

TEMAZEPAM- temazepam capsule
PD-Rx Pharmaceuticals, Inc.

Temazepam Capsules, USP 
(temazepam)

Rx only

WARNING: RISKS FROM CONCOMITANT USE WITH OPIOIDS; ABUSE, MISUSE, AND ADDICTION; and DEPENDENCE AND WITHDRAWAL REACTIONS

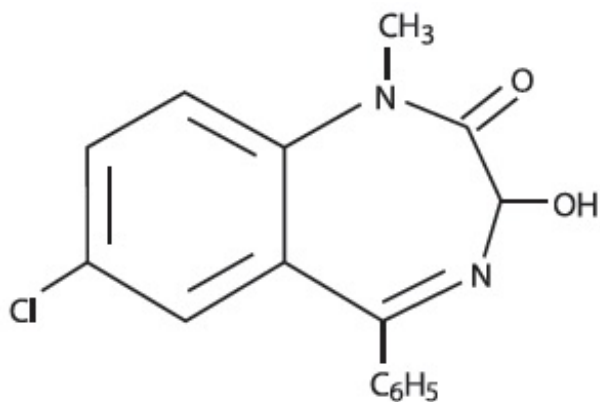
Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of these drugs in patients for whom alternative treatment options are inadequate. Limit dosages and durations to the minimum required. Follow patients for signs and symptoms of respiratory depression and sedation.

The use of benzodiazepines, including temazepam, exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death. Abuse and misuse of benzodiazepines commonly involve concomitant use of other medications, alcohol, and/or illicit substances, which is associated with an increased frequency of serious adverse outcomes. Before prescribing temazepam and throughout treatment, assess each patient's risk for abuse, misuse, and addiction (see WARNINGS).

The continued use of benzodiazepines, including Temazepam, may lead to clinically significant physical dependence. The risks of dependence and withdrawal increase with longer treatment duration and higher daily dose. Abrupt discontinuation or rapid dosage reduction of temazepam after continued use may precipitate acute withdrawal reactions, which can be life-threatening. To reduce the risk of withdrawal reactions, use a gradual taper to discontinue temazepam or reduce the dosage (see DOSAGE AND ADMINISTRATION and WARNINGS).

DESCRIPTION

Temazepam is a benzodiazepine hypnotic agent. The chemical name is 7-chloro-1,3-dihydro-3-hydroxy-1-methyl-5-phenyl-2H-1, 4-benzodiazepin-2-one, and the structural formula is:



$C_{16}H_{13}ClN_2O_2$

MW = 300.74

Temazepam is a white, crystalline substance, very slightly soluble in water and sparingly soluble in alcohol USP.

Temazepam capsules, 7.5 mg, 15 mg, 22.5 mg and 30 mg, are for oral administration.

7.5 mg, 15 mg, 22.5 mg and 30 mg Capsules Active Ingredient: temazepam USP

7.5 mg Capsules

Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, FD&C Red #40 and titanium dioxide.

May also include: sodium lauryl sulfate. Imprinting ink may contain ammonium hydroxide, ethanol, isopropyl alcohol, butanol, shellac, potassium hydroxide, propylene glycol, and black iron oxide.

15 mg Capsules

Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, FD&C Blue #1, FD&C yellow # 6, gelatin and titanium dioxide.

May also include: sodium lauryl sulfate. Imprinting ink may contain ammonium hydroxide, ethanol, isopropyl alcohol, butanol, shellac, potassium hydroxide, propylene glycol, and black iron oxide.

22.5 mg Capsules

Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, FD&C Blue #1, FD&C Red #40, gelatin and titanium dioxide.

May also include: sodium lauryl sulfate. Imprinting ink may contain ammonium hydroxide, ethanol, isopropyl alcohol, butanol, shellac, potassium hydroxide, propylene glycol, and black iron oxide.

30 mg Capsules

Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, gelatin and titanium dioxide.

May also include: sodium lauryl sulfate. Imprinting ink may contain ammonium hydroxide, ethanol, isopropyl alcohol, butanol, shellac, potassium hydroxide, propylene glycol, and black iron oxide.

CLINICAL PHARMACOLOGY

Pharmacokinetics

In a single and multiple dose absorption, distribution, metabolism, and excretion (ADME) study, using ^3H labeled drug, temazepam was well absorbed and found to have minimal (8%) first pass metabolism. There were no active metabolites formed and the only significant metabolite present in blood was the O-conjugate. The unchanged drug was 96% bound to plasma proteins. The blood level decline of the parent drug was biphasic with the short half-life ranging from 0.4 to 0.6 hours and the terminal half-life from 3.5 to 18.4 hours (mean 8.8 hours), depending on the study population and method of determination. Metabolites were formed with a half-life of 10 hours and excreted with a half-life of approximately 2 hours. Thus, formation of the major metabolite is the rate limiting step in the biodisposition of temazepam. There is no accumulation of metabolites. A dose-proportional relationship has been established for the area under the plasma concentration/time curve over the 15 to 30 mg dose range.

Temazepam was completely metabolized through conjugation prior to excretion; 80% to 90% of the dose appeared in the urine. The major metabolite was the O-conjugate of temazepam (90%); the O-conjugate of N-desmethyl temazepam was a minor metabolite (7%).

Bioavailability, Induction, and Plasma Levels

Following ingestion of a 30 mg temazepam capsule, measurable plasma concentrations were achieved 10 to 20 minutes after dosing with peak plasma levels ranging from 666 to 982 ng/mL (mean 865 ng/mL) occurring approximately 1.2 to 1.6 hours (mean 1.5 hours) after dosing.

