These highlights do not include all the and effectively. See full preso

HIGHLIGHTS OF PRESCRIBING

TRAZODONE hydrochloride tablets USP.

Initial U.S. Approval: 1981

### WARNING: SHICIDALITY AND ANTIDEPRESSANT DRUGS

for complete boxed warning. Increased risk of suicidal thinking and behavior in children cents and young adults takin isorder (MDD) and other psychiate disorders. Trazodone is not approfor use in pediatric patients (5.1).

---INDICATIONS AND USAGE--ire indicated for the treatment of

• Efficacy was established in trials formulation in patients with major denressive disorder (14)

## - DOSAGE AND ADMINISTRATION -Starting dose: 150 mg in divided doses daily. May be increased by 50 mg per day every three to four

davs. Maximum dose: 400 mg per

- day in divided doses (2). · Trazodone hydrochloride tablet should be taken shortly after a meal
- Tablets should be swallowed whole or should not be chewed or crushed (2). · When discontinued, gradual dose
- reduction is recommended (2). - DOSAGE FORMS AND STRENGTHS -
- ----CONTRAINDICATIONS----None (4)
- -- WARNINGS AND PRECAUTIONS --

suicidal thinking and behavior (5.1) · Serotonin Syndrome or Neuroleptic Reactions: Have been reported with antidepressants. Discontinue trazodone hydrochloride tablets and initiate supportive treatment (5.2, 7).

- · Activation of Mania/Hypomania Screen for bipolar disorder and monitor for mania/hypomania (5.3
- . QT Prolongation: Increases the QT prolonged QT interval (5.4).

799-33-100522

· Use in Patients With Heart Disease:

Use with caution in patients with

FULL PRESCRIBING INFORMATION: 7 DRUG INTERACTIONS CONTENTS\* Warning: Suicidality and

## INTIDEPRESSANT DRUGS INDICATIONS AND USAGE CONTRAINDICATIONS WARNINGS AND PRECAUTIONS

Worsening and Serotonin Syndrome or Neuroleptic Malignan

Syndrome (NMS)-Like Screening Patients for Bipola Disorder and Monitoring for

5.4 QT Prolongation and Risk of Sudden Death
5.5 Use in Patients With Heart

5.6 Orthostatic Hypotension and

16 HOW SUPPLIED/STORAGE AND Abnormal Bleeding Interaction With MAOIs

MEDICATION GUIDE 5.11 Potential for Cognitive and \*Sections or subsections omitted from the Full Prescribing Information

6 ADVERSE REACTIONS

are not listed.

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS

ants increased the risk compared to placebo of suicidal thinking and uicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders Anvone considering the use of trazodone hydrochloride tablets or any other essant in a child, adolescent, or young adult must halance this risk compared to placebo in adults beyond age 24: there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Trazodone hydro 5.2

### Orthostatic Hypotension and Syncope: INDICATIONS AND USAGE

Abnormal Bleeding: May increase

NSAIDs, aspirin, or other drugs that

affect coagulation may compound

Interaction With MAOIs: Do not use

monoamine oxidase inhibitors (5.8, 7)

patients of this risk and how/when

to seek medical attention (5.9).

sociation with SIADH (5.10)

Potential for Cognitive and Motor

skills. Advise patients to use caution

when operating machinery (5.11).

Discontinuation Symptoms: May

taper trazodone hydrochloride tablets

---- ADVERSE REACTIONS ----

and monitor for symptoms (5.12).

dizziness, constipation, vision blurred (6)

. CYP3A4 Inhibitors: May necessitate

loride tablets (7)

To report SUSPECTED ADVERSE

REACTIONS, contact TEVA USA.

FDA at 1-800-FDA-1088 or

www.fda.gov/medwatch.

at 1-866-832-8537 or

depressants (7).

lower dose of

CYP3A4 Inducers (e.g.,

hydrochloride tablets (7).

increased serum levels (7).

with caution (8.6, 8.7)

Digoxin or Phenytoin: Monitor

· Warfarin: Monitor for increased or

decreased prothrombin time (7).

-- USE IN SPECIFIC POPULATIONS --

USE IN SPECIFIC POPULATIONS

rsina Mothers

Geriatric Use Renal Impairment

DRUG ABUSE AND DEPENDENCE

10.2 Management of Overdose

CLINICAL PHARMACOLOGY

Mechanism of Action

Pediatric Use

10.1 Human Experience

13 NONCLINICAL TOXICOLOGY

14 CLINICAL STUDIES

INFORMATION 17.1 Information for Patients

7 PATIENT COUNSELING

13.1 Carcinogenesis, Mutage

• CNS Depr

occur with abrupt discon

pairment: Has potential to impair gment, thinking, and motor

hloride Tablets USP are indicated for the treatment of major er (MDD) in adults. The efficacy of Trazodone Hydrochloride ormulation of trazodone Isee Clinical Studies (14)1.

