

TRAZODONE HYDROCHLORIDE- trazodone hydrochloride tablet
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DIRECT RX

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WARNING: SUICIDAL THOUGHTS AND BEHAVIORS

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Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies. Closely monitor all antidepressant-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors [see Warnings and Precautions (5.1)]. Trazodone is not approved for use in pediatric patients [see Use in Specific Populations (8.4)].

Trazodone hydrochloride tablets are indicated for the treatment of major depressive disorder (MDD) in adults.

2.1 Dose Selection

An initial dose of 150 mg/day in divided doses is suggested. The dosage should be initiated at a low-dose and increased gradually, noting the clinical response and any evidence of intolerance. Occurrence of drowsiness may require the administration of a major portion of the daily dose at bedtime or a reduction of dosage.

The dose may be increased by 50 mg/day every 3 to 4 days. The maximum dose for outpatients usually should not exceed 400 mg/day in divided doses. Inpatients (i.e., more severely depressed patients) may be given up to but not in excess of 600 mg/day in divided doses.

Once an adequate response has been achieved, dosage may be gradually reduced, with subsequent adjustment depending on therapeutic response.

2.2 Important Administration Instructions

Trazodone hydrochloride tablets can be swallowed whole or administered as a half tablet by breaking the tablet along the score line.

Trazodone hydrochloride tablets should be taken shortly after a meal or light snack.

2.3 Screen for Bipolar Disorder Prior to Starting Trazodone

Prior to initiating treatment with trazodone hydrochloride tablets or another antidepressant, screen patients for a personal or family history of bipolar disorder, mania, or hypomania [see Warnings and Precautions (5.7)].

2.4 Switching to or from Monoamine Oxidase Inhibitor Antidepressant

At least 14 days must elapse between discontinuation of a monoamine oxidase inhibitor (MAOI) antidepressant and initiation of trazodone hydrochloride tablets. In addition, at

least 14 days must elapse after stopping trazodone hydrochloride tablets before starting an MAOI antidepressant [see Contraindications (4), Warnings and Precautions (5.2)].

2.5 Dosage Recommendations for Concomitant Use with Strong CYP3A4 Inhibitors or Inducers

Coadministration with Strong CYP3A4 Inhibitors

Consider reducing trazodone dose based on tolerability when trazodone is coadministered with a strong CYP3A4 inhibitor [see Drug Interactions (7.1)].

Coadministration with Strong CYP3A4 Inducers

Consider increasing trazodone dose based on therapeutic response when trazodone is coadministered with a strong CYP3A4 inducer [see Drug Interactions (7.1)].

2.6 Discontinuation of Treatment with Trazodone

Adverse reactions may occur upon discontinuation of trazodone [See Warnings and Precautions (5.8)]. Gradually reduce the dosage rather than stopping trazodone abruptly whenever possible.

Trazodone hydrochloride tablets, USP are available in the following strengths:

Trazodone hydrochloride tablets USP, 50 mg are white to off-white, round-shape, biconvex beveled tablets, bisect on one side and plain on other side. The bisected side of tablet is debossed with '8' on upper side of bisect and '05' on lower side of bisect.

Trazodone hydrochloride tablets USP, 100 mg are white to off-white, round-shape, biconvex beveled tablets, bisect on one side and plain on other side. The bisected side of tablet is debossed with '8' on upper side of bisect and '06' on lower side of bisect.

Trazodone hydrochloride tablets USP, 150 mg are white to off-white, oval-shape, flat faced beveled tablets having one full bisect and two trisect notches on one side and two trisects on other side. The full bisected side of tablet is debossed with '8' on one side of bisect and '07' on other bisect segments.

Trazodone hydrochloride tablets USP, 300 mg are white to off-white, oval-shape, flat faced beveled tablets having one full bisect and two trisect notches on one side and two trisects on other side. The full bisected side of tablet is debossed with '8' on one side of bisect and '08' on other bisect segment.

Trazodone hydrochloride tablets are contraindicated in:

Patients taking, or within 14 days of stopping, monoamine oxidase inhibitors (MAOIs), including MAOIs such as linezolid or intravenous methylene blue, because of an increased risk of serotonin syndrome [see Warnings and Precautions (5.2), Drug Interactions (7.1)].

5.1 Suicidal Thoughts and Behaviors in Pediatric and Young Adult Patients

In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included approximately 77,000 adult patients and over 4,400 pediatric patients, the incidence of suicidal thoughts and behaviors in pediatric and young adult patients was greater in antidepressant-treated patients than in placebo-treated patients. The drug-placebo differences in the number of cases of suicidal thoughts and behaviors per 1,000 patients treated are provided in Table 1.

No suicides occurred in any of the pediatric studies. There were suicides in the adult studies, but the number was not sufficient to reach any conclusion about antidepressant drug effect on suicide.

Table 1 Risk Differences of the Number of Cases of Suicidal Thoughts or Behaviors in the Pooled Placebo-Controlled Trials of Antidepressants in Pediatric and Adult Patients

Age Range
(years)

Drug-Placebo Difference in Number of Patients of
Suicidal Thoughts or Behaviors per 1,000 Patients Treated
Increases Compared to Placebo

< 18

14 additional patients

18 to 24

5 additional patients

Decreases Compared to Placebo

25 to 64

1 fewer patient

≥ 65

6 fewer patients

It is unknown whether the risk of suicidal thoughts and behaviors in pediatric and young adult patients extends to longer-term use, i.e., beyond four months. However, there is substantial evidence from placebo-controlled maintenance trials in adults with MDD that antidepressants delay the recurrence of depression.

Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing trazodone, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

5.2 Serotonin Syndrome

Serotonin-norepinephrine reuptake inhibitors (SNRIs) and SSRIs, including trazodone, can precipitate serotonin syndrome, a potentially life-threatening condition. The risk is increased with concomitant use of other serotonergic drugs (including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, amphetamines, and St. John's Wort) and with drugs that impair metabolism of serotonin, i.e., MAOIs [see Contraindications (4), Drug Interactions (7.1)]. Serotonin syndrome can also occur when these drugs are used alone.

Serotonin syndrome signs and symptoms may include mental status changes (e.g., agitation, hallucinations, delirium, and coma), autonomic instability (e.g., tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g., tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

The concomitant use of trazodone with MAOIs is contraindicated. In addition, do not initiate trazodone in a patient being treated with MAOIs such as linezolid or intravenous methylene blue. No reports involved the administration of methylene blue by other routes (such as oral tablets or local tissue injection). If it is necessary to initiate treatment with an MAOI such as linezolid or intravenous methylene blue in a patient taking trazodone, discontinue trazodone before initiating treatment with the MAOI [see Contraindications (4), Drug Interactions (7.1)].

Monitor all patients taking trazodone for the emergence of serotonin syndrome. Discontinue treatment with trazodone and any concomitant serotonergic agents immediately if the above symptoms occur, and initiate supportive symptomatic treatment. If concomitant use of trazodone with other serotonergic drugs is clinically warranted, inform patients of the increased risk for serotonin syndrome and monitor for symptoms.

5.3 Cardiac Arrhythmias

Clinical studies indicate that trazodone hydrochloride may be arrhythmogenic in patients with preexisting cardiac disease. Arrhythmias identified include isolated PVCs, ventricular couplets, tachycardia with syncope, and torsade de pointes. Postmarketing events, including torsade de pointes have been reported at doses of 100 mg or less with the immediate-release form of trazodone. Trazodone should also be avoided in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes and/or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and the presence of congenital prolongation of the QT interval. Trazodone is not recommended for use during the initial recovery phase of myocardial infarction. Caution should be used when administering trazodone to patients with cardiac disease and such patients should be closely monitored, since antidepressant drugs (including trazodone) may cause cardiac arrhythmias [see Adverse Reactions (6.2)].

Trazodone prolongs the QT/QTc interval. The use of trazodone should be avoided in patients with known QT prolongation or in combination with other drugs that are inhibitors of CYP3A4 (e.g.,

itraconazole, clarithromycin, voriconazole), or known to prolong QT interval including Class 1A antiarrhythmics (e.g., quinidine, procainamide) or Class 3 antiarrhythmics (e.g., amiodarone, sotalol), certain antipsychotic medications (e.g., ziprasidone, chlorpromazine, thioridazine), and certain antibiotics (e.g., gatifloxacin). Concomitant administration of drugs may increase the risk of cardiac arrhythmia [see Drug Interactions (7.1)].

5.4 Orthostatic Hypotension and Syncope

Hypotension, including orthostatic hypotension and syncope has been reported in patients receiving trazodone hydrochloride. Concomitant use with an antihypertensive may require a reduction in the dose of the antihypertensive drug.

5.5 Increased Risk of Bleeding

Drugs that interfere with serotonin reuptake inhibition, including trazodone, increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), other antiplatelet drugs, warfarin, and other anticoagulants may add to this risk. Case reports and epidemiological studies (case-control and cohort design) have demonstrated an association between use of drugs that interfere with serotonin reuptake and the occurrence of gastrointestinal bleeding. Bleeding events related to drugs that interfere with serotonin reuptake have ranged from ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages.

Inform patients about the risk of bleeding associated with the concomitant use of trazodone and antiplatelet agents or anticoagulants. For patients taking warfarin, carefully monitor coagulation indices when initiating, titrating, or discontinuing trazodone.

5.6 Priapism

Cases of priapism (painful erections greater than 6 hours in duration) have been reported in men receiving trazodone. Priapism, if not treated promptly, can result in irreversible damage to the erectile tissue. Men who have an erection lasting greater than 4 hours, whether painful or not, should immediately discontinue the drug and seek emergency medical attention [see Adverse Reactions (6.2), Overdosage (10)].

Trazodone should be used with caution in men who have conditions that might predispose them to priapism (e.g., sickle cell anemia, multiple myeloma, or leukemia), or in men with anatomical deformation of the penis (e.g., angulation, cavernosal fibrosis, or Peyronie's disease).

5.7 Activation of Mania or Hypomania

In patients with bipolar disorder, treating a depressive episode with trazodone or another antidepressant may precipitate a mixed/manic episode. Activation of mania/hypomania has been reported in a small proportion of patients with major affective disorder who were treated with antidepressants. Prior to initiating treatment with trazodone, screen patients for any personal or family history of bipolar disorder, mania, or hypomania [see Dosage and Administration (2.3)].

5.8 Discontinuation Syndrome

Adverse reactions after discontinuation of serotonergic antidepressants, particularly after abrupt discontinuation, include: nausea, sweating, dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g., paresthesia, such as electric shock sensations), tremor, anxiety, confusion, headache, lethargy, emotional lability, insomnia, hypomania, tinnitus, and seizures. A gradual reduction in dosage rather than abrupt cessation is recommended whenever possible [See Dosage and Administration (2.6)].

5.9 Potential for Cognitive and Motor Impairment

Trazodone may cause somnolence or sedation and may impair the mental and/or physical ability required for the performance of potentially hazardous tasks. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are reasonably certain that the drug treatment does not affect them adversely.

5.10 Angle-Closure Glaucoma

The pupillary dilation that occurs following use of many antidepressant drugs including trazodone may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy. Avoid use of antidepressants, including trazodone, in patients with untreated anatomically narrow angles.

5.11 Hyponatremia

Hyponatremia may occur as a result of treatment with SNRIs and SSRIs, including trazodone. Cases with serum sodium lower than 110 mmol/L have been reported. Signs and symptoms of hyponatremia include headache, difficulty concentrating, memory impairment, confusion, weakness, and unsteadiness, which can lead to falls. Signs and symptoms associated with more severe and/or acute cases have included hallucination, syncope, seizure, coma, respiratory arrest, and death. In many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH).