In a 7 day study, in which subjects were given a 30 mg temazepam capsule 1 hour before retiring, steady-state (as measured by the attainment of maximal trough concentrations) was achieved by the third dose. Mean plasma levels of temazepam (for days 2 to 7) were 260 ± 210 ng/mL at 9 hours and 75 ± 80 ng/mL at 24 hours after dosing. A slight trend toward declining 24 hour plasma levels was seen after day 4 in the study, however, the 24 hour plasma levels were quite variable.

At a dose of 30 mg once-a-day for 8 weeks, no evidence of enzyme induction was found in man.

Elimination Rate of Benzodiazepine Hypnotics and Profile of Common Untoward Effects

The type and duration of hypnotic effects and the profile of unwanted effects during administration of benzodiazepine hypnotics may be influenced by the biologic half-life of the administered drug and for some hypnotics, the half-life of any active metabolites formed. Benzodiazepine hypnotics have a spectrum of half-lives from short (<4 hours) to long (>20 hours). When half-lives are long, drug (and for some drugs their active metabolites) may accumulate during periods of nightly administration and be associated with impairments of cognitive and/or motor performance during waking hours; the

possibility of interaction with other psychoactive drugs or alcohol will be enhanced. In contrast, if half-lives are shorter, drug (and, where appropriate, its active metabolites) will be cleared before the next dose is ingested, and carry-over effects related to excessive sedation or CNS depression should be minimal or absent. However, during nightly use for an extended period, pharmacodynamic tolerance or adaptation to some effects of benzodiazepine hypnotics may develop. If the drug has a short elimination half-life, it is possible that a relative deficiency of the drug, or, if appropriate, its active metabolites (i.e., in relationship to the receptor site) may occur at some point in the interval between each night's use. This sequence of events may account for 2 clinical findings reported to occur after several weeks of nightly use of rapidly eliminated benzodiazepine hypnotics, namely, increased wakefulness during the last third of the night, and the appearance of increased signs of daytime anxiety.

Controlled Trials Supporting Efficacy

Temazepam improved sleep parameters in clinical studies. Residual medication effects ("hangover") were essentially absent. Early morning awakening, a particular problem in the geriatric patient, was significantly reduced.

Patients with chronic insomnia were evaluated in 2 week, placebo controlled sleep laboratory studies with temazepam at doses of 7.5 mg, 15 mg, and 30 mg, given 30 minutes prior to bedtime. There was a linear dose-response improvement in total sleep time and sleep latency, with significant drug-placebo differences at 2 weeks occurring only for total sleep time at the 2 higher doses, and for sleep latency only at the highest dose.

In these sleep laboratory studies, REM sleep was essentially unchanged and slow wave sleep was decreased. No measurable effects on daytime alertness or performance occurred following temazepam treatment or during the withdrawal period, even though a transient sleep disturbance in some sleep parameters was observed following withdrawal of the higher doses. There was no evidence of tolerance development in the sleep laboratory parameters when patients were given temazepam nightly for at least 2 weeks.

In addition, normal subjects with transient insomnia associated with first night adaptation to the sleep laboratory were evaluated in 24 hour, placebo controlled sleep laboratory studies with temazepam at doses of 7.5 mg, 15 mg, and 30 mg, given 30 minutes prior to bedtime. There was a linear dose-response improvement in total sleep time, sleep latency and number of awakenings, with significant drug-placebo differences occurring for sleep latency at all doses, for total sleep time at the 2 higher doses and for number of awakenings only at the 30 mg dose.

INDICATIONS & USAGE

Temazepam Capsules, USP are indicated for the short-term treatment of insomnia (generally 7 to 10 days). For patients with short-term insomnia, instructions in the prescription should indicate that Temazepam Capsules should be used for short periods of time (7 to 10 days).

The clinical trials performed in support of efficacy were 2 weeks in duration with the final formal assessment of sleep latency performed at the end of treatment.

WARNINGS

Risks from Concomitant Use with Opioids

Concomitant use of benzodiazepines, including Temazepam, and opioids may result in profound sedation, respiratory depression, coma, and death. Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug related mortality compared to use of opioids alone. If a decision is made to prescribe Temazepam concomitantly with opioids, prescribe the lowest effective dosages and minimum durations of concomitant use, and follow patients closely for signs and symptoms of respiratory depression and sedation. In patients already receiving an opioid analgesic, prescribe a lower initial dose of Temazepam than indicated in the absence of an opioid and titrate based on clinical response. If an opioid is initiated in a patient already taking Temazepam, prescribe a lower initial dose of the opioid and titrate based upon clinical response.

Advise both patients and caregivers about the risks of respiratory depression and sedation when Temazepam is used with opioids. Advise patients not to drive or operate heavy machinery until the effects of concomitant use with the opioid have been determined (see *PRECAUTIONS*, Drug Interactions).

Abuse, Misuse, and Addiction

The use of benzodiazepines, including temazepam, exposes users to the risks of abuse, misuse, and addiction, which can lead to overdose or death. Abuse and misuse of benzodiazepines often (but not always) involve the use of doses greater than the maximum recommended dosage and commonly involve concomitant use of other medications, alcohol, and/or illicit substances, which is associated with an increased frequency of serious adverse outcomes, including respiratory depression, overdose, or death (see DRUG ABUSE AND DEPENDENCE, Abuse).

Before prescribing temazepam and throughout treatment, assess each patient's risk for abuse, misuse, and addiction (e.g., using a standardized screening tool). Use of temazepam, particularly in patients at elevated risk, necessitates counseling about the risks and proper use of temazepam along with monitoring for signs and symptoms of abuse, misuse, and addiction. Prescribe the lowest effective dosage; avoid or minimize concomitant use of CNS depressants and other substances associated with abuse, misuse, and addiction (e.g., opioid analgesics, stimulants); and advise patients on the proper disposal of unused drug. If a substance use disorder is suspected, evaluate the patient and institute (or refer them for) early treatment, as appropriate.

