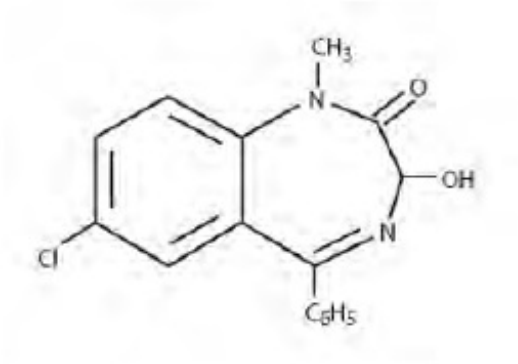
STRAZEPAM - temazepam, choline
Physician Therapeutics LLC

Disclaimer: This drug has not been found by FDA to be safe and effective, and this labeling has not been approved by FDA. For further information about unapproved drugs, click here.

Strazepam

DESCRIPTION Temazepam is a benzodiazepine hypnotic agent. The chemical name is 7-chloro 1,3-dihydro-3-hydroxyl-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, 15 mg and 30 mg, are for oral administration. 15 mg and 30 mg Capsules Active Ingredient: temazepam USP 15 mg Capsules Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, FDandC Blue #1, FDandC yellow # 5, FDandC yellow # 6, gelatin and titanium dioxide.

May also include: benzyl alcohol, butylparaben, sodium lauryl sulfate, edetate calcium disodium, methylparaben, propyl paraben and sodium propionate. Imprinting ink may contain ammonium hydroxide, ethanol, 2-propanol, butanol, pharmaceutical shellac, potassium hydroxide, propylene glycol, black iron oxide, and other ingredents. 30 mg Capsules Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, gelatin and titanium dioxide. May also include: benzyl alcohol, butylparaben, sodium lauryl sulfate, edetate calcium disodium, methylparaben, propyl paraben and sodium propionate. Imprinting ink may contain ammonium hydroxide, ethanol, 2-propanol, butanol, pharmaceutical shellac, potassium hydroxide, propylene glycol, black iron oxide, and other ingredents. Structural Formula

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 doseresponse 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 AND 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.

CONTRAINDICATIONS Benzodiazepines may cause fetal harm when administered to a pregnant

woman. An increased risk of congenital malformations associated with the use of diazepam and chlordiazepoxide during the first trimester of pregnancy has been suggested in several studies. Transplacental distribution has resulted in neonatal CNS depression following the ingestion of therapeutic doses of a benzodiazepine hypnotic during the last weeks of pregnancy. Reproduction studies in animals with temazepam were performed in rats and rabbits. In a perinatalpostnatal study in rats, oral doses of 60 mg/kg/day resulted in increasing nursling 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.

Temazepam is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. Patients should be instructed to discontinue the drug prior to becoming pregnant. The possibility that a woman of childbearing potential may be pregnant at the time of institution of therapy should be considered.

WARNINGS 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 "sleepdriving" (i.e., driving while not fully awake after ingestion of a sedativehypnotic, with amnesia for the event) have been reported. These events can occur in sedativehypnoticnaive 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 sleepdriving, 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. Withdrawal symptoms (of the barbiturate type) have occurred after the abrupt discontinuation of benzodiazepines (see DRUG ABUSE AND DEPENDENCE).

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.

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; and 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 (see CONTRAINDICATIONS).

Information for Patients The text of a patient Medication Guide is printed at the end of this insert. To assure safe and effective use of temazepam, the information and instructions provided in this patient Medication Guide should be discussed with patients. Special Concerns "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 (see WARNINGS). 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.

Laboratory Test 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 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 Pregnancy Category X (see CONTRAINDICATIONS).

Nursing Mothers It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when temazepam is administered to a nursing woman.

Pediatric Use Safety and effectiveness in pediatric patients have not been established.

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 Abuse and addiction are separate and distinct from physical dependence and tolerance. Abuse is characterized by misuse of the drug for non-medical purposes, often in combination with other psychoactive substances. Physical dependence is a state of adaptation that is manifested by a specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug and/or administration of an antagonist. Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time. Tolerance may occur to both the desired and undesired effects of drugs and may develop at different rates for different effects. Addiction is a primary, chronic, neurobiological disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. Drug addiction is a treatable disease, utilizing a multidisciplinary approach, but relapse is common.

Controlled Substance Temazepam is a controlled substance in Schedule IV.