In patients with symptomatic hyponatremia, discontinue trazodone and institute appropriate medical intervention. Elderly patients, patients taking diuretics, and those who are volume-depleted may be at greater risk of developing hyponatremia with SSRIs and SNRIs [see Use in Specific Populations (8.5)].

The following serious adverse reactions are described elsewhere in the labeling:

Suicidal Thoughts and Behavior in Children, Adolescents and Young Adults [see Boxed Warning and Warnings and Precautions (5.1)]

Serotonin Syndrome [see Warnings and Precautions (5.2)]

Cardiac Arrhythmias (see Warnings and Precautions (5.3)]

Orthostatic Hypotension and Syncope [see Warnings and Precautions (5.4)]

Increased Risk of Bleeding [see Warnings and Precautions (5.5)]

Priapism [see Warnings and Precautions (5.6)]

Activation of Mania or Hypomania [see Warnings and Precautions (5.7)]

Discontinuation Syndrome [see Warnings and Precautions (5.8)]

Potential for Cognitive and Motor Impairment [see Warnings and Precautions (5.9)]

Angle-Closure Glaucoma [see Warnings and Precautions (5.10)]

Hyponatremia [see Warnings and Precautions (5.11)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Table 2 Common Adverse Reactions Occurring in $\geq 2\%$ of Trazodone-treated Patients and Greater than the Rate of Placebo-Treated Patients as Observed in Controlled Clinical Studies

Inpatients

Outpatients

Trazodone

Placebo

Trazodone

Placebo

142

95

157

158

Allergic

Skin Condition/Edema

3%

1%

7%
1%
Autonomic
Blurred Vision
6%
4%
15%
4%
Constipation
7%
4%
8%
6%
Dry Mouth
15%
8%
34%
20%
Cardiovascular
Hypertension
20%
1%
1%
*
Hypotension
7%
1%
4%
0
Syncope
3%
2%
5%
1%
CNS
Confusion
5%
0
6%
8%
Decreased Concentration
3%
2%
1%
0
Disorientation
2%
0
*
0
Dizziness/Light-Headedness
20%
5%

28%

15%

Drowsiness

24%

6%

41%

20%

Fatigue

11%

4%

6%

3%

Headache

10%

5%

20%

16%

Nervousness

15%

11%

6%

8%

Gastrointestinal

Abdominal/Gastric Disorder

4%

4%

6%

4%

Diarrhea

0

1%

5%

1%

Nausea/Vomiting

10%

1%

13%

10%

Musculoskeletal

Aches/Pains

6%

3%

5%

3%

Neurological

Incoordination

5%

0

2%

*

Tremors

3%

1%

5%
4%
Other
Eyes Red/Tired/Itching
3%
0
0
0
Head Full-Heavy
3%
0
0
0
Malaise
3%
0
0
0
Nasal/Sinus Congestion
3%
0
6%
3%
Weight Gain
1%
0
5%
2%
Weight Loss
*
3%
6%
3%

Other adverse reactions occurring at an incidence of <2% with the use of trazodone hydrochloride in the controlled clinical studies: akathisia, allergic reaction, anemia, chest pain, delayed urine flow, early menses, flatulence, hallucinations/delusions, hematuria, hypersalivation, hypomania, impaired memory, impaired speech, impotence, increased appetite, increased libido, increased urinary frequency, missed periods, muscle twitches, numbness, paresthesia, retrograde ejaculation, shortness of breath, and tachycardia/palpitations. Occasional sinus bradycardia has occurred in long-term studies.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of trazodone. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency or establish a causal relationship to drug exposure:

Blood and lymphatic system disorders: hemolytic anemia, leukocytosis

Cardiac disorders: cardiospasm, congestive heart failure, conduction block, orthostatic hypotension and syncope, palpitations, bradycardia, atrial fibrillation, myocardial infarction, cardiac arrest, arrhythmia, ventricular ectopic activity, including ventricular tachycardia and QT prolongation. Prolonged QT interval, torsade de pointes, and ventricular tachycardia have been reported at doses of 100 mg per day or less [see Warnings and Precautions (5.3)].

Endocrine disorders: inappropriate ADH syndrome

Eye disorders: diplopia

Gastrointestinal disorders: increased salivation, nausea/vomiting

General disorders and administration site conditions: chills, edema, unexplained death, weakness

Hepatobiliary disorders: cholestasis, jaundice, hyperbilirubinemia, liver enzyme alterations

Investigations: increased amylase

Metabolism and nutrition disorders: methemoglobinemia

Nervous system disorders: aphasia, ataxia, cerebrovascular accident, extrapyramidal symptoms, grand mal seizures, paresthesia, tardive dyskinesia, vertigo

Psychiatric disorders: abnormal dreams, agitation, anxiety, hallucinations, insomnia, paranoid reaction, psychosis, stupor

Renal and urinary disorders: urinary incontinence, urinary retention

Reproductive system and breast disorders: breast enlargement or engorgement, clitorism, lactation, priapism [see Warnings and Precautions (5.6)]

Respiratory, thoracic and mediastinal disorders: apnea

Skin and subcutaneous tissue disorders: alopecia, hirsutism, leukonychia, pruritus, psoriasis, rash, urticaria

Vascular disorders: vasodilation

MAOIs

MAOIs should not be used within 14 days of trazodone [see Warnings and Precautions (5.8)].

Central Nervous System (CNS) Depressants

Trazodone may enhance the response to alcohol, barbiturates, and other CNS depressants.