Dependence and Withdrawal Reactions

To reduce the risk of withdrawal reactions, use a gradual taper to discontinue temazepam or reduce the dosage (a patient-specific plan should be used to taper the dose) (see DOSAGE AND ADMINISTRATION, Discontinuation or Dosage Reduction of

temazepam).

Patients at an increased risk of withdrawal adverse reactions after benzodiazepine discontinuation or rapid dosage reduction include those who take higher dosages, and those who have had longer durations of use.

Acute Withdrawal Reactions

The continued use of benzodiazepines, including temazepam, may lead to clinically significant physical dependence. Abrupt discontinuation or rapid dosage reduction of temazepam after continued use, or administration of flumazenil (a benzodiazepine antagonist) may precipitate acute withdrawal reactions, which can be life-threatening (e.g., seizures) (see DRUG ABUSE AND DEPENDENCE, Dependence).

Protracted Withdrawal Syndrome

In some cases, benzodiazepine users have developed a protracted withdrawal syndrome with withdrawal symptoms lasting weeks to more than 12 months (see DRUG ABUSE AND DEPENDENCE, Dependence).

Sleep disturbance may be the presenting manifestation of an underlying physical and/or psychiatric disorder. Consequently, a decision to initiate symptomatic treatment of insomnia should only be made after the patient has been carefully evaluated. **The failure of insomnia to remit after 7 to 10 days of treatment may indicate the presence of a primary psychiatric and/or medical illness that should be evaluated.** Worsening of insomnia may be the consequence of an unrecognized psychiatric or physical disorder as may the emergence of new abnormalities of thinking or behavior. Such abnormalities have also been reported to occur in association with the use of drugs with central nervous system depressant activity, including those of the benzodiazepine class. Because some of the worrisome adverse effects of benzodiazepines, including temazepam, appear to be dose related (see **PRECAUTIONS** and **DOSAGE AND ADMINISTRATION**), it is important to use the lowest possible effective dose. Elderly patients are especially at risk.

Some of these changes may be characterized by decreased inhibition, e.g., aggressiveness and extroversion that seem out of character, similar to that seen with alcohol. Other kinds of behavioral changes can also occur, for example, bizarre behavior, agitation, hallucinations, and depersonalization. Complex behaviors such as "sleep-driving" (i.e., driving while not fully awake after ingestion of a sedative-hypnotic, with amnesia for the event) have been reported. These events can occur in sedative-hypnotic-naïve as well as in sedative-hypnotic-experienced persons. Although behaviors such as sleep-driving may occur with temazepam alone at therapeutic doses, the use of alcohol and other CNS depressants with temazepam appears to increase the risk of such behaviors, as does the use of temazepam at doses exceeding the maximum recommended dose. Due to the risk to the patient and the community, discontinuation of temazepam should be strongly considered for patients who report a "sleep-driving" episode. Other complex behaviors (e.g., preparing and eating food, making phone calls, or having sex) have been reported in patients who are not fully awake after taking a sedative-hypnotic. As with "sleep-driving", patients usually do not remember these events. Amnesia and other neuro-psychiatric symptoms may occur unpredictably. In primarily depressed patients, worsening of depression, including suicidal thinking has been reported in association with the use of sedative/hypnotics.

It can rarely be determined with certainty whether a particular instance of the abnormal behaviors listed above is drug induced, spontaneous in origin, or a result of an underlying psychiatric or physical disorder. Nonetheless, the emergence of any new

behavioral sign or symptom of concern requires careful and immediate evaluation.

Because Temazepam can cause drowsiness and a decreased level of consciousness, patients, particularly the elderly, are at higher risk of falls.

Severe Anaphylactic and Anaphylactoid Reactions

Rare cases of angioedema involving the tongue, glottis or larynx have been reported in patients after taking the first or subsequent doses of sedative-hypnotics, including temazepam. Some patients have had additional symptoms such as dyspnea, throat closing, or nausea and vomiting that suggest anaphylaxis. Some patients have required medical therapy in the emergency department. If angioedema involves the tongue, glottis or larynx, airway obstruction may occur and be fatal. Patients who develop angioedema after treatment with temazepam should not be rechallenged with the drug.

Neonatal Sedation and Withdrawal Syndrome

Use of temazepam late in pregnancy can result in sedation (respiratory depression, lethargy, hypotonia) and/or withdrawal symptoms (hyperreflexia, irritability, restlessness, tremors, inconsolable crying, and feeding difficulties) in the neonate (see PRECAUTIONS, Pregnancy). Monitor neonates exposed to Restoril during pregnancy or labor for signs of sedation and monitor neonates exposed to temazepam during pregnancy for signs of withdrawal; manage these neonates accordingly.

PRECAUTIONS

General

Since the risk of the development of oversedation, dizziness, confusion, and/or ataxia increases substantially with larger doses of benzodiazepines in elderly and debilitated patients, 7.5 mg of temazepam is recommended as the initial dosage for such patients.

Temazepam should be administered with caution in severely depressed patients or those in whom there is any evidence of latent depression; it should be recognized that suicidal tendencies may be present and protective measures may be necessary.

The usual precautions should be observed in patients with impaired renal or hepatic function and in patients with chronic pulmonary insufficiency.

If temazepam is to be combined with other drugs having known hypnotic properties or CNS-depressant effects, consideration should be given to potential additive effects.