Abuse and Dependence Withdrawal symptoms, similar in character to those noted with barbiturates and alcohol (convulsions, tremor, abdominal, and muscle cramps, vomiting, and sweating), have occurred following abrupt discontinuance of benzodiazepines. The more severe withdrawal symptoms have usually been limited to those patients who received excessive doses over an extended period of time.

Generally milder withdrawal symptoms (e.g., dysphoria and insomnia) have been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months. Consequently, after extended therapy at doses higher than 15 mg, abrupt discontinuation should generally be avoided and a gradual dosage tapering schedule followed. As with any hypnotic, caution must be exercised in administering temazepam to individuals known to be addiction-prone or to those whose history suggests they may increase the dosage on their own initiative. It is desirable to limit repeated prescriptions without adequate medical supervision.

OVERDOSAGE

Manifestations of acute overdosage of temazepam can be expected to reflect the CNS effects of the drug and include somnolence, confusion, and coma, with reduced or absent reflexes, respiratory depression, and hypotension. The oral LD50 of temazepam was 1963 mg/kg in mice, 1833 mg/kg in rats, and >2400 mg/kg in rabbits.

Treatment If the patient is conscious, vomiting should be induced mechanically or with emetics. Gastric lavage should be employed utilizing concurrently a cuffed endotracheal tube if the patient is unconscious to prevent aspiration and pulmonary complications. Maintenance of adequate pulmonary ventilation is essential. The use of pressor agents intravenously may be necessary to combat hypotension. Fluids should be administered intravenously to encourage diuresis. The value of dialysis has not been determined. If excitation occurs, barbiturates should not be used. It should be borne in mind that multiple agents may have been ingested. Flumazenil (Romazicorn®)*, a specific benzodiazepine receptor antagonist, is indicated for the complete or partial reversal of the sedative effects of benzodiazepines and may be used in situations when an overdose with a benzodiazepine is known or suspected. Prior to the administration of flumazenil, necessary measures should be instituted to secure airway, ventilation, and intravenous access. Flumazenil is intended as an adjunct to, not as a substitute for, proper management of benzodiazepine overdose. Patients treated with flumazenil should be monitored for re-sedation, respiratory depression, and other residual benzodiazepine effects for an appropriate period after treatment. The prescriber should be aware of a risk of seizure in association with flumazenil treatment, particularly in long-term benzodiazepine users and in cyclic antidepressant overdose. The complete flumazenil package insert including CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS should be consulted prior to use. Up-to-date information about the treatment of overdose can often be obtained from a certified Regional Poison Control Center. Telephone numbers of certified Regional Poison Control Centers are listed in the Physicians' Desk References®**

DOSAGE AND 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.

HOW SUPPLIED Temazepam Capsules USP 15 mg Green opaque cap and white opaque body, imprinted "15 mg" on cap and "Novel 121" on the body in black ink.

Bottle of 100.....NDC 67877-146-01
Bottle of 500.....NDC 67877-146-05

30 mg White opaque cap and body, imprinted "30 mg" on cap and "Novel 123" on the body in black ink.
Bottle of 100.....NDC 67877-147-01
Bottle of 500.....NDC 67877-147-05

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

*Romazicon is the registered trademark of Hoffman-LaRoche Inc.

**Trademark of Medical Economics Company, Inc.

Manufactured by:

Distributed by: Novel Laboratories, Inc.

ASCEND Laboratories, LLC Somerset, NJ 08873

Montvale, NJ 07645

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

MEDICATION GUIDE TEMAZEPAM Capsules, USP C-IV (temazepam) Read the Medication Guide that comes with TEMAZEPAM before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your doctor about your medical condition or treatment.

What is the most important information I should know about TEMAZEPAM? 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: • driving a car ("sleep-driving") • making and eating food • talking on the phone • having sex • sleep-walking Call your doctor right away if you find out that you have done any of the above activities after taking TEMAZEPAM. Important: 1. Take TEMAZEPAM exactly as prescribed • Do not take more TEMAZEPAM than prescribed. • Take TEMAZEPAM right before you get in bed, not sooner. 2. Do not take TEMAZEPAM if you: • drink alcohol • take other medicines that can make you sleepy. Talk to your doctor about all of your medicines. Your doctor will tell you if you can take TEMAZEPAM with your other medicines • cannot get a full night's sleep

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What is TEMAZEPAM? TEMAZEPAM is a sedative-hypnotic (sleep) medicine. TEMAZEPAM 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 • waking up often during the night TEMAZEPAM is not for children. TEMAZEPAM is a federally controlled substance (C-IV) because it 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 doctor if you have ever abused or been dependent on alcohol, prescription medicines or street drugs.