Cytochrome P450 3A4 Inhibitors

In vitro drug metabolism studies suggest that there is a potential for drug interactions when trazodone is given with cytochrome P450 3A4 (CYP3A4) inhibitors. The effect of short-term administration of ritonavir (200 mg twice daily, 4 doses) on the pharmacokinetics of a single dose of trazodone (50 mg) has been studied in 10 healthy subjects. The C_{max} of trazodone increased by 34%, the AUC increased 2.4 fold, the half-life increased by 2.2 fold, and the clearance decreased by 52%. Adverse effects including nausea, hypotension, and syncope were observed when ritonavir and trazodone were coadministered. It is likely that ketoconazole, indinavir, and other CYP3A4 inhibitors such as itraconazole may lead to substantial increases in trazodone plasma concentrations with the potential for adverse effects. If trazodone is used with a potent CYP3A4 inhibitor, the risk of cardiac arrhythmia may be increased [see Warnings and Precautions (5.4)] and a lower dose of trazodone should be considered.

Cytochrome P450 Inducers (e.g., Carbamazepine)

Carbamazepine induces CYP3A4. Following coadministration of carbamazepine 400 mg per day with trazodone 100 mg to 300 mg daily, carbamazepine reduced plasma concentrations of trazodone and m-chlorophenylpiperazine (an active metabolite) by 76% and 60% respectively, compared to pre-carbamazepine values. Patients should be closely monitored to see if there is a need for an increased dose of trazodone when taking both drugs.

Digoxin and Phenytoin

Increased serum digoxin or phenytoin levels have been reported in patients receiving trazodone concurrently with either of these drugs. Monitor serum levels and adjust dosages as needed.

Serotonergic Drugs

Based on the mechanism of action of trazodone and the potential for serotonin syndrome, caution is advised when trazodone is coadministered with other drugs that may affect the neurotransmitter systems [see Warnings and Precautions (5.2)].

NSAIDs, Aspirin, or Other Drugs Affecting Coagulation or Bleeding

Due to a possible association between serotonin modulating drugs and gastrointestinal bleeding, patients should be monitored for and cautioned about the potential risk of bleeding associated with the concomitant use of trazodone and NSAIDs, aspirin, or other drugs that affect coagulation or bleeding [see Warnings and Precautions (5.7)].

Warfarin

There have been reports of altered (either increased or decreased) prothrombin times in taking both warfarin and trazodone.

7.1 Drugs Having Clinically Important Interactions with Trazodone

Table 3 Clinically Important Drug Interactions with Trazodone

Monoamine Oxidase Inhibitors (MAOIs)

Clinical Impact:

The concomitant use of MAOIs and serotonergic drugs including trazodone increases the risk of serotonin syndrome.

Intervention:

Trazodone is contraindicated in patients taking MAOIs, including MAOIs such as linezolid or intravenous methylene blue [see Contraindications (4), Dosage and Administration (2.3, 2.4), and Warnings and Precautions (5.2)].

Examples:

isocarboxazid, moclobemide, phenelzine, selegiline, tranylcypromine

Other Serotonergic Drugs

Clinical Impact:

The concomitant use of serotonergic drugs including trazodone and other serotonergic drugs increases the risk of serotonin syndrome.

Intervention:

Monitor patients for signs and symptoms of serotonin syndrome, particularly during trazodone initiation. If serotonin syndrome occurs, consider discontinuation of trazodone and/or concomitant serotonergic drugs [see Warnings and Precautions (5.2)].

Examples:

triptans, antidepressants (tricyclic and serotonin uptake inhibitors), fentanyl, lithium, tramadol, tryptophan, buspirone, and St. John's Wort

Antiplatelet Agents and Anticoagulants

Clinical Impact:

Serotonin release by platelets plays an important role in hemostasis. The concurrent use of an antiplatelet agent or anticoagulant with trazodone may potentiate the risk of bleeding.

Intervention:

Inform patients of the increased risk of bleeding with the concomitant use of trazodone and antiplatelet agents and anticoagulants. For patients taking warfarin, carefully monitor the international normalized ratio (INR) when initiating or discontinuing trazodone [see Warnings and Precautions (5.5)].

Examples:

warfarin, rivaroxaban, dabigatran, clopidogrel

Strong CYP3A4 Inhibitors

Clinical Impact:

The concomitant use of trazodone and strong CYP3A4 inhibitors increased the exposure of trazodone compared to the use of trazodone alone.

Intervention:

If trazodone is used with a potent CYP3A4 inhibitor, the risk of adverse reactions, including cardiac arrhythmias, may be increased and a lower dose of trazodone should be considered [see Dosage and Administration (2.5), Warnings and Precautions (5.3)].

Examples:

itraconazole, ketoconazole, clarithromycin, indinavir

Strong CYP3A4 Inducers

Clinical Impact:

The concomitant use of trazodone and strong CYP3A4 inducers decreased the exposure of trazodone compared to the use of trazodone alone.

Intervention:

Patients should be closely monitored to see if there is a need for an increased dose of trazodone when taking CYP3A4 inducers [see Dosage and Administration (2.5)].

Examples:

rifampin, carbamazepine, phenytoin, St. John's wort

Digoxin and Phenytoin

Clinical Impact:

Digoxin and phenytoin are narrow therapeutic index drugs. Concomitant use of trazodone can increase digoxin or phenytoin concentrations.

Intervention:

Measure serum digoxin or phenytoin concentrations before initiating concomitant use of trazodone. Continue monitoring and reduce digoxin or phenytoin dose as necessary.

Examples:

digoxin, phenytoin

Central Nervous System (CNS) Depressants

Clinical Impact:

Trazodone may enhance the response CNS depressants.

Intervention:

Patients should be counseled that trazodone may enhance the response to alcohol, barbiturates, and other CNS depressants.

Examples:

alcohol, barbiturates

QT Interval Prolongation

Clinical Impact:

Concomitant use of drugs that prolong the QT interval may add to the QT effects of trazodone and increase the risk of cardiac arrhythmia.