## DOSAGE AND ADMINISTRATION

a reduction of dosage. Trazodone hydrochloride tablets should be taken shortly after a meal or light snack Dose Selection

An initial dose of 150 mg/day in divided doses is suggested. 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. Patients should be monitored for withdrawal symptoms when discontinuing

of MDD has not been evaluated. While there is no body of evidence available to 5.3 nswer the question of how long a patient treated with trazodone hydrochloride tablets should continue the drug, it is generally recommended that treatment be continued for several months after an initial response. Patients should be naintained on the lowest effective dose and be periodically reassessed to

Important Administration Instructions

razodone hydrochloride tablets are scored to provide flexibility in dosing. Trazodone hydrochloride tablets can be swallowed whole or administered as a half tablet by breaking the tablet along the score line

### DOSAGE FORMS AND STRENGTHS

determine the continued need for maintenance treatment.

de tablets are available in the following strengths 300 mg: White, oval, flat-faced, beveled-edge tablet with one side scored with a full bisect and having two partial trisects. Debossed with borr/733 on one side and 100 100 100 on the other side with the middle 100 perpendicular QT/QT

## ----DRUG INTERACTIONS----

### WARNINGS AND PRECAUTIONS

5.1 Clinical Worsening and Suicide Risk
Patients with major depressive disorder (MDD), both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal deation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders and these disorders themselves are the strongest predictors of suicide. There has been a long standing concern, however, that ntidepressants may have a role in inducing worsening of depression and the phase of myocardial infarction. pergence of suicidality in certain patients during the early phases of treatment SSRIs and others) showed that these drugs increase the risk of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults (ages 18 to 24) with MDD and other psychiatric disorders. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction with antidepressants compared to placebo in adults aged 65 and older.

. Nursing Mothers: Use with caution he pooled analyses of placebo-controlled trials in children and adoles with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders included a total of 24 short-term trials of 9 antidepressant drugs in over 4,000 patients. The pooled analyses of placebo-controlled trials in adults with MDD or other psychiatric disorders included a total of 295 short-term trials (median duration of 2 months) of 11 antidepressant drugs in over approved in pediatric patients (8.4). · Renal or Hepatic Impairment: Use 77,000 patients. There was considerable variation in risk of suicidality among 5.6 Orthostatic Hypotension and Syncope See 17 for PATIENT COUNSELING drugs, but a tendency toward an increase in the younger patients for almost all rugs studied. There were differences in absolute risk of suicidality across the (drug vs. placebo), however, were relatively stable within age strata and across Revised: 01/2014 dications. These risk differences (drug-placebo difference in the number of cases of suicidality per 1,000 patients treated) are provided in Table 1.

## District Difference is North and

Age Range	Cases of Suicidality per 1,000 Patients Treated
	Increases Compared to Placebo
< 18	14 additional cases
18 to 24	5 additional cases
	Decreases Compared to Placebo
25 to 64	1 fewer case

No suicides occurred in any of the nediatric trials. There were suicides in the drug effect on suicide.

beyond several months. However, there is substantial evidence from placebocontrolled maintenance trials in adults with depression that the use of ntidepressants can delay the recurrence of depression

All patients being treated with antidepressants for any indication should d appropriately and observed closely for clinical worsening, nd unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either

The following symptoms, anxiety, agitation, panic attacks, insomnia, irritability, ypomania, and mania, have been reported in adult and pediatric patients being eated with antidepressants for major depressive disorder as well as for other ndications, both psychiatric and nonpsychiatric. Although a causal link between he emergence of such symptoms and either the worsening of depression and/or he emergence of suicidal impulses has not been established, there is concern at such symptoms may represent precursors to emerging suicidality.

Consideration should be given to changing the therapeutic regimen, including sistently worse, or who are experiencing emergent suicidality or symptoms that might be precursors to worsening depression or suicidality, especially if oms are severe, abrupt in onset, or were not part of the patient's

Families and caregivers of patients being treated with antidepressants for major depressive disorder or other indications, both psychiatric and nonpsychiatric, should be alerted about the need to monitor patients for the emergence of agitation, irritability, unusual changes in behavior, and the other symptoms described above, as well as the emergence of suicidality, and to report such symptoms immediately to healthcare providers. Such monitoring should include daily observation by families and caregivers. escriptions for trazodone should be written for the smallest quantity of ablets consistent with good patient management, in order to reduce the risk

# Serotonin Syndrome or Neurolentic Malignant Syndrome (NMS)-

neuroleptic malignant syndrome (MMS)-like reactions have been reported with

antidepressants alone and may occur with trazodone treatment, but particularly with concomitant use of other serotoninergic drugs (including SSRIs, SNRIs and triptans) and with drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors [MAOIs]), or with antipsychotics or other dopamine antagonists. Serotonin syndrome symptoms may include mental tatus changes (e.g., agitation, hallucinations, and coma), autonomic instability e.g., tachycardia, labile blood pressure, and hyperthermia), neuromuscular berrations (e.g., hyperreflexia, incoordination) and/or gastrointestina ymptoms (e.g., nausea, vomiting, and diarrhea). Serotonin syndrome, in ts most severe form, can resemble neuroleptic malignant syndrome, which ludes hyperthermia, muscle rigidity, autonomic instability with possible rapid ctuation of vital signs, and mental status changes.