Who should not take TEMAZEPAM?

Do not take TEMAZEPAM if you are pregnant or planning to become pregnant. TEMAZEPAM may cause birth defects or harm a fetus (unborn baby). TEMAZEPAM may not be right for you. Before starting TEMAZEPAM, tell your doctor about all of your health conditions, including if you:
• have a history of depression, mental illness, or suicidal • have a history of drug or alcohol abuse or addiction
• have kidney or liver disease
• have a lung disease or breathing problems
• are breastfeeding Tell your doctor about all of the medicines you take including prescription and nonprescription medicines, vitamins and herbal supplements. Medicines can interact with each other, sometimes causing serious side effects. Do not take TEMAZEPAM with other medicines that can make you sleepy. Know the medicines you take. Keep a list of your medicines with you to show your doctor and pharmacist each time you get a new medicine. How should I take TEMAZEPAM? • Take TEMAZEPAM exactly as prescribed. Do not take more TEMAZEPAM than prescribed for you.

• 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.
• Call your doctor if your insomnia worsens or is not better within 7 to 10 days. This may mean that there is another condition causing your sleep problems.
• If you take too much TEMAZEPAM or overdose, call your doctor or poison control center right

away, or get emergency treatment. What are the possible side effects of TEMAZEPAM? Possible serious side effects of TEMAZEPAM include:
• getting out of bed while not being fully awake and do an activity that you do not know you are doing. (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.
• memory loss
• anxiety
• severe allergic reactions. Symptoms include swelling of the tongue or throat, trouble breathing, and nausea and vomiting. Get emergency medical help if you get these symptoms after taking TEMAZEPAM. Call your doctor right away if you have any of the above side effects or any other side effects that worry you while using TEMAZEPAM.

The most common side effects of TEMAZEPAM are:
• drowsiness
• headache
• tiredness
• nervousness
• dizziness
• nausea
• "hangover" feeling the day after taking TEMAZEPAM

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. You may have withdrawal symptoms if you stop taking TEMAZEPAM suddenly. Withdrawal symptoms can be serious and include seizures. Mild withdrawal symptoms include a depressed mood and trouble sleeping. Talk to your doctor to check if you need to stop TEMAZEPAM slowly. These are not all the side effects of TEMAZEPAM. Ask your doctor or pharmacist for more information. How should I store TEMAZEPAM? • Store TEMAZEPAM at room temperature, 68° to 77°F (20° to 25°C). • Keep TEMAZEPAM and all medicines out of reach of children. General Information about 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 share TEMAZEPAM with other people, even if you think they have the same symptoms that you have. It may harm them and it is against the law. This Medication Guide summarizes the most important information about TEMAZEPAM. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about TEMAZEPAM that is written for healthcare professionals. What are the ingredients in TEMAZEPAM? TEMAZEPAM is a federally controlled substance (C-IV) because it 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 doctor if you have ever abused or been dependent on alcohol, prescription medicines or street drugs. 15mg and 30mg Capsules

Active Ingredient: temazepam USP 15 mg Capsules

Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, FDandC Blue #1, FDandC yellow # 5, FDandC yellow # 6, gelatin and titanium dioxide. May also include: benzyl alcohol ,butylparaben, sodium lauryl sulfate, edetate calcium disodium, methylparaben, propyl paraben and sodium propionate. Imprinting ink may contain ammonium hydroxide, ethanol, 2-propanol, butanol, pharmaceutical shellac, potassium hydroxide, propylene glycol, black iron oxide, and other ingredents. 30 mg Capsules Inactive Ingredients: Corn starch, lactose anhydrous, magnesium stearate, sodium lauryl sulfate, gelatin and titanium dioxide. May also include: benzyl alcohol ,butylparaben, sodium lauryl sulfate, edetate calcium disodium, methylparaben, propyl paraben and sodium propionate. Imprinting ink

may contain ammonium hydroxide, ethanol, 2-propanol, butanol, pharmaceutical shellac, potassium hydroxide, propylene glycol, black iron oxide, and other ingredents.