Intervention:

Avoid the use of trazodone in combination with other drugs known to prolong QTc [see Warnings and Precautions (5.3)].

Examples:

Class 1A antiarrhythmics: quinidine, procainamide, disopyramide; Class 3 antiarrhythmics: amiodarone, sotalol;

Antipsychotics: ziprasidone, chlorpromazine, thioridazine; Antibiotics: gatifloxacin

8.1 Pregnancy

Teratogenic Effects

Pregnancy Category C

Trazodone hydrochloride has been shown to cause increased fetal resorption and other adverse effects on the fetus in the rat when given at dose levels approximately 6 to 9 times the maximum recommended human dose (MRHD) of 400 mg/day on mg/m² in adolescents. There is also an increase in congenital anomalies in the rabbit at approximately 6 to 17 times the MRHD on mg/m² basis in adolescents. There are no adequate and well-controlled studies in pregnant women. Trazodone hydrochloride should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data

No teratogenic effects were observed when trazodone was given to pregnant rats and rabbits during the period of organogenesis at oral doses up to 450 mg/kg/day. This dose is 9 and 17 times, in rats and rabbits, respectively, the maximum recommended human dose (MRHD) of 400 mg/day on mg/m² basis in adolescents. Increased fetal resorption and other adverse effects on the fetus in rats at 6 to 9 times the MRHD and increase in congenital anomalies in rabbits at 6 to 17 times the MRHD on mg/m² basis in adolescents were observed.

8.3 Nursing Mothers

Trazodone and/or its metabolites have been found in the milk of lactating rats, suggesting that the drug may be secreted in human milk. Caution should be exercised when trazodone is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in the pediatric population have not been established. Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric patients [see Boxed Warning, Warnings and Precautions (5.1)].

8.5 Geriatric Use

Reported clinical literature and experience with trazodone has not identified differences in responses between elderly and younger patients. However, as experience in the elderly with trazodone hydrochloride is limited, it should be used with caution in geriatric patients.

Serotonergic antidepressants have been associated with cases of clinically significant hyponatremia in elderly patients who may be at greater risk for this adverse reaction [see Warnings and Precautions (5.11)].

8.6 Renal Impairment

Trazodone has not been studied in patients with renal impairment. Trazodone should be used with caution in this population.

8.7 Hepatic Impairment

Trazodone has not been studied in patients with hepatic impairment. Trazodone should be used with caution in this population.

9.1 Controlled Substance

Trazodone hydrochloride tablets are not a controlled substance.

9.2 Abuse

Although trazodone hydrochloride has not been systematically studied in preclinical or clinical studies for its potential for abuse, no indication of drug-seeking behavior was seen in the clinical studies with trazodone hydrochloride.

Death from overdose has occurred in patients ingesting trazodone and other CNS depressant drugs concurrently (alcohol; alcohol and chloral hydrate and diazepam; amobarbital; chlordiazepoxide; or meprobamate).

The most severe reactions reported to have occurred with overdose of trazodone alone have been priapism, respiratory arrest, seizures, and ECG changes, including QT prolongation. The reactions reported most frequently have been drowsiness and vomiting. Overdosage may cause an increase in incidence or severity of any of the reported adverse reactions.

There is no specific antidote for trazodone hydrochloride overdose.

In managing overdosage, consider the possibility of multiple drug involvement.

For current information on the management of poisoning or overdose, contact a poison control center (1-800-222-1222 or www.poison.org).

Trazodone hydrochloride is a selective serotonin reuptake inhibitor and 5HT₂ receptor antagonist. Trazodone hydrochloride, USP is a triazolopyridine derivative designated as 2-[3-[4-(3-chlorophenyl)-1-piperazinyl]propyl]-1,2,4-triazolo[4,3-a]pyridin-3(2H)-one hydrochloride. It is a white to off-white, crystalline powder which is sparingly soluble in chloroform and in water. The structural formula is represented as follows:

[Trazodone Hydrochloride Tablets USP]

Molecular Formula: C₁₉H₂₂ClN₅O•HCl

Molecular Weight: 408.33

Each trazodone hydrochloride tablet, USP for oral administration contains 50 mg, 100 mg, 150 mg or 300 mg of trazodone hydrochloride, USP. In addition, each tablet contains the following inactive ingredients: colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, pregelatinized starch, sodium lauryl sulfate, and sodium starch glycolate.

The USP Dissolution Test is pending.

12.1 Mechanism of Action

The mechanism of trazodone's antidepressant action is not fully understood, but is thought to be related to its enhancement of serotonergic activity in the CNS. Trazodone is both a selective serotonin reuptake inhibitor (SSRI) and a 5HT₂ receptor antagonist and the net result of this action on serotonergic transmission and its role in trazodone's antidepressant effect is unknown.

12.2 Pharmacodynamics

Preclinical studies have shown that trazodone selectively inhibits neuronal reuptake of serotonin (K_i = 367 nM) and acts as an antagonist at 5-HT_{2A} (K_i = 35.6 nM) serotonin receptors. Trazodone is also an antagonist at several other monoaminergic receptors including 5-HT_{2B} (K_i = 78.4 nM), 5-HT_{2C} (K_i = 224 nM), α_{1A} (K_i = 153 nM), α_{2C} (K_i = 155 nM) receptors and it is a partial agonist at 5HT_{1A} (K_i = 118 nM) receptor.

Trazodone antagonizes alpha 1-adrenergic receptors, a property which may be associated with postural hypotension.

12.3 Pharmacokinetics

Absorption

In humans, trazodone hydrochloride is absorbed after oral administration without selective localization in any tissue. When trazodone hydrochloride is taken shortly after ingestion of food, there may be an

increase in the amount of drug absorbed, a decrease in maximum concentration and a lengthening in the time to maximum concentration. Peak plasma levels occur approximately one hour after dosing when trazodone hydrochloride is taken on an empty stomach or 2 hours after dosing when taken with food.