Treatment with trazodone hydrochloride tablets and any concomitant serotonergic or antidopaminergic agents, including antipsychotics, should tinued immediately if the above reactions occur and supportive symptomatic treatment should be initiated.

razodone hydrochloride tablets should not be used within 14 days of an MAOI [see Warnings and Precautions (5.8) and Drug Interactions (7)].

If concomitant treatment with trazodone hydrochloride tablets and an SSRI SNRI or a 5-hydroxytryptamine receptor agonist (triptan) is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases.

The concomitant use of trazodone hydrochloride tablets with serotonin precursors (such as tryptophan) is not recommended.

### Screening Patients for Bipolar Disorder and Monitoring for Mania/

such an episode with an antidepressant alone may increase the likelihood of precipitation of a mixed/manic episode in patients at risk for bipolar disorder. Whether any of the symptoms described for clinical worsening and suicide risk represent such a conversion is unknown. However, prior to initiating treatment with an antidepressant, patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history f suicide, bipolar disorder, and depression. It should be noted that trazodone de tablets are not approved for use in treating bipolar depression. OT Prolongation and Risk of Sudden Death

### Trazodone is known to prolong the $\mathrm{QT/QT_C}$ interval. Some drugs that prolong th $\mathrm{QT/QT_C}$ interval can cause torsade de pointes with sudden, unexplained death The relationship of QT prolongation is clearest for larger increases (20 msec and reater) but it is possible that smaller OT/OT, prob

Although torsade de pointes has not been observed with the use of trazodone hydrochloride tablets at recommended doses in premarketing trials, experience is too limited to rule out an increased risk. However, there have been ting reports of torsade de pointes with the immediate-release form of 100 mg per day or less. Use in Patients With Heart Diseas

ypomagnesemia, or a genetic predisposition to prolonged QT/QT

## loride is not recommended for use during the initial recovery

Caution should be used when administering trazodone hydrochloride tablets to patients with cardiac disease and such patients should be closely monitored ssant drugs (including trazodone hydrochloride) may cause cardiac arrhythmias.

QT prolongation has been reported with trazodone therapy [see Warnings and Precautions (5.4)]. Clinical studies in patients with preexisting cardiac disease indicate that trazodone hydrochloride may be arrhythmogenic in some patients n that population. Arrhythmias identified include isolated PVCs, ventricular couplets, tachycardia with syncope, and torsade de pointes. Postmarketin events have been reported at doses of 100 mg or less with the immediate release form of trazodone.

inhibitors of CYP3A4 may increase the risk of cardiac arrhythmia

in patients receiving trazodone hydrochloride. Cond

rketing data have shown an association between use of drugs that interfere with serotonin reuntake and the occurrence of dastro bleeding. While no association between trazodone and bleeding vents, in particular GI bleeding, was shown, patients should be cautioned about potential risk of bleeding associated with the concomitant use of trazodone and NSAIDs aspirin, or other drugs that affect coagulation or bleeding. Other bleeding events elated to SSRIs and SNRIs have ranged from ecchymosis, hematoma, enistaxis

### 5.8 Interaction With MAOIs

n patients receiving serotonergic drugs in combination with a monoamine xidase inhibitor (MAOI), there have been reports of serious, sometimes fatal reactions including hyperthermia, rigidity, myoclonus, autonomic instability with rapid fluctuation in vital signs, and mental status changes that include extreme agitation progressing to delirium and coma. These reactions have also been reported in patients who have recently discontinued antidepressant treatment and have been started on an MAOI. Some cases presented with features resembling neuroleptic malignant syndrome. Furthermore, limited nimal data on the effects of combined use of serotoneroic antid zodone hydrochloride tablets should not be used in combination with an MAOI or within 14 days of discontinuing treatment with an MAOI. Similarly, at least 14 days should be allowed after stopping trazodone hydroc

### Priapism

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 reater than 6 hours, whether painful or not, should imme and Overdosage (10)1.

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).