The possibility of a synergistic effect exists with the co-administration of temazepam and diphenhydramine. One case of stillbirth at term has been reported 8 hours after a pregnant patient received temazepam and diphenhydramine. A cause and effect relationship has not yet been determined (seeCONTRAINDICATIONS)

Information for Patients

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

Risks from Concomitant Use with Opioids

Advise both patients and caregivers about the risks of potentially fatal respiratory depression and sedation when temazepam is used with opioids and not to use such drugs concomitantly unless supervised by a healthcare provider. Advise patients not to

drive or operate heavy machinery until the effects of concomitant use with the opioid have been determined (see WARNINGS, Risks from Concomitant Use with Opioids and PRECAUTIONS, Drug Interactions).

Abuse, Misuse, and Addiction

Inform patients that the use of temazepam, even at recommended dosages, exposes users to risks of abuse, misuse, and addiction, which can lead to overdose and death, especially when used in combination with other medications (e.g., opioid analgesics), alcohol, and/or illicit substances. Inform patients about the signs and symptoms of benzodiazepine abuse, misuse, and addiction; to seek medical help if they develop these signs and/or symptoms; and on the proper disposal of unused drug (see WARNINGS, Abuse, Misuse, and Addiction and DRUG ABUSE AND DEPENDENCE). Withdrawal Reactions

Inform patients that the continued use of temazepam may lead to clinically significant physical dependence and that abrupt discontinuation or rapid dosage reduction of temazepam may precipitate acute withdrawal reactions, which can be life-threatening. Inform patients that in some cases, patients taking benzodiazepines have developed a protracted withdrawal syndrome with withdrawal symptoms lasting weeks to more than 12 months. Instruct patients that discontinuation or dosage reduction of temazepam may require a slow taper (see WARNINGS, Dependence and Withdrawal Reactions and DRUG ABUSE AND DEPENDENCE).

“Sleep-Driving” and Other Complex Behaviors

There have been reports of people getting out of bed after taking a sedative-hypnotic and driving their cars while not fully awake, often with no memory of the event. If a patient experiences such an episode, it should be reported to his or her doctor immediately, since “sleep-driving” can be dangerous. This behavior is more likely to occur when temazepam is taken with alcohol or other central nervous system depressants (seeWARNINGS). Other complex behaviors (e.g., preparing and eating food, making phone calls, or having sex) have been reported in patients who are not fully awake after taking a sedative-hypnotic. As with "sleep-driving", patients usually do not remember these events.

Advise patients that increased drowsiness and decreased consciousness may increase the risk of falls in some patients.

Pregnancy

Advise pregnant females that use of temazepam late in pregnancy can result in sedation (respiratory depression, lethargy, hypotonia) and/or withdrawal symptoms (hyperreflexia, irritability, restlessness, tremors, inconsolable crying, and feeding difficulties) in newborns (see Warnings, Neonatal Sedation and Withdrawal Syndrome and Precautions, Pregnancy). Instruct patients to inform their healthcare provider if they are pregnant.

Nursing

Instruct patients to notify their healthcare provider if they are breastfeeding or intend to breastfeed. Instruct breastfeeding patients using temazepam to monitor infants for excessive sedation, poor feeding and poor weight gain, and to seek medical attention if they notice these signs (see Precautions, Nursing Mothers).

Laboratory Tests

The usual precautions should be observed in patients with impaired renal or hepatic function and in patients with chronic pulmonary insufficiency.

Abnormal liver function tests as well as blood dyscrasias have been reported with benzodiazepines.

Drug Interactions

The concomitant use of benzodiazepines and opioids increases the risk of respiratory depression because of actions at different receptor sites in the CNS that control respiration. Benzodiazepines interact at GABAA sites and opioids interact primarily at mu receptors. When benzodiazepines and opioids are combined, the potential for benzodiazepines to significantly worsen opioid-related respiratory depression exists. Limit dosage and duration of concomitant use of benzodiazepines and opioids, and monitor patients closely for respiratory depression and sedation.

The benzodiazepines, including temazepam, produce additive CNS-depressant effects when co-administered with other CNS depressants such as alcohol, barbiturates, antipsychotics, sedative/hypnotics, anxiolytics, antidepressants, narcotic analgesics, sedative antihistamines, anticonvulsants, and anesthetics.

The pharmacokinetic profile of temazepam does not appear to be altered by orally administered cimetidine dosed according to labeling.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies were conducted in rats at dietary temazepam doses up to 160 mg/kg/day for 24 months and in mice at dietary doses of 160 mg/kg/day for 18 months. No evidence of carcinogenicity was observed although hyperplastic liver nodules were observed in female mice exposed to the highest dose. The clinical significance of this finding is not known.

Fertility in male and female rats was not adversely affected by Temazepam.

No mutagenicity tests have been done with Temazepam.

Pregnancy

Risk Summary

Neonates born to mothers using benzodiazepines late in pregnancy have been reported to experience symptoms of sedation and/or neonatal withdrawal (see WARNINGS, Neonatal Sedation and Withdrawal Syndrome and Clinical Considerations). Available data from published observational studies of pregnant women exposed to benzodiazepines do not report a clear association with benzodiazepines and major birth defects (see Data).

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated risk of major birth defects and of miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Benzodiazepines cross the placenta and may produce respiratory depression, hypotonia and sedation in neonates. Monitor neonates exposed to Temazepam during pregnancy or labor for signs of sedation, respiratory depression, hypotonia, and feeding problems. Monitor neonates exposed to Temazepam during pregnancy for signs of withdrawal. Manage these neonates accordingly (see WARNINGS, Neonatal Sedation and Withdrawal Syndrome).