Metabolism

In vitro studies in human liver microsomes show that trazodone is metabolized, via oxidative cleavage, to an active metabolite, m-chlorophenylpiperazine (mCPP) by CYP3A4. Other metabolic pathways that may be involved in the metabolism of trazodone have not been well characterized. Trazodone is extensively metabolized; less than 1% of an oral dose is excreted unchanged in the urine.

Elimination

In some patients trazodone may accumulate in the plasma.

Protein Binding

Trazodone is 89 to 95% protein bound in vitro at concentrations attained with therapeutic doses in humans.

Carcinogenesis

No drug- or dose-related occurrence of carcinogenesis was evident in rats receiving trazodone in daily oral doses up to 7.3 times the maximum recommended human dose (MRSD) of 400 mg/day on mg/m² basis.

Mutagenesis

No genotoxicity studies were conducted with trazodone.

Impairment of Fertility

Trazodone has no effect on fertility in rats at doses up to 6 times the MRHD on mg/m² basis in adolescents.

The efficacy and safety of trazodone hydrochloride were established from inpatient and outpatient trials of the trazodone immediate release formulation in the treatment of major depressive disorder.

Trazodone Hydrochloride Tablets USP, 150 mg are white to off-white, oval-shape, flat faced beveled tablets having one full bisect and two trisect notches on one side and two trisects on other side. The full bisected side of tablet is debossed with '8' on one side of bisect and '07' on other bisect segments

Directions for using the correct score when breaking the tablet, please refer to the following:

-For 100 mg, break the score on either the left or right side of the tablet (one-third of a tablet).

[Trazodone Hydrochloride Tablets USP]

-For 150 mg, break the score down the middle of the tablet (one-half of a tablet).

[Trazodone Hydrochloride Tablets USP]

-For 200 mg, break the score on either the left or right side of the tablet (two-thirds of a tablet).

[Trazodone Hydrochloride Tablets USP]

-For 300 mg, use the entire tablet.

[Trazodone Hydrochloride Tablets USP]

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

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

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

Suicidal Thoughts and Behaviors

Advise patients and caregivers to look for the emergence of suicidality, especially early during treatment and when the dosage is adjusted up or down and instruct them to report such symptoms to the healthcare provider [see Box Warning and Warnings and Precautions (5.1)].

Dosage and Administration

Advise patients that trazodone hydrochloride tablets should be taken shortly after a meal or light snack. Advise patients regarding the importance of following dosage titration instructions [see Dosage and Administration (2)].

Serotonin Syndrome

Caution patients about the risk of serotonin syndrome, particularly with the concomitant use of trazodone hydrochloride tablets with other serotonergic drugs including triptans, tricyclic antidepressants, fentanyl, lithium, tramadol, tryptophan, buspirone, amphetamines, St. John's Wort, and with drugs that impair metabolism of serotonin (in particular, MAOIs, both those intended to treat psychiatric disorders and also others, such as linezolid). Patients should contact their health care provider or report to the emergency room if they experience signs or symptoms of serotonin syndrome [see Warnings and Precautions (5.2) and Drug Interactions (7)].

Activation of Mania/Hypomania

Advise patients and their caregivers to observe for signs of activation of mania/hypomania and instruct them to report such symptoms to the healthcare provider [see Warnings and Precautions (5.7)].

Increased Risk of Bleeding

Inform patients about the concomitant use of trazodone hydrochloride tablets with aspirin, NSAIDs, other antiplatelet drugs, warfarin, or other anticoagulants because the combined use of drugs that interfere with serotonin reuptake and these medications has been associated with an increased risk of bleeding. Advise them to inform their health care providers if they are taking or planning to take any prescription or over-the-counter medications that increase the risk of bleeding [see Warnings and Precautions (5.5)].

Discontinuation Syndrome

Advise patients not to abruptly discontinue trazodone hydrochloride tablets and to discuss any tapering regimen with their healthcare provider. Adverse reactions can occur when trazodone hydrochloride tablets are discontinued [see Warnings and Precautions (5.8)].

Concomitant Medications

Advise patients to inform their health care providers if they are taking, or plan to take any prescription or over-the-counter medications since there is a potential for interactions [see Drug Interactions (7.1)].

What is the most important information I should know about trazodone hydrochloride tablets?

Antidepressant medicines, depression or other serious mental illnesses, and suicidal thoughts or actions: Talk to your healthcare provider about:

All risks and benefits of treatment with antidepressant medicines

All treatment choices for depression or other serious mental illnesses

1. Antidepressant medicines may increase suicidal thoughts or actions in some children, teenagers, and young adults within the first few months of treatment.

2. Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Some people may have a higher risk of having suicidal thoughts or actions. These include people who have or have a family history of bipolar illness (also called manic-depressive illness) or suicidal thoughts or actions.

3. How can I watch for and try to prevent suicidal thoughts and actions?

Pay close attention to any changes, especially sudden changes in mood, behaviors, thoughts, or feelings. This is very important when an antidepressant medicine is started or when the dose is changed. Call your healthcare provider right away to report new or sudden changes in mood, behavior, thoughts or feelings.

Keep all follow-up visits with your healthcare provider as scheduled. Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

Call a healthcare provider right away if you have any of the following symptoms, especially if they are new, worse, or worry you:

Thoughts about suicide or dying

Attempts to commit suicide

New or worse depression

New or worse anxiety

Feeling very agitated or restless

Panic attacks

Trouble sleeping (insomnia)

New or worse irritability

Acting aggressive, being angry or violent

Acting on dangerous impulses

An extreme increase in activity and talking (mania)

Other unusual changes in behavior or mood

What else do I need to know about antidepressant medicines?