## 5.10 Hynonatremia

many cases, this hyponatremia appears to be the result of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Cases with serum sodium lower than 110 mmol/L have been reported. Elderly patients may be t greater risk of developing hyponatremia with antidepressants. Also, patients aking diuretics or who are otherwise volume-depleted can be at greater risk. Discontinuation of trazodone hydrochloride tablets should be considered in atients with symptomatic hyponatremia and appropriate medical intervention should be instituted Signs and symptoms of hyponatremia include headache, difficulty cor

## included hallucination, syncope, seizure, coma, respiratory arrest, and death. Trazodone hydrochloride tablets may cause somnolence or sedation and

ment confusion weakness and unsteadiness which can lead to

may impair the mental and/or physical ability required for the performance

hazardous machinery, including automobiles, until they are reasonably certain  $\mathcal{P}_{\mathbf{q}}$ that the drug treatment does not affect them adversely.

Discontinuation Symptoms 5.12 should be gradually reduced before complete discontinuation of the treatment.

ADVERSE REACTIONS The following serious adverse reactions are described elsewhere in the labeling: Clinical Worsening and Suicide Risk [see Boxed Warning and Warnings and

Serotonin Syndrome or NMS-Like Reactions [see Warnings and Precautions]

· QT Prolongation and Risk of Sudden Death [see Warnings and Precautions

 Hyponatremia Isee Warnings and Precautions (5.10). • Cognitive and Motor Impairment [see Warnings and Precautions (5.11)] • Discontinuation Symptoms [see Warnings and Precautions (5.12)]

The most common adverse reactions (reported in  $\geq$  5% and at twice the rate Somnolence/sedation, dizziness, constination, vision blurred

Table 2 presents the summary of adverse events (AEs) leading to discontinuati

• Priapism [see Warnings and Precautions (5.9)]

Action Taken (≥ 1%) Incidence and Incidence 2x Placebo				
Trazodone				
	N = 202			
Somnolence/Sedation	8 (4%)			
Dizziness	7 (3.5%)			
Confusional state	2 (1%)			
Coordination abnormal	2 (1%)			
Headache	2 (1%)			
Nausea	2 (1%)			
Balance disorder/Gait disturbance	2 (1%)			

events reported in representative controlled clinical studies conducted to evaluate the safety and efficacy of trazodone hydrochloride.

The figures cited cannot be used to predict concisely the incidence of untoward vents in the course of usual medical practice where natient characteristics and other factors often differ from those which prevailed in the clinical trials. Thes incidence figures, also, cannot be compared with those obtained from other clinical studies involving related drug products and placebo as each group of drug trials is conducted under a different set of conditions Table 3: Adverse Reactions: Percentage of Patients (> 2%) as Observed in

	<u>Irazodone</u>		<u>Irazodone</u>		pipolar iliness (also called manic-depressive
Number of Patients	142	95	157	158	illness) or suicidal thoughts or actions.
% of Patients Reporting					• -
Allergic	0.0	4.4	7	4.0	3. How can I watch for and try to prevent
Skin Condition/Edema	2.8	1.1	7	1.3	suicidal thoughts and actions?
Autonomic Blurred Vision	6.3	4.2	14.7	3.8	<ul> <li>Pay close attention to any changes, especially</li> </ul>
Constipation	7	4.2	7.6	5.7	
Dry Mouth	14.8	8.4	33.8	20.3	sudden changes in mood, behaviors,
Cardiovascular		0.1	00.0	20.0	thoughts, or feelings. This is very important
Hypertension	2.1	1.1	1.3	*	when an antidepressant medicine is started
Hypotension	7	1.1	3.8	0	or when the dose is changed.
Shortness of Breath	*	1.1	1.3	0	
Syncope	2.8	2.1	4.5	1.3	• Call your healthcare provider right away to
Tachycardia/Palpitations	0	0	7	7	report new or sudden changes in mood,
CNS					behavior, thoughts or feelings.
Anger/Hostility	3.5	6.3	1.3	2.5	
Confusion	4.9	0	5.7	7.6	• Keep all follow-up visits with your healthcare
Decreased Concentration	2.8	2.1	1.3	0	, provider as scheduled. Call your healthcare
Disorientation	2.1	0		0	provider between visits as needed, especially
Dizziness/Light-Headedness	19.7	5.3	28	15.2	
Drowsiness Excitement	23.9 1.1	6.3 1.1	40.8 5.1	19.6 5.7	if you are worried about symptoms.
Fatique	11.3	4.2	5.7	2.5	Call a healthcare provider right away if
Headache	9.9	5.3	19.8	15.8	you have any of the following symptoms,
Insomnia	9.9	10.5	6.4	12	
Impaired Memory	1.4	0	*	*	especially if they are new, worse, or worry
Nervousness	14.8	10.5	6.4	8.2	you:
Gastrointestinal					Thoughts about suicide or dying
Abdominal/Gastric Disorder	3.5	4.2	5.7	4.4	1
Bad Taste in Mouth	1.4	0	0	0	<ul> <li>Attempts to commit suicide</li> </ul>
Diarrhea	0	1.1	4.5	1.9	New or worse depression
Nausea/Vomiting	9.9	1.1	12.7	9.5	·
Musculoskeletal					<ul> <li>New or worse anxiety</li> </ul>
Musculoskeletal Aches/Pains	5.6	3.2	5.1	2.5	Feeling very agitated or restless
Neurological	4.9	0	1.9	0	
Incoordination Paresthesia	1.4	0	0	*	<ul><li>Panic attacks</li></ul>
Tremors	2.8	1.1	5.1	3.8	Trouble sleeping (insomnia)
Sexual Function	2.0	1.1	0.1	0.0	,
Decreased Libido	*	1.1	1.3	*	New or worse irritability
Other					<ul> <li>Acting aggressive, being angry or violent</li> </ul>
Decreased Appetite	3.5	5.3	0	*	
Eyes Red/Tired/Itching	2.8	0	0	0	<ul> <li>Acting on dangerous impulses</li> </ul>
Head Full-Heavy	2.8	0	0	0	• An extreme increase in activity and talking
Malaise	2.8	0	0	0	
Nasal/Sinus Congestion	2.8	0	5.7	3.2	(mania)
Nightmares/Vivid Dreams	*	1.1	5.1	5.7	<ul> <li>Other unusual changes in behavior or</li> </ul>
Sweating/Clamminess	1.4	1.1	*	*	mood
Tinnitus	1.4	0	0	*	
Weight Gain	1.4	0 3.2	4.5	1.9 2.5	What else do I need to know about
Weight Loss	_	3.2	5.7	2.5	, antidepressant medicines?