Data

Human Data

Published data from observational studies on the use of benzodiazepines during pregnancy do not report a clear association with benzodiazepines and major birth defects. Although early studies reported an increased risk of congenital malformations with diazepam and chlordiazepoxide, there was no consistent pattern noted. In addition, the majority of more recent case-control and cohort studies of benzodiazepine use during pregnancy, which were adjusted for confounding exposures to alcohol, tobacco and other medications, have not confirmed these findings.

Animal Data

Reproduction studies in animals with temazepam were performed in rats and rabbits. In a perinatal-postnatal study in rats, oral doses of 60 mg/kg/day resulted in increasing nursing mortality. Teratology studies in rats demonstrated increased fetal resorptions at doses of 30 and 120 mg/kg in one study and increased occurrence of rudimentary ribs, which are considered skeletal variants, in a second study at doses of 240 mg/kg or higher. In rabbits, occasional abnormalities such as exencephaly and fusion or asymmetry of ribs were reported without dose relationship. Although these abnormalities were not found in the concurrent control group, they have been reported to occur randomly in historical controls. At doses of 40 mg/kg or higher, there was an increased incidence of the 13th rib variant when compared to the incidence in concurrent and historical controls.

Nursing Mothers

Risk Summary

Temazepam is present in breast milk. There are reports of sedation, poor feeding and poor weight gain in infants exposed to benzodiazepines through breast milk. The effects of temazepam on milk production are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for temazepam and any potential adverse effects on the breastfed infant from temazepam or from the underlying maternal condition.

Clinical Considerations

Infants exposed to temazepam through breast milk should be monitored for sedation, poor feeding and poor weight gain.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Clinical studies of Temazepam did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in response between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy commonly observed in this population. Temazepam 7.5 mg is recommended as the initial dosage for patient aged 65 and over since the risk of the development of oversedation, dizziness, confusion, ataxia and/or falls increases substantially with larger doses of benzodiazepines in elderly and debilitated patients.

ADVERSE REACTIONS

During controlled clinical studies in which 1076 patients received temazepam at bedtime, the drug was well tolerated. Side effects were usually mild and transient. Adverse reactions occurring in 1% or more of patients are presented in the following table:

	Temazepam % Incidence (n=1076)	Placebo % Incidence (n=783)
Drowsiness	9.1	5.6
Headache	8.5	9.1
Fatigue	4.8	4.7
Nervousness	4.6	8.2
Lethargy	4.5	3.4
Dizziness	4.5	3.3
Nausea	3.1	3.8
Hangover	2.5	1.1
Anxiety	2.0	1.5
Depression	1.7	1.8
Dry Mouth	1.7	2.2
Diarrhea	1.7	1.1
Abdominal Discomfort	1.5	1.9
Euphoria	1.5	0.4
Weakness	1.4	0.9
Confusion	1.3	0.5
Blurred Vision	1.3	1.3
Nightmares	1.2	1.7
Vertigo	1.2	0.8

The following adverse events have been reported less frequently (0.5% to 0.9%):

Central Nervous System-anorexia, ataxia, equilibrium loss, tremor, increased dreaming

Cardiovascular-dyspnea, palpitations

Gastrointestinal-vomiting

Musculoskeletal-backache

Special Senses-hyperhidrosis, burning eyes

Amnesia, hallucinations, horizontal nystagmus, and paradoxical reactions including restlessness, overstimulation and agitation were rare (less than 0.5%).

DRUG ABUSE AND DEPENDENCE

Controlled Substance

Temazepam Capsules contains temazepam, a Schedule IV controlled substance.

Abuse

Temazepam is a benzodiazepine and a CNS depressant with a potential for abuse and addiction. Abuse is the intentional, non-therapeutic use of a drug, even once, for its desirable psychological or physiological effects. Misuse is the intentional use, for therapeutic purposes, of a drug by an individual in a way other than prescribed by a healthcare provider or for whom it was not prescribed. Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use (e.g., continuing drug use despite harmful consequences, giving a higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence. Even taking benzodiazepines as prescribed may put patients at risk for abuse and misuse of their medication. Abuse and misuse of benzodiazepines may lead to addiction.

Abuse and misuse of benzodiazepines often (but not always) involve the use of doses greater than the maximum recommended dosage and commonly involve concomitant use of other medications, alcohol, and/or illicit substances, which is associated with an increased frequency of serious adverse outcomes, including respiratory depression, overdose, or death. Benzodiazepines are often sought by individuals who abuse drugs and other substances, and by individuals with addictive disorders (see WARNINGS, Abuse, Misuse, and Addiction).

The following adverse reactions have occurred with benzodiazepine abuse and/or misuse: abdominal pain, amnesia, anorexia, anxiety, aggression, ataxia, blurred vision, confusion, depression, disinhibition, disorientation, dizziness, euphoria, impaired concentration and memory, indigestion, irritability, muscle pain, slurred speech, tremors, and vertigo.

The following severe adverse reactions have occurred with benzodiazepine abuse and/or misuse: delirium, paranoia, suicidal ideation and behavior, seizures, coma, breathing difficulty, and death. Death is more often associated with polysubstance use (especially benzodiazepines with other CNS depressants such as opioids and alcohol).

Dependence

Physical Dependence

Temazepam may produce physical dependence from continued therapy. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug. Abrupt discontinuation or rapid dosage reduction of benzodiazepines or administration of flumazenil, a benzodiazepine antagonist, may precipitate acute withdrawal reactions, including seizures, which can be life-threatening. Patients at an increased risk of withdrawal adverse reactions after benzodiazepine discontinuation or rapid dosage reduction include those who take higher dosages (i.e., higher and/or more frequent doses) and those who have had longer durations of use (see WARNINGS, Dependence and Withdrawal Reactions).

