dose and severity of pretreatment pain. Peak serum levels of TALWIN occur between 1 and 3 hours after oral administration and the elimination half-life in plasma ranges between 2 to 5 hours. There is considerable variability between individuals in terms of the rate of TALWIN metabolism which may also account for the variability in analgesic response.

Oral bioavailability is low and somewhat variable between patients.

Metabolism:

TALWIN is extensively metabolized in the liver.

Excretion:

The metabolites are excreted by the kidney with only a small amount of unchanged drug excreted in the urine. Approximately 60% of an oral dose is eliminated in the urine in 24 hours.

Special Populations and Conditions

Pediatrics: Individuals under 18 years of age should not take TALWIN.

Hepatic Impairment:

Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment. Extensive liver disease appears to predispose to a higher incidence of side effects (e.g. marked apprehension, anxiety, dizziness, sleepiness) with the usual clinical dose, and may be the result of decreased metabolism of the drug by the liver.

Renal Impairment:

Although laboratory tests have not indicated that **TALWIN** causes or increases renal impairment, the drug should be administered with caution to patients with such impairment.

STORAGE AND STABILITY

Store between 15 and 30°C.

DOSAGE FORMS, COMPOSITION AND PACKAGING**Composition:**

Round, flat, bevelled white tablets of 50 mg engraved with “FTL” on one side and “50” on the other side.

Medicinal ingredient: Each tablet contains pentazocine hydrochloride equivalent to 50 mg base.

TALWIN is included in the Schedule to the Narcotic Control Act.

Non-medicinal ingredients: Aerosil, avicel, cornstarch, dibasic calcium phosphate, magnesium stearate, kolliphor, sodium metabisulphite.

Packaging:

- Blisters of 100 (10 x 10) tablets.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

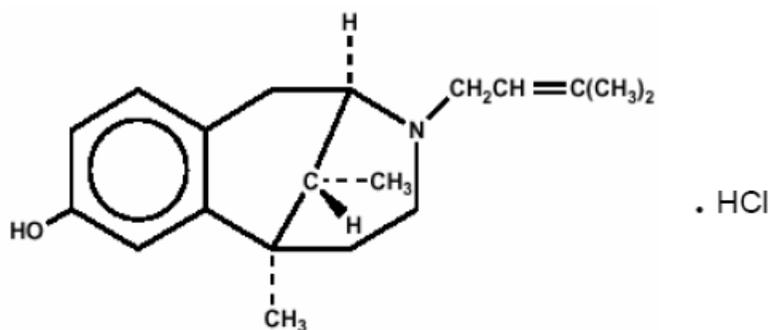
Proper name: pentazocine hydrochloride

Chemical name: 2R*,6R*,11R*)-1,2,3,4,5,6-Hexahydro-6,11-dimethyl-3-(3-methyl-2-butenyl)-2,6-methano-3-benzazocin-8-ol hydrochloride

Molecular formula and molecular mass:

$C_{19}H_{27}NO \cdot HCl$ M.W. 321.88

Structural formula:



Physicochemical Properties:

pentazocine hydrochloride is a white, crystalline substance soluble in acidic aqueous solutions.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PART III: PATIENT MEDICATION INFORMATION

® TALWIN®

pentazocine hydrochloride tablets, 50 mg

Read this carefully before you start taking **TALWIN** 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 **TALWIN**.

Serious Warnings and Precautions

- **Even if you take TALWIN as prescribed you are at a risk for opioid addiction, abuse and misuse. This can lead to overdose and death.**
- **When you take TALWIN it must be swallowed whole. Do not cut, break, crush, chew, or 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 TALWIN. This is less likely to happen if you take it as prescribed by your doctor. Babies are at risk of life-threatening breathing problems if their mothers take opioids while pregnant or nursing.**
- **You should never give anyone your TALWIN. They could die from taking it. If a person has not been prescribed TALWIN, taking even one dose can cause a fatal overdose. This is especially true for children.**
- **If you took TALWIN 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 TALWIN 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 TALWIN used for?

TALWIN is used to manage your pain.

How does TALWIN work?

TALWIN 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.

What are the ingredients in TALWIN?

Medicinal ingredient: pentazocine hydrochloride

Non-medicinal ingredients: Aerosil, avicel, cornstarch, dibasic calcium phosphate, magnesium stearate, kolliphor, sodium metabisulphite.