Manufactured by: Novel Laboratories, Inc Somerset, NJ 08873

Distributed by: ASCEND Laboratories, LLC Montvale, NJ 07645

ALPI-147-05-00 Rev: 06/09

ASCEND Laboratories, LLC NDC 67877-146-01

TEMAZEPAM CIV Capsules, USP

15 mg

Rx only

100 capsules

INGREDIENTS

Name	Type	Strength	Moiety	UNII	Preferred Substance
temazepam	Active	15 mg In 1	temazepam	CHB1QD2QSS	TEMAZEPAM
starch, corn	Inactive			O8232NY3SJ	STARCH, CORN
anhydrous lactose	Inactive			3SY5LH9PMK	ANHYDROUS LACTOSE
magnesium stearate	Inactive			70097M6I30	MAGNESIUM STEARATE
sodium lauryl sulfate	Inactive			368GB5141J	SODIUM LAURYL SULFATE
FDandC BLUE NO. 1	Inactive			H3R47K3TBD	FDandC BLUE NO. 1
FDandC YELLOW NO. 5	Inactive			I753WB2F1M	FDandC YELLOW NO. 5
FDandC YELLOW NO. 6	Inactive			H77VEI93A8	FDandC YELLOW NO. 6
gelatin	Inactive			2G86QN327L	GELATIN
titanium dioxide	Inactive			15FIX9V2JP	TITANIUM DIOXIDE
benzyl alcohol	Inactive			LKG8494WBH	BENZYL ALCOHOL
butylparaben	Inactive			3QPI1U3FV8	BUTYLPARABEN
sodium lauryl sulfate	Inactive			368GB5141J	SODIUM LAURYL SULFATE
edetate calcium disodium	Inactive			25IH6R4SGF	EDETATE CALCIUM DISODIUM
methylparaben	Inactive			A2I8C7HI9T	METHYLPARABEN
propylparaben	Inactive			Z8IX2SC1OH	PROPYLPARABEN
sodium propionate	Inactive			DK6Y9P42IN	SODIUM PROPIONATE
ammonia	Inactive			5138Q19F1X	AMMONIA
alcohol	Inactive			3K9958V90M	ALCOHOL

isopropyl alcohol	Inactive			ND2M416302	ISOPROPYL ALCOHOL
butyl alcohol	Inactive			8PJ61P6TS3	BUTYL ALCOHOL
shellac	Inactive			46N107B71O	SHELLAC
potassium hydroxide	Inactive			WZH3C48M4T	POTASSIUM HYDROXIDE
propylene glycol	Inactive			6DC9Q167V3	PROPYLENE GLYCOL
ferrosoferric oxide	Inactive			XM0M87F357	FERROSOFERRIC OXIDE

Packaged by Bryant Ranch

North Hollywood CA 91605

Temazepam 15mg(CIV)

Capsule Compare to Restore 15mg(CIV)

Capsule

MYLAN PHARMACEUTICALS NC #30

EXP 11/09 NDC 6362916192 NANA LOT 10973

Rx Only

Do Not Drink Alcohol

May Cause Drowsiness/No Alcohol

Sentra PM™PRODUCT INFORMATION

Sentra PM (U.S. patent pending) capsules by oral administration. A specially formulated Medical Food product, consisting of a proprietary blend of amino acids and polyphenol ingredients in specific proportions, for the dietary management of the metabolic processes of sleep disorders (SD). Must be administered under physician supervision.

Medical Foods Medical Food products are often used in hospitals (e.g., for burn victims or kidney dialysis patients) and outside of a hospital setting under a physician’s care for the dietary management of diseases in patients with particular medical or metabolic needs due to their disease or condition. Congress defined "Medical Food" in the Orphan Drug Act and Amendments of 1988 as "a system which is formulated to be consumed or administered enterally [or orally] under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation." Medical Foods are complex formulated products, requiring sophisticated and exacting technology. Sentra PM has been developed, manufactured, and labeled in accordance with both the statutory and the FDA regulatory definition of a Medical Food. Sentra PM must be used while the patient is under the ongoing care of a physician.