To reduce the risk of withdrawal reactions, use a gradual taper to discontinue temazepam or reduce the dosage (see DOSAGE and ADMINISTRATION, Discontinuation or Dosage Reduction of Temazepam and WARNINGS, Dependence and Withdrawal Reactions).

Acute Withdrawal Signs and Symptoms

Acute withdrawal signs and symptoms associated with benzodiazepines have included abnormal involuntary movements, anxiety, blurred vision, depersonalization, depression, derealization, dizziness, fatigue, gastrointestinal adverse reactions (e.g., nausea, vomiting, diarrhea, weight loss, decreased appetite), headache, hyperacusis, hypertension, irritability, insomnia, memory impairment, muscle pain and stiffness, panic attacks, photophobia, restlessness, tachycardia, and tremor. More severe acute withdrawal signs and symptoms, including life-threatening reactions, have included catatonia, convulsions, delirium tremens, depression, hallucinations, mania, psychosis, seizures, and suicidality.

Protracted Withdrawal Syndrome

Protracted withdrawal syndrome with benzodiazepines is characterized by anxiety, cognitive impairment, depression, insomnia, formication, motor symptoms (e.g., weakness, tremor, muscle twitches), paresthesia, and tinnitus that persists beyond 4 to 6 weeks after initial benzodiazepine withdrawal. Protracted withdrawal symptoms may last weeks to more than 12 months. As a result, there may be difficulty in differentiating withdrawal symptoms from potential re-emergence or continuation of symptoms for which the benzodiazepine was being used.

Tolerance

Tolerance to temazepam may develop from continued therapy. Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose). Tolerance to the therapeutic effect of temazepam may develop; however, little tolerance develops to the amnestic reactions and other cognitive impairments caused by benzodiazepines.

OVERDOSAGE

Overdosage of benzodiazepines is characterized by central nervous system depression ranging from drowsiness to coma. In mild to moderate cases, symptoms can include drowsiness, confusion, dysarthria, lethargy, hypnotic state, diminished reflexes, ataxia, and hypotonia. Rarely, paradoxical or disinhibitory reactions (including agitation, irritability, impulsivity, violent behavior, confusion, restlessness, excitement, and talkativeness) may occur. In severe overdosage cases, patients may develop respiratory depression and coma. Overdosage of benzodiazepines in combination with other CNS depressants (including alcohol and opioids) may be fatal (see WARNINGS, Abuse, Misuse, and Addiction). Markedly abnormal (lowered or elevated) blood pressure, heart rate, or respiratory rate raise the concern that additional drugs and/or alcohol are involved in the overdosage.

In managing benzodiazepine overdosage, employ general supportive measures, including intravenous fluids and airway management. Flumazenil, a specific benzodiazepine receptor antagonist indicated for the complete or partial reversal of the sedative effects of benzodiazepines in the management of benzodiazepine overdosage, can lead to withdrawal and adverse reactions, including seizures, particularly in the context of mixed overdosage with drugs that increase seizure risk (e.g., tricyclic and

tetracyclic antidepressants) and in patients with long-term benzodiazepine use and physical dependency. The risk of withdrawal seizures with flumazenil use may be increased in patients with epilepsy. Flumazenil is contraindicated in patients who have received a benzodiazepine for control of a potentially life-threatening condition (e.g., status epilepticus). If the decision is made to use flumazenil, it should be used as an adjunct to, not as a substitute for, supportive management of benzodiazepine overdose. See the flumazenil injection Prescribing Information.

Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

DOSAGE & ADMINISTRATION

While the recommended usual adult dose is 15 mg before retiring, 7.5 mg may be sufficient for some patients, and others may need 30 mg. In transient insomnia, a 7.5 mg dose may be sufficient to improve sleep latency. In elderly or debilitated patients, it is recommended that therapy be initiated with 7.5 mg until individual responses are determined.

Discontinuation or Dosage Reduction of Temazepam Capsules

To reduce the risk of withdrawal reactions, use a gradual taper to discontinue temazepam or reduce the dosage. If a patient develops withdrawal reactions, consider pausing the taper or increasing the dosage to the previous tapered dosage level. Subsequently decrease the dosage more slowly (see WARNINGS, Dependence and Withdrawal Reactions and DRUG ABUSE AND DEPENDENCE: Dependence).

HOW SUPPLIED

Temazepam Capsules USP

15 mg

Blue opaque cap and white opaque body, imprinted “15 mg” on cap and “Novel 121” on the body in black ink.

NDC 55289-196-14 Bottles of 14

NDC 55289-196-30 Bottles of 30

NDC 55289-196-60 Bottles of 60

NDC 55289-196-90 Bottles of 90

NDC 55289-196-01 Bottles of 100

NDC 55289-196-82 Bottles of 500

Dispense in a well-closed, light-resistant container with a child-resistant closure.

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

MEDICATION GUIDE

TEMAZEPAM (tem az' e pam) Capsules, C-IV

What is the most important information I should know about temazepam?

- **temazepam is a benzodiazepine medicine. Taking benzodiazepines with opioid medicines, alcohol, or other central nervous system depressants (including street drugs) can cause severe drowsiness, breathing problems (respiratory depression), coma and death.** Get emergency help right away if any of the following happens:
 - shallow or slowed breathing
 - breathing stops (which may lead to the heart stopping)
 - excessive sleepiness (sedation)

Do not drive or operate heavy machinery until you know how taking temazepam and opioids affects you.