Never stop an antidepressant medicine without first talking to a healthcare provider. Stopping an antidepressant medicine suddenly can cause other symptoms.

Antidepressants are medicines used to treat depression and other illnesses. It is important to discuss all the risks of treating depression and also the risks of not treating it. You should discuss all treatment choices with your healthcare provider, not just the use of antidepressants.

Antidepressant medicines have other side effects. Talk to your healthcare provider about the side effects of your medicines.

Antidepressant medicines can interact with other medicines. Know all of the medicines that you take. Keep a list of all medicines to show your healthcare provider. Do not start new medicines without first checking with your healthcare provider.

It is not known if trazodone hydrochloride tablets are safe and effective in children.

What are trazodone hydrochloride tablets?

Trazodone hydrochloride tablets are a prescription medicine used in adults to treat major depressive disorder (MDD). Trazodone hydrochloride tablets belong to a class of medicines known as SSRIs (or selective serotonin reuptake inhibitors).

Do not take trazodone hydrochloride tablets:

If you take a monoamine oxidase inhibitor (MAOI). Ask your healthcare provider or pharmacist if you are not sure if you take an MAOI, including the antibiotic linezolid, and intravenous methylene blue.

Do not take an MAOI within 2 weeks of stopping trazodone hydrochloride tablets unless directed to do so by your healthcare provider.

Do not start trazodone hydrochloride tablets if you stopped taking an MAOI in the last 2 weeks unless directed to do so by your healthcare provider.

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

have heart problems, including QT prolongation or a family history of it

have ever had a heart attack

have bipolar disorder

have liver or kidney problems

have other serious medical conditions

are pregnant or plan to become pregnant. Trazodone hydrochloride tablets may harm your unborn baby. Talk to your healthcare provider if you are pregnant or plan to become pregnant.

are breastfeeding or plan to breastfeed. It is not known if trazodone hydrochloride passes into your breast milk. You and your healthcare provider should decide if you will take trazodone hydrochloride tablets or breastfeed.

have taken a Monoamine Oxidase Inhibitor (MAOI) or if you have stopped taking an MAOI in the last 2 weeks.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Using trazodone hydrochloride tablets with certain other medicines can affect each other causing serious side effects.

Especially tell your healthcare provider if you take:

triptans used to treat migraine headache

medicines used to treat mood, anxiety, psychotic or thought disorders, including tricyclics, lithium, SSRIs, SNRIs, buspirone, or antipsychotics

tramadol

over-the-counter supplements such as tryptophan or St. John's Wort

nonsteroidal anti-inflammatory drugs (NSAIDs)

aspirin

warfarin (Coumadin, Jantoven)

phenytoin (Mesantoin)

diuretics

Know the medicines you take. Keep a list of them and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take trazodone hydrochloride tablets?

Take trazodone hydrochloride tablets exactly as your healthcare provider tells you.

Trazodone hydrochloride tablets should be taken shortly after a meal or light snack.

If you feel drowsy after taking trazodone hydrochloride tablets, talk to your healthcare provider. Your healthcare provider may change your dose or the time of day you take your trazodone hydrochloride tablets.

Do not stop taking trazodone hydrochloride tablets without talking to your healthcare provider.

Trazodone hydrochloride tablets should be swallowed whole or broken in half along the score line. Do not chew or crush trazodone hydrochloride tablets. Tell your healthcare provider if you cannot swallow trazodone either whole or as a half tablet.

If you take too much trazodone hydrochloride tablets, call your healthcare provider, your Poison

Control Center at 1-800-222-1222, or go to the nearest emergency room right away.

What should I avoid while taking trazodone hydrochloride tablets?

Do not drive, operate heavy machinery, or do other dangerous activities until you know how trazodone hydrochloride tablets affects you. Trazodone hydrochloride tablets can slow your thinking and motor skills.

Do not drink alcohol or take other medicines that make you sleepy or dizzy while taking trazodone hydrochloride tablets until you talk with your healthcare provider. Trazodone hydrochloride tablets may make your sleepiness or dizziness worse if you take it with alcohol or other medicines that cause sleepiness or dizziness.

What are the possible side effects of trazodone hydrochloride tablets?

Trazodone hydrochloride tablets can cause serious side effects or death, including:

See “What is the most important information I should know about trazodone hydrochloride tablets?”

Serotonin syndrome. Symptoms of serotonin syndrome include: agitation, hallucinations, problems with coordination, fast heartbeat, tight muscles, trouble walking, sweating, fever, nausea, vomiting, and diarrhea.

Irregular or fast heartbeat or faint (QT prolongation)

Low blood pressure. You feel dizzy or faint when you change positions (go from sitting to standing)

Unusual bruising or bleeding

Erection lasting for more than 6 hours (priapism)

Feeling high or in a very good mood, then becoming irritable, or having too much energy, feeling like you have to keep talking or do not sleep (mania).

Withdrawal symptoms. Symptoms of withdrawal can include anxiety, agitation, and sleep problems. Do not stop taking trazodone hydrochloride tablets without talking to your healthcare provider.

Visual problems.

eye pain

changes in vision

swelling or redness in or around the eye

Only some people are at risk for these problems. You may want to undergo an eye examination to see if you are at risk and receive preventative treatment if you are.

Low sodium in your blood (hyponatremia). Symptoms of hyponatremia include: headache, feeling weak, feeling confused, trouble concentrating, memory problems and feeling unsteady when you walk.

Get medical help right away, if you have any of the symptoms listed above.

The most common side effects of trazodone hydrochloride tablets include:

swelling

blurred vision

dizziness

sleepiness

tiredness

diarrhea

stuffy nose

weight loss

These are not all the possible side effects of trazodone hydrochloride tablets. 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 trazodone hydrochloride tablets?