SLEEP DISORDERS (SD)
SD as a Metabolic Deficiency Disease A critical component of the definition of a Medical Food is the requirement for a distinctive nutritional deficiency. FDA scientists have proposed a physiologic definition of a distinctive nutritional deficiency as follows: “the dietary management of patients with specific diseases requires, in some instances, the ability to meet nutritional requirements that differ substantially from the needs of healthy persons. For example, in establishing the recommended dietary allowances for general, healthy population, the Food and Nutrition Board of the Institute of Medicine

National Academy of Sciences, recognized that different or distinctive physiologic requirements may exist for certain persons with "special nutritional needs arising from metabolic disorders, chronic diseases, injuries, premature birth, other medical conditions and drug therapies. Thus, the distinctive nutritional needs associated with a disease reflect the total amount needed by a healthy person to support life or maintain homeostasis, adjusted for the distinctive changes in the nutritional needs of the patient as a result of the effects of the disease process on absorption, metabolism, and excretion." It was also proposed that in patients with certain disease states who respond to nutritional therapies, a physiologic deficiency of the nutrient is assumed to exist. For example, if a patient with sleep disorders responds to a tryptophan formulation by improving the duration and quality of sleep, a deficiency of tryptophan is assumed to exist.

Patients with sleep disorders are known to have nutritional deficiencies of tryptophan, choline, flavonoids, and certain antioxidants. Patients with sleep disorders frequently exhibit reduced plasma levels of tryptophan and have been shown to respond to oral administration of tryptophan or a 5-hydoxytryptophan formulation. Research has shown that tryptophan reduced diets result in a fall of circulating tryptophan. Patients with sleep disorders have activation of the tryptophan degradation pathway that increases the turnover of tryptophan leading to a reduced level of production of serotonin for a given tryptophan blood level. Research has also shown that a genetic predisposition can lead to increased tryptophan requirements in certain patients with sleep disorders.

Choline is required to fully potentiate acetylcholine synthesis by brain neurons. A deficiency of choline leads to reduced acetylcholine production by the neurons. Low fat diets, frequently used by patients with sleep disorders, are usually choline deficient. Flavonoids potentiate the production of acetylcholine by the neurons thereby inducing REM sleep. Low fat diets and diets deficient in flavonoid rich foods result in inadequate flavonoid concentrations, impeding acetylcholine production in certain patients with sleep disorders. Provision of tryptophan, choline, and flavonoids with antioxidants, in specific proportions can restore the production of beneficial serotonin and acetylcholine, thereby improving sleep quality.

PRODUCT DESCRIPTION

Primary Ingredients

Sentra PM consists of a proprietary blend of amino acids, cocoa, ginkgo biloba and flavonoids in specific proportions. These ingredients fall into the category of "Generally Regarded as Safe" (GRAS) as defined by the Food and Drug Administration (FDA) (Sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act). A GRAS substance is distinguished from a food additive on the basis of the common knowledge about the safety of the substance for its intended use. The standard for an ingredient to achieve GRAS status requires not only technical demonstration of non-toxicity and safety, but also general recognition of safety through widespread usage and agreement of that safety by experts in the field. Many ingredients have been determined by the U.S. Food and Drug Administration (FDA) to be GRAS, and are listed as such by regulation, in Volume 21 Code of Federal Regulations (CFR) Sections 182, 184, and 186.

Amino Acids

Amino Acids are the building blocks of protein. All amino acids are GRAS listed as they have been ingested by humans for thousands of years. The doses of the amino acids in Sentra PM are equivalent to those found in the usual human diet; however the formulation uses specific ratios of the key ingredients to elicit a therapeutic response. Patients with sleep disorders may require an increased amount of certain amino acids that cannot be obtained from normal diet alone. Tryptophan, for example, is an obligatory amino acid. The body cannot make tryptophan and must obtain tryptophan from the diet. Tryptophan is needed to produce serotonin. Serotonin is required to induce sleep. Patients with sleep disorders have altered serotonin metabolism. Some patients with sleep disorders have a resistance to the use of tryptophan that is similar to the mechanism found in insulin resistance that is genetically

determined. Patients with sleep disorders frequently cannot acquire sufficient tryptophan from the diet without ingesting a prohibitively large amount of calories, particularly protein rich calories.

Flavonoids

Flavonoids are a group of phytochemical compounds found in all vascular plants including fruits and vegetables. They are a part of a larger class of compounds known as polyphenols. Many of the therapeutic or health benefits of colored fruits and vegetables, cocoa, red wine, and green tea are directly related to their flavonoid content. The specially formulated flavonoids found in Sentra PM cannot be obtained from conventional foods in the necessary proportions to elicit a therapeutic response.