- **Risk of abuse, misuse, and addiction.** There is a risk of abuse, misuse, and addiction with benzodiazepines including temazepam which can lead to overdose and serious side effects including coma and death.
- **Serious side effects including coma and death have happened in people who have abused or misused benzodiazepines, including temazepam.** These serious side effects may also include delirium, paranoia, suicidal thoughts or actions, seizures, and difficulty breathing . **Call your healthcare provider or go to the nearest hospital emergency room right away if you get any of these serious side effects.**
- **You can develop an addiction even if you take temazepam as prescribed by your healthcare provider**
- **Take temazepam exactly as your healthcare provider prescribed.**
- Do not share your temazepam with other people.
- Keep TEMAZEPAM in a safe place and away from children.
- **Physical dependence and withdrawal reactions.** Temazepam can cause physical dependence and withdrawal reactions.
- **Do not suddenly stop taking temazepam.** Stopping temazepam suddenly can cause serious and life- threatening side effects, including, unusual movements, responses, or expressions, seizures, sudden and severe mental or nervous system changes, depression, seeing or hearing things that others do not see or hear, an extreme increase in activity or talking, losing touch with reality, and suicidal thoughts or actions. **Call your healthcare provider or go to the nearest hospital emergency room right away if you get any of these symptoms.**
- **Some people who suddenly stop benzodiazepines have symptoms that can last for several weeks to more than 12 months,** including, anxiety, trouble remembering, learning, or concentrating, depression, problems sleeping, feeling like insects are crawling under your skin, weakness, shaking, muscle twitching, burning or prickling feeling in your hands, arms, legs or feet, and ringing in your ears.
- Physical dependence is not the same as drug addiction. Your healthcare provider can tell you more about the differences between physical dependence and drug addiction.
- Do not take more temazepam than prescribed or take temazepam for longer than prescribed.
- After taking temazepam, you may get up out of bed while not being fully awake and do an activity that you do not know you are doing. The next morning, you may not remember that you did anything during the night. You have a higher chance for doing these activities if you drink alcohol or take other medicines that make you sleepy with temazepam. Reported activities include:

- o driving a car (“sleep-driving”)
- o making and eating food
- o talking on the phone
- o having sex
- o sleep-walking

Call your healthcare provider right away if you find out that you have done any of the above activities after taking temazepam.

What is temazepam?

- Temazepam is a prescription sleep medicine. TEMA ZEPAM is used in adults for the short-term (usually 7 to 10 days) treatment of a sleep problem called insomnia. Symptoms of insomnia include trouble falling asleep and waking up often during the night.

- **Temazepam is a federal controlled substance (C-IV) because it contains temazepam that can be abused or lead to dependence.** Keep temazepam in a safe place to prevent misuse and abuse. Selling or giving away temazepam may harm others, and is against the law. Tell your healthcare provider if you have ever abused or been dependent on alcohol, prescription medicines or street drugs.

- It is not known if temazepam is safe and effective in children.
- It is not known if temazepam is safe and effective for use longer than 2 weeks.

Do not take temazepam if you:

- are allergic to temazepam or any of the ingredients in temazepam. See the end of this Medication Guide for a complete list of ingredients in temazepam.

Before you take temazepam, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of depression, mental illness or, suicidal thoughts
- have a history of drug or alcohol abuse or addiction
- have lung disease or breathing problems
- are pregnant or plan to become pregnant.
 - Taking temazepam late in pregnancy may cause your baby to have symptoms of sedation (breathing problems, sluggishness, low muscle tone), and/or withdrawal symptoms (jitteriness, irritability, restlessness, shaking, excessive crying, feeding problems)
 - Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment with temazepam.
- are breastfeeding, or plan to breastfeed. temazepam can pass through your breast milk.
 - Breastfeeding during treatment with temazepam may cause your baby to have sleepiness, feeding problems, and decreased weight gain.
 - Talk to your healthcare provider about the best way to feed your baby if you take temazepam.

Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking temazepam with certain other medicines can cause side effects or affect how well temazepam or the other medicines work. Do not start or stop other medicines

without talking to your healthcare provider.

Do not take temazepam with other medicines that can make you sleepy unless your healthcare provider tells you to.

How should I take temazepam?

- **See “What is the most important information I should know about temazepam?”**

- Take temazepam exactly as your healthcare providers tell you to take it. Take temazepam right before you get into bed.

- Do not take temazepam unless you are able to get a full night’s sleep before you must be active again.

- If you take too much temazepam or overdose, get emergency treatment right away.

What are the possible side effects of temazepam?

temazepam may cause serious side effects, including:

- **See “What is the most important information I should know about temazepam?”**

- **Abnormal thoughts and behavior.**Symptoms include more outgoing or aggressive behavior than normal, confusion, agitation, hallucinations, worsening of depression, and suicidal thoughts.

- **Severe allergic reactions.**Symptoms include swelling of the tongue or throat, trouble breathing, and nausea and vomiting. Get emergency medical help right away if you have these symptoms after taking temazepam.

Temazepam can make you sleepy or dizzy and can slow your thinking and motor skills.

- Do not drive, operate heavy machinery, or do other dangerous activities until you know how temazepam affects you.

- **Do not drink alcohol or take other drugs that may make you sleepy or dizzy while taking temazepam talking to your healthcare provider.**When taken with alcohol or other drugs that cause sleepiness or

- dizziness, temazepam may make your sleepiness or dizziness much worse.

The most common side effects of temazepam include:

- drowsiness
- headache
- tiredness
- nervousness
- dizziness
- nausea

You may still feel drowsy the next day after taking temazepam. **Do not drive or do other dangerous activities after taking temazepam until you feel fully awake.**

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

How should I store TEMAZEPAM?

- Store temazepam between 68°F to 77°F (20°C to 25°C).