In addition to the relatively common (i.e., greater than 1%) untoward events enumerated above, the following adverse events have been reported to occur in association with the use of trazodone hydrochloride in the controlled clinical studies; akathisia, allergic reaction, anemia, chest pain, delayed urine flow.

## **MEDICATION GUIDE**

Trazodone Hydrochloride (traz' oh done hye" droe klor' ide) Tablets USP

Read the Medication Guide that comes with trazodone hydrochloride tablets before antidepressants. you start taking it and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. Talk to your healthcare Antidepressant medicines can interact with provider or pharmacist if there is something other medicines. Know all of the medicines you do not understand or you want to learn that you take. Keep a list of all medicines to about trazodone hydrochloride tablets.

## should know about trazodone hydrochloride your healthcare provider. tablets?

Antidepressant medicines, depression or other approved for use in children. Talk to your serious mental illnesses, and suicidal thoughts healthcare provider for more information or actions: Talk to your healthcare provider What are trazodone hydrochloride tablets?

- All risks and benefits of treatment with antidepressant medicines depressive disorder in adults.
- 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.
- 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.
- 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
- 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
- Thoughts about suicide or dying Attempts to commit suicide
- New or worse depression New or worse anxiety
- 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

can cause other symptoms.

ntidepressant medicines? Never stop an antidepressant medicine without first talking to a healthcare provider. Stopping an antidepressant medicine suddenly

Antidepressants are medicines used to Xtreat 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

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

show your healthcare provider. Do not start What is the most important information I new medicines without first checking with 4. Trazodone hydrochloride tablets **are not** 

> or actions: Talk to your healthcare provider Trazodone hydrochloride tablets are a prescription medicine used to treat major

## What should I tell my healthcare provider before taking trazodone hydrochloride

Before you take trazodone hydrochloride tablets tell your healthcare provider 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 or
- 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 non-prescription medicines, vitamins, and herbal supplements.

Using trazodone hydrochloride tablets with certain other medicines can affect each other causing serious side effects 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 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
- hydrochloride tablets. Do not stop taking trazodone hydrochloride tablets without talking to your healthcare provider.

time of day you take your trazodone

 Trazodone hydrochloride tablets should can cause other symptoms. be swallowed whole or broken in half along the score line. Do not chew or crush

**MEDICATION GUIDE** Trazodone Hydrochloride (traz' oh done hye" droe klor' ide) Tablets USP Read the Medication Guide that comes

information does not take the place of talking to your healthcare provider about your medical

> What is the most important information I should know about trazodone hydrochloride your healthcare provider. tablets?

about trazodone hydrochloride tablets.

- All risks and benefits of treatment with antidepressant medicines
- · All treatment choices for depression or other serious mental illnesses . Antidepressant medicines may increase suicidal thoughts or actions in some
- 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
- 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
- · Attempts to commit suicide New or worse depression

New or worse anxiety

Thoughts about suicide or dying

· Feeling very agitated or restless Panic attacks

mood

 Trouble sleeping (insomnia) New or worse irritability

Acting on dangerous impulses

- Acting aggressive, being angry or violent
- · Other unusual changes in behavior or

What else do I need to know about antidepressant medicines? Never stop an antidepressant medicine without first talking to a healthcare provider.