Other Ingredients

Sentra PM contains the following inactive or other ingredients, as fillers, excipients, and colorings: magnesium stearate, microcrystalline cellulose, Maltodextrin NF, gelatin (as the capsule material).

Physical Description

Sentra PM is a yellow to light brown powder. Sentra PM contains L-Glutamic Acid, 5-Hydroxytryptophan as Griffonia Seed Extract, Acetylcarnitine HCL, Choline Bitartrate, Cinnamon, Cocoa, Ginkgo Biloba, and Hawthorn Berry.

CLINICAL PHARMACOLOGY

Mechanism of Action

Sentra PM acts by restoring and maintaining the balance of the neurotransmitters, serotonin and acetylcholine, that are associated with sleep disorders.

Metabolism

The amino acids in Sentra PM are primarily absorbed by the stomach and small intestines. All cells metabolize the amino acids in Sentra PM. Circulating tryptophan and choline blood levels determine the production of serotonin and acetylcholine.

Excretion

Sentra PM is not an inhibitor of cytochrome P450 1A2, 2C9, 2C19, 2D6, or 3A4. These isoenzymes are principally responsible for 95% of all detoxification of drugs, with CYP3A4 being responsible for detoxification of roughly 50% of drugs. Amino acids do not appear to have an effect on drug metabolizing enzymes.

INDICATIONS FOR USE

Sentra PM is intended for the clinical dietary management of the metabolic processes associated with sleep disorders.

CLINICAL EXPERIENCE

The administration of Sentra PM has demonstrated significant functional improvement in the quality and quantity of sleep when used for the dietary management of the metabolic processes associated with sleep disorders. Administration of Sentra PM results in the induction and maintenance of sleep in patients with sleep disorders. Sentra PM has no effect on normal blood pressure.

PRECAUTIONS AND CONTRAINDICATIONS

Sentra PM is contraindicated in an extremely small number of patients with hypersensitivity to any of the nutritional components of Sentra PM.

ADVERSE REACTIONS

Oral supplementation with L-tryptophan or choline at high doses up to 15 grams daily is generally well tolerated. The most common adverse reactions of higher doses — from 15 to 30 grams daily — are nausea, abdominal cramps, and diarrhea. Some patients may experience these symptoms at lower doses. The total combined amount of amino acids in each Sentra PM capsule does not exceed 400 mg.

DRUG INTERACTIONS
Sentra PM does not directly influence the pharmacokinetics of prescription drugs. Clinical experience has shown that administration of Sentra PM may allow for lowering the dose of co-administered drugs under physician supervision.

OVERDOSE
There is a negligible risk of overdose with Sentra PM as the total dosage of amino acids in a one month supply (60 capsules) is less than 24 grams. Overdose symptoms may include diarrhea, weakness, and nausea.

POST-MARKETING SURVEILLANCE
Post-marketing surveillance has shown no serious adverse reactions. Reported cases of mild rash and itching may have been associated with allergies to Sentra PM flavonoid ingredients, including cinnamon, cocoa, and chocolate. The reactions were transient in nature and subsided within 24 hours.

DOSAGE AND ADMINISTRATION
Recommended Administration For the dietary management of the metabolic processes associated with sleep disorders. Take (2) capsules daily at bedtime. An additional dose of one or two capsules may be taken after awakenings during the night. As with most amino acid formulations Sentra PM should be taken without food to increase the absorption of key ingredients.

How Supplied
Sentra PM is supplied in red and white, size 0 capsules in bottles of 60 capsules.

Physician Supervision
Sentra PM is a Medical Food product available by prescription only and must be used while the patient is under ongoing physician supervision.

Sentra PM is supplied to physicians in a recyclable plastic bottle with a child-resistant cap.

U.S. patents pending.