- **Keep temazepam and all medicines out of the reach of children.**

General information about the safe and effective use of temazepam.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use temazepam for a condition for which it was not prescribed. Do not give temazepam to other people, even if they have the same symptoms that you have. It may harm them. You can ask your healthcare provider or pharmacist for information about temazepam that is written for healthcare professionals.

What are the ingredients in temazepam?**7.5mg, 15mg, 22.5mg and 30mg Capsules**

Active Ingredient: temazepam USP

7.5 mg Capsules

Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, FD&C Red #40 and titanium dioxide.

May also include: sodium lauryl sulfate. Imprinting ink may contain ammonium hydroxide, ethanol, isopropyl alcohol, butanol, shellac, potassium hydroxide, propylene glycol, and black iron oxide.

15 mg Capsules

Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, FD&C Blue #1, FD&C yellow # 6, gelatin and titanium dioxide.

May also include: sodium lauryl sulfate. Imprinting ink may contain ammonium hydroxide, ethanol, isopropyl alcohol, butanol, shellac, potassium hydroxide, propylene glycol, and black iron oxide.

22.5 mg Capsules

Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, FD&C Blue #1, FD&C Red #40, gelatin and titanium dioxide.

May also include: sodium lauryl sulfate. Imprinting ink may contain ammonium hydroxide, ethanol, isopropyl alcohol, butanol, shellac, potassium hydroxide, propylene glycol, and black iron oxide.

30 mg Capsules

Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, gelatin and titanium dioxide.

May also include: sodium lauryl sulfate. Imprinting ink may contain ammonium hydroxide, ethanol, isopropyl alcohol, butanol, shellac, potassium hydroxide, propylene glycol, and black iron oxide.

If you would like more information, call Novel Laboratories, Inc. at 1-866-403-7592

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

Manufactured by:

Novel Laboratories, Inc

Somerset, NJ 08873

Distributed by:

ASCEND Laboratories, LLC

Parsippany, NJ 07054

SAP Code: 272731

Rev: 08/2023

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

TEMAZEPAM CIV

Capsules, USP 15 mg PHARMACIST: PLEASE DISPENSE WITH
MEDICATION GUIDE PROVIDED SEPARATELY Rx only

Keep this and all drugs out of the reach of children.
Storage: Store at 20°-25°C (68°-77°F) [See USP Controlled Room Temperature]. Protect from light and moisture. Dispense in a tight, light-resistant container as defined in the USP using a child resistant closure.
Usual Adult Dosage:
See package insert
May Cause Drowsiness. Use Caution While Driving Or Performing Tasks Requiring Mental Alertness. Avoid Alcohol. Do not accept if seal over bottle opening is broken or missing.

NDC 55289-196-82


TEMAZEPAM
15 mg
Each capsule contains:
Temazepam USP 15 mg
500 Capsules

Rx Only




3 55289 19682 2

Marketed and Packaged by:
PD-Rx Pharmaceuticals, Inc
Oklahoma City, OK 73127
1-405-942-3040 v. 8.19.0

Manufactured by:
Novel Laboratories, Inc.
Somerset, NJ 08873

 GTIN: 00355289196822
SNO: D20A120001
EXP: 11/2021
LOT: D20A12

TEMAZEPAM CIV

Capsules, USP 15 mg

Rx only

TEMAZEPAM

temazepam capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:55289-196(NDC:67877-146)	
Route of Administration	ORAL	DEA Schedule	CIV	
Active Ingredient/Active Moiety				
Ingredient Name			Basis of Strength	Strength
TEMAZEPAM (UNII: CHB1QD2QSS) (TEMAZEPAM - UNII:CHB1QD2QSS)			TEMAZEPAM	15 mg
Inactive Ingredients				
Ingredient Name			Strength	
STARCH, CORN (UNII: O8232NY3SJ)				
ANHYDROUS LACTOSE (UNII: 3SY5LH9PMK)				
MAGNESIUM STEARATE (UNII: 70097M6I3O)				
SODIUM LAURYL SULFATE (UNII: 368GB5141J)				
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)				
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)				
AMMONIA (UNII: 5138Q19F1X)				
ALCOHOL (UNII: 3K9958V90M)				
ISOPROPYL ALCOHOL (UNII: ND2M416302)				
BUTYL ALCOHOL (UNII: 8PJ61P6TS3)				
SHELLAC (UNII: 46N107B71O)				
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)				
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)				
FERROSOFERRIC OXIDE (UNII: XM0M87F357)				
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)				
GELATIN (UNII: 2G86QN327L)				
Product Characteristics				
Color	blue (blue opaque cap) , white (white opaque body)		Score	no score
Shape	CAPSULE		Size	19mm
Flavor			Imprint Code	15;mg;Novel;121
Contains				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:55289-196-14	14 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	02/05/2016	
2	NDC:55289-196-30	30 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	02/05/2016	
3	NDC:55289-196-60	60 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	02/05/2016	
4	NDC:55289-196-90	90 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	12/13/2018	
5	NDC:55289-196-01	100 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	02/05/2016	

6	NDC:55289-196-82	500 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	04/20/2020	
Marketing Information				
Marketing Category	Application Number or Monograph Citation		Marketing Start Date	Marketing End Date
ANDA	ANDA071456		04/21/1987	

Labeler - PD-Rx Pharmaceuticals, Inc. (156893695)

Registrant - PD-Rx Pharmaceuticals, Inc. (156893695)

Establishment			
Name	Address	ID/FEI	Business Operations
PD-Rx Pharmaceuticals, Inc.		156893695	repack(55289-196)

Revised: 10/2025

PD-Rx Pharmaceuticals, Inc.