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.

with trazodone hydrochloride tablets before you start taking it and each time you get a Antidepressant medicines have other side refill. There may be new information. This **effects.** Talk to your healthcare provider about the side effects of your medicines.

condition or treatment. Talk to your healthcare Antidepressant medicines can interact with provider or pharmacist if there is something other medicines. Know all of the medicines you do not understand or you want to learn that you take. Keep a list of all medicines to show your healthcare provider. Do not start new medicines without first checking with

4. Trazodone hydrochloride tablets are not Antidepressant medicines, depression or other approved for use in children. Talk to your serious mental illnesses, and suicidal thoughts healthcare provider for more information.

> What are trazodone hydrochloride tablets? Trazodone hydrochloride tablets are a prescription medicine used to treat major depressive disorder in adults.

What should I tell my healthcare provider

before taking trazodone hydrochloride

Before you take trazodone hydrochloride tablets tell your healthcare provider if you: children, teenagers, and young adults

- 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 bipolar illness (also called manic-depressive 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 or
  - 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 non-prescription medicines, vitamins, and herbal supplements.

Using trazodone hydrochloride tablets with certain other medicines can affect each other causing serious side effects

them and show it to your healthcare provider and pharmacist when you get a new medicine. How should I take trazodone hydrochloride tablets?

Know the medicines you take. Keep a list of

• Take trazodone hydrochloride tablets

provider may change your dose or the

time of day you take your trazodone

- exactly as your healthcare provider tells Trazodone hydrochloride tablets should be
- taken shortly after a meal or light snack. • If you feel drowsy after taking trazodone An extreme increase in activity and talking hydrochloride tablets, talk to your healthcare provider. Your healthcare
  - hydrochloride tablets. Do not stop taking trazodone hydrochloride tablets without talking to your healthcare provider.
- Stopping an antidepressant medicine suddenly Trazodone hydrochloride tablets should
  - be swallowed whole or broken in half along the score line. Do not chew or crush

healthcare provider if you cannot swallow tablets?

trazodone either whole or as a half tablet. • If you take too much trazodone hydrochloride, call your doctor 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 affect 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 vou talk with your healthcare provider. Trazodone hydrochloride tablets may make vour 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 hvdrochloride tablets?

Trazodone hydrochloride tablets can cause serious side effects or death. See "What is the most important information I should know about trazodone hydrochloride tablets?"

### Serious side effects include:

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

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

### The most common side effects of trazodone hydrochloride tablets include:

- Sleepiness
- Dizziness
- Constipation
- Blurry vision

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of trazodone hydrochloride tablets. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088

# trazodone hydrochloride tablets. Tell your How should I store trazodone hydrochloride $\chi$

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

This Medication Guide summarizes the most important information about trazodone hydrochloride tablets. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about trazodone hydrochloride tablets that is written for health professionals.

For more information, call 1-888-838-2872.

### What are the ingredients in trazodone hydrochloride tablets?

Active ingredient: trazodone hydrochloride Inactive ingredients: colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, pregelatinized corn starch, sodium lauryl sulfate and sodium starch glycolate.

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

### TEVA PHARMACEUTICALS USA Sellersville, PA 18960

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## healthcare provider if you cannot swallow tablets? trazodone either whole or as a half tablet.

• If you take too much trazodone hydrochloride, call your doctor 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 affect 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 vour 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. See "What is the most important information I should know about trazodone hydrochloride tablets?"

### Serious side effects include:

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

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

### The most common side effects of trazodone hydrochloride tablets include:

- Sleepiness
- Dizziness
- Constipation
- Blurry vision

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of trazodone hydrochloride tablets. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

## trazodone hydrochloride tablets. Tell your How should I store trazodone hydrochloride winches, numbness, and including QT prolongation. The reactions reported most frequently have been retrograde elevations. 6.2 Postmarketing Experience

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

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.

This Medication Guide summarizes the most important information about trazodone hydrochloride tablets. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about trazodone hvdrochloride tablets that is written for health | professionals.

For more information, call 1-888-838-2872.

### What are the ingredients in trazodone hydrochloride tablets? Active ingredient: trazodone hydrochloride

Inactive ingredients: colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, pregelatinized corn starch, sodium lauryl sulfate and sodium starch glycolate. This Medication Guide has been approved by

the U.S. Food and Drug Administration. TEVA PHARMACEUTICALS USA Sellersville, PA 18960

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diospasm, cerebrovascular accident, chills, cholestasis, clitorism, congestive

heart failure, diplopia, edema, extrapyramidal symptoms, grand mal seizures, hallucinations, hemolytic anemia, hirsutism, hyperbilirubinemia, increased amylase, increased salivation, insomnia, leukocytosis, leukonychia, jaundice,

lactation, liver enzyme alterations, methemoglobinemia, nausea/vomiting

sodilation, vertigo, and weakness.