Manufactured by Arizona Nutritional Supplements, Inc. Chandler AZ 85225

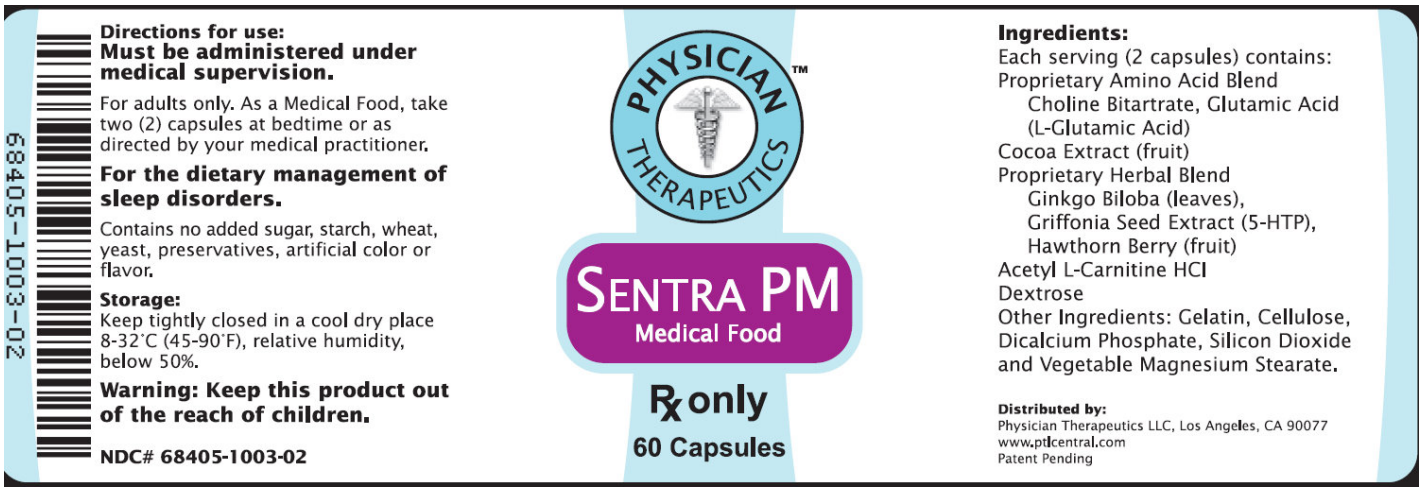
Distributed by Physician Therapeutics LLC, Los Angeles, CA 90077. www.ptlcentral.com