Store trazodone hydrochloride tablets at room temperature between 68°F to 77°F (20°C to 25°C).

Keep in tight container

Keep out of the light

Safely throw away medicine that is out of date or no longer needed.

Keep trazodone hydrochloride tablets and all medicines out of the reach of children.

General information about the safe and effective use of trazodone hydrochloride tablets.

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

What are the ingredients in trazodone hydrochloride tablets?

Active ingredient: trazodone hydrochloride, USP

Inactive ingredients: 50 mg and 100 mg: hypromellose, lactose monohydrate, magnesium stearate, polydextrose, polyethylene glycol, povidone, pregelatinized corn starch, silicon dioxide, and titanium dioxide.

Distributed by:

Par Pharmaceutical

Chestnut Ridge, NY 10977

8183136

Revised: 06/17

R7

D

**TRAZODONE
HYDROCHLORIDE
150mg 30 Tabs**

Generic For: **DESYREL**
Each tablet contains 150mg of trazodone hydrochloride, USP

Lot#
Prod# 473-30

Discard After: 02/19

Alpharetta, GA 30005

Caution: Federal law prohibits transfer of this drug to any person other than the patient for whom it was prescribed.

RX ONLY-KEEP OUT OF REACH OF CHILDREN

Dosage: See package insert. Store between 68-77 degrees F

M

Take with food or milk. May cause DROWSINESS. ALCOHOL may INTENSIFY this effect. Use care when operating dangerous machinery.

TRAZODONE HYDROCHLORIDE 15
NDC 61919-473-30 30 Tab
Lot Exp Date 02/19
Mfg NDC 68382-807-05

TRAZODONE HYDROCHLORIDE 15
NDC 61919-473-30 30 Tab
Lot Exp Date 02/19
Mfg NDC 68382-807-05

TRAZODONE HYDROCHLORIDE 15
NDC 61919-473-30 30 Tab
Lot Exp Date 02/19
Mfg NDC 68382-807-05

TRAZODONE HYDROCHLORIDE 15
NDC 61919-473-30 30 Tab
Lot Exp Date 02/19
Mfg NDC 68382-807-05

Diret By: Zydus Pharmaceuticals USA, Inc.
Parsippany, NJ 08634
NDC 68382-807-05

Mfg Lot:
1/23/2018

DIRECT

D **TRAZODONE HCl**
50mg 90 Tabs

Generic For: **DESYREL**
*Each tablet contains: Trazodone hydrochloride 50mg

Lot# **Prod# 386-90** Discard After: **09/18**

Packaged and Distributed By: **DIRECT Rx** Alphaletta, GA 30005

Mfg For: **Qualitest Pharmaceuticals Inc**
Huntsville, AL 35811
NDC 0603-6160-32

Mfg Lot: **10/11/2017**

M **TRAZODONE HCl 50mg**
HDC 61919-386-90 90 Tabs
Lot Exp Date **09/18**
NDC **0603-6160-32**

TRAZODONE HCl 50mg
HDC 61919-386-90 90 Tabs
Lot Exp Date **09/18**
NDC **0603-6160-32**

TRAZODONE HCl 50mg
HDC 61919-386-90 90 Tabs
Lot Exp Date **09/18**
NDC **0603-6160-32**

TRAZODONE HCl 50mg
HDC 61919-386-90 90 Tabs
Lot Exp Date **09/18**
NDC **0603-6160-32**

Caution: Federal law prohibits transfer of this drug to any person other than the patient for whom it was prescribed.
RX ONLY-KEEP OUT OF REACH OF CHILDREN
Dosage: See package insert. Store between 68-77 degrees F

NDC 61919-386-90

May cause DROWSINESS. ALCOHOL may INTENSIFY this effect. Use care when operating dangerous machinery. Take with food or milk.

number | Revision | Effective Date | Form Name | Page

TRAZODONE HYDROCHLORIDE

trazodone hydrochloride tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:61919-473(NDC:68382-807)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TRAZODONE HYDROCHLORIDE (UNII: 6E8Z08LRNM) (TRAZODONE - UNII:YBK48B XK30)	TRAZODONE HYDROCHLORIDE	150 mg

Inactive Ingredients

Ingredient Name	Strength
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6B30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
STARCH, PREGELATINIZED CORN (UNII: O8232NY3SJ)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	

Product Characteristics

Color	white (WHITE TO OFF WHITE)	Score	3 pieces
Shape	OVAL	Size	17mm
Flavor		Imprint Code	8;07
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
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1	NDC:61919-473-30	30 in 1 BOTTLE; Type 0: Not a Combination Product	03/07/2018
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Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA205253	03/07/2018	

TRAZODONE HYDROCHLORIDE

trazodone hydrochloride tablet, film coated

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:61919-386(NDC:0603-6160)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TRAZODONE HYDROCHLORIDE (UNII: 6E8ZO8LRNM) (TRAZODONE - UNII:YBK48BXX30)	TRAZODONE HYDROCHLORIDE	50 mg

Inactive Ingredients

Ingredient Name	Strength
HYPROMELLOSES (UNII: 3NXW29V3WO)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYDEXTROSE (UNII: VH2XOU12IE)	
POVIDONE (UNII: FZ989GH94E)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
STARCH, CORN (UNII: O8232NY3SJ)	
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WJQ0SDW1A)	

Product Characteristics

Color	white	Score	2 pieces
Shape	ROUND	Size	9mm
Flavor		Imprint Code	61;60;V
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:61919-386-90	90 in 1 BOTTLE; Type 0: Not a Combination Product	04/25/2019	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA072192	04/25/2019	

Labeler - DIRECT RX (079254320)

Registrant - DIRECT RX (079254320)

Establishment

Name	Address	ID/FEI	Business Operations
DIRECT RX		079254320	repack(61919-473) , relabel(61919-386)

Revised: 4/2019

DIRECT RX