DRUG INTERACTIONS

Cytochrome P450 3A4 Inhibitors

Central Nervous System (CNS) Depressants

Precautions (5.8)

most frequently), paresthesia, paranoid reaction, priapism [see Warnings and Precautions (5.9) and Patient Counseling Information (17.1)], pruritus, soriasis, psychosis, rash, stupor, inappropriate ADH syndrome, tardive

skinesia, unexplained death, urinary incontinence, urinary retention, urticaria,

Cardiovascular system effects which have been reported include the following:

conduction block, orthostatic hypotension and syncope, palpitations, bradycardia, atrial fibrillation, myocardial infarction, cardiac arrest, arrhythmia, ventricular ectopic activity, including ventricular tachycardia and QT

intes, and ventricular tachycardia have been reported with the immediate

elease form of trazodone at doses of 100 mg per day or less [see Warnings

razodone may enhance the response to alcohol, barbiturates, and other CNS

clearance decreased by 52%. Adverse effects including nausea, hypotension

and syncope were observed when ritonavir and trazodone were coadministered

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-chlorophenlypiperazine (an active

Increased serum digoxin or phenytoin levels have been reported in patients

receiving trazodone concurrently with either of these drugs. Monitor serum

Based on the mechanism of action of trazodone and the notential for serotoni

syndrome, caution is advised when trazodone is coadministered with other drugs that may affect the neurotransmitter systems [see Warnings and

Oue to a possible association between serotonin modulating drugs and

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

### done hydrochloride received from **10.2 Management of Overdose**Illowing: abnormal dreams, agitation, There is no specific antidote for trazodone hydrochloride overdose. Spontaneous reports regarding trazodone hydrochloride received from postmarketing experience include the following: abnormal dreams, agitation, alopecia, anxiety, aphasia, apnea, ataxia, breast enlargement or engorgement,

depressive disorder. Ensure an adequate airway, oxygenation and ventilation. Monitor cardiac rhythm

General supportive and symptomatic measures are also recommende Induction of emesis is not recommended. Gastric lavage with a large bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion, or in symptomatic patients. Activated charcoal should be administered. Forced digresis may be useful in facilitating elimination

In managing overdosage, consider the possibility of multiple drug involvement

### rolongation. In postmarketing surveillance, prolonged QT interval, torsade de DESCRIPTION

to tricyclic, tetracyclic, or other known antidepressant agents. 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(2*H*)-one hydrochloride. It is a white, odorless crystalline powder which is MAOIs MAOIs should not be used within 14 days of trazodone [see Warnings and freely soluble in water. The structural formula is represented as follows:

In vitro frog 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 Each tablet, for oral administration, contains 300 mg of trazodone hydrochlorid USP. In addition, each tablet contains colloidal silicon dioxide, magnesiur 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 stearate, microcrystalline cellulose, pregelatinized corn starch, sodium lauryl sulfate and sodium starch glycolate. CLINICAL PHARMACOLOGY

### Mechanism of Action

The mechanism of trazodone's antidepressant action is not fully understood, but is thought to be related to its potentiation of serotonergic activity in the CNS. 12.2 Pharmacodynamics
Preclinical studies have shown that trazodone selectively inhibits neurona

before you start taking it and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. Talk to your reuptake of serotonin and acts as an antagonist at 5-HT-2A/2C serotonin healthcare provider or pharmacist if there is something you do not understand Trazodone is not a monoamine oxidase inhibitor and, unlike amphetamine-type

What is the most important information I should know about trazodone drugs, does not stimulate the central nervous system hydrochloride tablets?
Antidepressant medicines, depression or other serious mental illnesses, and

Trazodone antagonizes alpha 1-adrenergic receptors, a property which may be

### 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 Absorption n humans, trazodone hydrochloride is well absorbed after oral administration

NONCLINICAL TOXICOLOGY

HOW SUPPLIED/STORAGE AND HANDLING

CLINICAL STUDIES

without selective localization in any tissue. When trazodone hydrochloride is without selective todalization in any tissue. When tradeolite hydrochindre 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.

n 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

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
No drug- or dose-related occurrence of carcinogenesis was evident in rats

ring trazodone in daily oral doses up to 300 mg/kg for 18 months.

and 100 100 100 on the other side with the middle 100 perpendicular to the others. Available in bottles of 100.

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

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

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

PATIENT COUNSELING INFORMATION

Information for Patients

children, teenagers and young adults.

Dispense in a tight, light-resistant container as defined in the USP, with a child-

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment

with trazodone hydrochloride and should counsel them in its appropriate use.

• There is a potential for increased risk of suicidal thoughts especially in

• The following symptoms should be reported to the physician; anxiety.

They should inform their physician if they have a history of bipolar disorder.

agitation, panic attacks, insomnia, irritability, hostility, aggress impulsivity, akathisia, hypomania and mania.