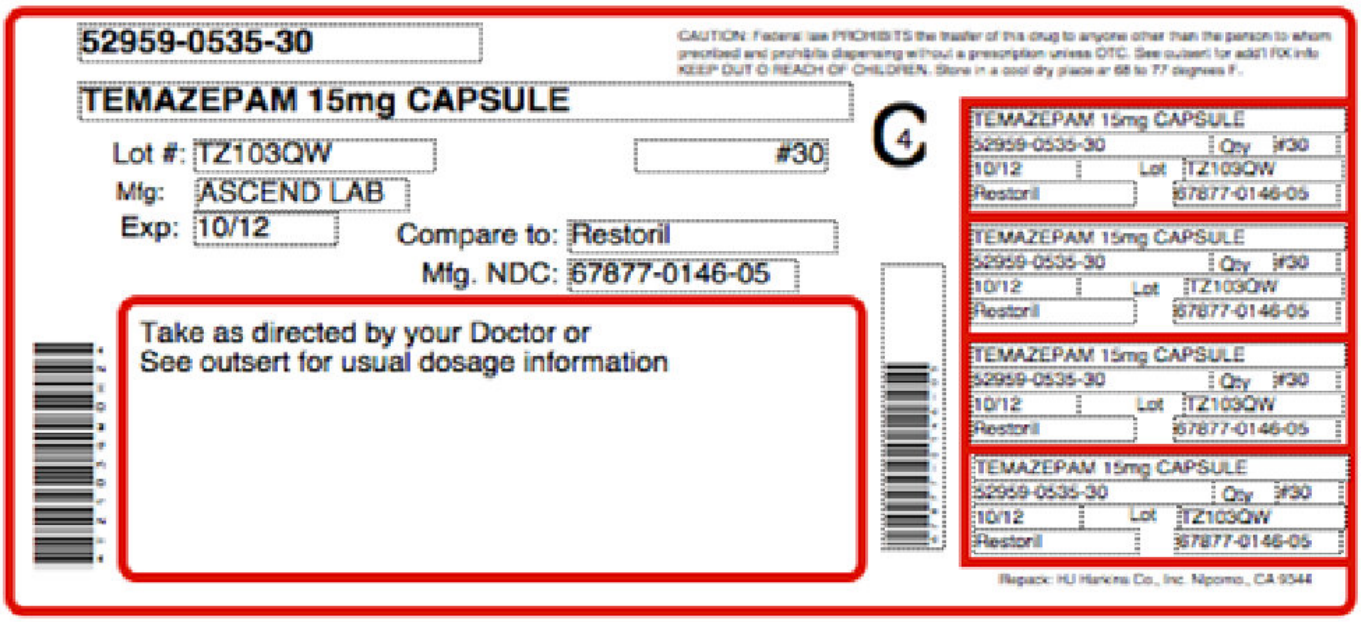
NDC # 68405-1003-02

Storage
Store at room temperature, 59-86OF (15-30OC). Protect from light and moisture.

PHYSICIAN THERAPEUTICS SENTRA PM Medical Food Rx only 60 Capsules Directions for use: Must be administered under medical supervision. For adults only. As a Medical Food, take two (2) capsules at bedtime or as directed by your medical practitioner. For the dietary management of sleep disorders. Contains no added sugar, starch, wheat, yeast, preservatives, artificial color or flavor. Storage: Keep tightly closed in a cool dry place 8-320 C (45-900F), relative humidity, below 50%. Warning: Keep this product out of the reach of children. NDC# 68405-1003-02 Ingredients: Each serving (2 capsules) contains: Proprietary Amino Acid blend Choline Bitartrate, Glutamic Acid (L-Glutamic Acid), Cocoa Extract (fruit), Proprietary Herbal Blend Ginkgo Biloba (leaves), Griffonia Seed Extract (5-HTP), Hawthorn Berry (fruit), Acetyl L-Carnitine HCl, Dextrose Other Ingredients: Gelatin, Cellulose, Dicalcium Phosphate, Silicon Dioxide and Vegetable Magnesium Stearate. Distributed by: Physician Therapeutics LLC, Los Angeles, CA 90077 www.ptlcentral.com Patent Pending

A Convenience Packed Medical Food and Drug Strazepam PHYSICIAN THERAPEUTICS Sentra PM 60 Capsules Temazepam 15 mg 30 Capsules No Refills Without Physician Authorization Rx Only NDC# 68405-8013-06 of this co-pack For the Dietary Management of Sleep Disorders. Two capsules at bedtime or as directed by physician. See product label and insert. Sentra PM Medical Food As prescribed by physician. See product label and product information insert. Temazepam 15mg Rx Drug Physician Therapeutics LLC Los Angeles, CA 90077 on November 21, 2006





STRAZEPAM

temazepam, choline kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:68405-013

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:68405-013-06	1 in 1 KIT		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 BOTTLE	30
Part 2	1 BOTTLE	60

Part 1 of 2

TEMAZEPAM

temazepam capsule

Product Information	
Item Code (Source)	NDC:52959-535(NDC:67877-146)
Route of Administration	ORAL

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: 70097M6I30)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
GELATIN (UNII: 2G86QN327L)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
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)	

Product Characteristics			
Color	blue (Blue opaque cap and white opaque body)	**Score**	no score

Shape	CAPSULE	**Size**	19mm
Flavor		**Imprint Code**	15mg;Novel121
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:52959-535-30	30 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA071456	02/15/2011	

Part 2 of 2

SENTRA PM 60

choline capsule

Product Information

Route of Administration	ORAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CHOLINE (UNII: N91BDP6H0X) (CHOLINE - UNII:N91BDP6H0X)	CHOLINE	250 mg

Inactive Ingredients

Ingredient Name	Strength
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
MALTODEXTRIN (UNII: 7CVR7L4A2D)	
GELATIN (UNII: 2G86QN327L)	

Product Characteristics

Color	red (RED)	**Score**	no score
Shape	CAPSULE	**Size**	21mm
Flavor		**Imprint Code**	;
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1		60 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
Medical Food		02/15/2011	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
unapproved drug other		02/15/2011	

Labeler - Physician Therapeutics LLC (931940964)

Establishment

Name	Address	ID/FEI	Business Operations
Novel Laboratories, Inc		793518643	manufacture

Establishment

Name	Address	ID/FEI	Business Operations
H.J. Harkins Company, Inc		147681894	repack

Establishment

Name	Address	ID/FEI	Business Operations
Targeted Medical Pharma, Inc.		126962740	manufacture

Revised: 8/2011 Physician Therapeutics LLC