TALWIN comes in the following dosage forms:

- Tablets, 50 mg

Do not use TALWIN if:

- your doctor did not prescribe it for you
- you are allergic to pentazocine hydrochloride or any of the other ingredients in TALWIN (see **What are the ingredients in TALWIN?**)
- 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 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, or recently had, a planned surgery
- you are pregnant or planning to become pregnant
- you are breastfeeding

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

- have a history of illicit or prescription drug or alcohol abuse
- have severe kidney, liver or lung disease
- have low blood pressure
- have past or current depression
- suffer from chronic or severe constipation
- have acute inflammation of the gallbladder or inflammation in the pancreas
- have blockage that inhibits the flow of urine through its normal path (the urinary tract)
- have porphyria (genetic disease in which your body builds-up chemicals with skin, nervous system or other symptoms)
- have chronic inflammation or blockage of all or part of your digestive tract or narrowing of the stomach.
- have problems with your thyroid, adrenal or prostate gland
- have, or had in the past, hallucinations or other severe mental problems
- suffer from migraines

Other warnings you should know about:

Opioid dependence and addiction: There are important differences between physical dependence and addiction. It is important that you talk to your doctor if you have questions or concerns about abuse, addiction or physical dependence.

Pregnancy, nursing, labor and delivery:

Do not use TALWIN while pregnant, nursing, during labor or delivery. Opioids can be transferred to your baby through breast milk, or while still in the womb. TALWIN can then cause life-threatening breathing problems in your unborn baby or nursing infant.

If you are pregnant and are taking TALWIN, 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 doctor will monitor and guide you on how to slowly stop taking TALWIN. 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 TALWIN. TALWIN can cause:

- drowsiness
- dizziness or
- lightheadedness

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

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 doctor may do tests, give you another medication, and slowly take you off TALWIN.

Serotonin Syndrome: TALWIN can cause Serotonin Syndrome, 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 Syndrome if you take TALWIN with certain anti-depressants or migraine medications.

Serotonin Syndrome 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.

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.

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 TALWIN:

- Alcohol. This includes prescription and non-prescription medications that contain alcohol. **Do not** drink alcohol while you are taking TALWIN. It can lead to:
 - drowsiness
 - unusually slow or weak breathing
 - serious side effects or
 - a fatal overdose
- other sedative drugs which may enhance the drowsiness caused by TALWIN
- other opioid analgesics (drugs used to treat pain)
- 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 TALWIN 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
- drugs used to treat migraines (e.g. triptans)
- St. John's Wort

How to take TALWIN:

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.

Usual Adult Starting Dose:

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.

Your doctor will prescribe the lowest dose that works to control your pain. It is recommended that you only take TALWIN for up to 7 days. If you need to take TALWIN for longer, your doctor will determine the best dose for you to lower the risk of side effects and overdose. Higher doses can lead to more side effects and a greater chance of overdose.

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

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

Stopping your Medication

If you have been taking TALWIN for more than a few days you should not stop taking it all of a sudden. Your doctor will monitor and guide you on how to slowly stop taking TALWIN. 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 TALWIN.

Refilling your Prescription for TALWIN:

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

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

Overdose:

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

Signs of overdose may include:

- unusually slow or weak breathing
- dizziness
- confusion
- extreme drowsiness

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 doctor before restarting your medication.

What are possible side effects from using TALWIN?

These are not all the possible side effects you may feel when taking TALWIN. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- Drowsiness
- Insomnia

- Sleepiness
- Dizziness
- Fainting
- Nausea, vomiting, or a poor appetite
- Dry mouth
- Headache
- Problems with vision
- Weakness, uncoordinated muscle movement
- Itching
- Sweating
- Constipation
- Low sex drive, impotence (erectile dysfunction), infertility

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

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			✓
Bowel Blockage (impaction): abdominal pain, severe constipation, nausea			✓
Withdrawal: nausea, vomiting, diarrhea, anxiety, shivering, cold and clammy skin, body aches, loss of appetite, sweating.		✓	

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	
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			✓

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.

<p>Reporting Side Effects</p> <p>You can report any suspected side effects associated with the use of health products to Health Canada by:</p> <ul style="list-style-type: none"> • 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. <p><i>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.</i></p>
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Storage:

- **Keep unused or expired TALWIN in a secure place to prevent theft, misuse or accidental exposure.**
- **Store between 15 and 30°C.**
- **Keep TALWIN 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 TALWIN, get emergency help right away.**

Disposal:

TALWIN 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 TALWIN:

- 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's website (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.sanofi.ca, or by calling 1-800-265-7927.

This leaflet was prepared by sanofi-aventis Canada Inc.

Last Revised: May 22, 2018