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)]. e patients trazodone may accumulate in the plasma.

to the following:

-For 300 mg, use the entire tablet

Patients should be warned that:

<u>Protein Binding</u> Trazodone is 89 to 95% protein bound *in vitro* at concentrations attained with  $\frac{Warfarin}{\text{There have been reports of altered (either increased or decreased) prothrombin}}$ therapeutic doses in humans.

## USE IN SPECIFIC POPULATIONS

NSAIDs, Aspirin, or Other Drugs Affecting Coagulation or Bleeding

## Pregnancy Category C

Digoxin and Phenytoin

Serotonergic Drugs

Precautions (5.2)].

levels and adjust dosages as needed.

oride has been shown to cause increased fetal resorption

and other adverse effects on the fetus in two studies using the rat when given at dose levels approximately 30 to 50 times the proposed maximum human dose. There was also an increase in congenital anomalies in one of three rabbit studies at approximately 15 to 50 times the maximum human dose. There The efficacy and safety of trazodone hydrochloride was established from <u>both</u> <u>inpatient and outpatient</u> trials of the trazodone immediate release formulation in the treatment of major depressive disorder 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. 300 mg; White, oval, flat-faced, beveled-edge tablet with one side scored with a full bisect and having two partial trisects. Debossed with barr/733 on one side 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 afety and effectiveness in the pediatric population have not been established -For 100 mg, break the score on either the left or right side of the tablet

# [see Boxed Warning and Warnings and Precautions (5.1)]. Trazodone (one-third of a tablet). hydrochloride should not be used in children or adolescents.

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 continuous control to the control of the control used with caution in geriatric patients.

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 (5.10)].

-For 200 mg, break the score on either the left or right side of the tablet (two-thirds of a tablet). 8.6 Renal Impairment done has not been studied in patients with renal impairment. Trazodone

### should be used with caution in this population 8.7 Henatic Impairment

## Trazodone has not been studied in patients with hepatic impairment. Trazodone should be used with caution in this population. 9 DRUG ABUSE AND DEPENDENCE 9.1 Controlled Substance

### azodone hydrochloride tablets are not a controlled substance Abuse

Although trazodone hydrochloride has not been systematically studied in 17 preclinical or clinical studies for its potential for abuse, no indication of drug-seeking behavior was seen in the clinical studies with trazodone hydrochloride. However, it is difficult to predict the extent to which a CNS-active drug will be misused, diverted, and abused. Consequently, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of trazodone hydrochloride (e.g., development of tolerance, incrementation of dose, drug-seeking behavior).

### OVERDOSAGE Human Experience

Death from overdose has occurred in patients ingesting trazodone and other CNS depressant drugs concurrently (alcohol; alcohol and chloral hydrate and azepam; 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,

 Serotonin syndrome could occur and symptoms may include changes
 have taken a Monoamine Oxidase Inhibitor (MAOI) or if you have stopped rowsiness and vomiting. Overdosage may cause an increase in incidence or everity of any of the reported adverse reactions.

management of overdosage with any drug effective in the treatment of major

 There is a notential risk of bleeding (including life-threatening hemorrhages) and bleeding related events (including ecchymosis, hematoma, epistaxis, and petechiae) with the concomitant use of trazodone hydrochloride and

NSAIDs, aspirin, or other drugs that affect coagulation or bleeding. Withdrawal symptoms including anxiety, agitation and sleep disturbances have been reported with trazodone. Clinical experience suggests that the dose should be gradually reduced

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

Patients should be counseled that:

light snack.

Trazodone may enhance the response to alcohol, barbiturates, and other Women who intend to become pregnant or who are breastfeeding should

TEVA PHARMACEUTICALS USA

MEDICATION GUIDE

Trazodone Hydrochloride (traz' oh done hye" droe klor' ide) Tablets USP

Read the Medication Guide that comes with trazodone hydrochloride tablets

r you want to learn about trazodone hydrochloride tablet

illness) or suicidal thoughts or actions.

. Thoughts about suicide or dving

· Attempts to commit suicide

· Feeling very agitated or restless

· Acting on dangerous impulses

· Acting aggressive, being angry or violent

An extreme increase in activity and talking (mania)

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

Other unusual changes in behavior or mood

. New or worse depression

• Trouble sleeping (insomni

· New or worse irritability

· New or worse anxiety

· Panic attacks

about symptoms.

medicine is started or when the dose is changed

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

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

symptoms, especially if they are new, worse, or worry you:

- discuss with a physician whether they should continue to use trazodone, since use in pregnant and nursing women is not recommended. **Important Administration Instructions** hydrochloride tablets can slow your thinking and motor skills Trazodone hydrochloride tablets should be swallowed whole or broken in Do not drink alcohol or take other medicines that make you sleeny. half along the score line.
- dizzy while taking trazodone hydrochloride tablets until you sleepy of your healthcare provider. Trazodone hydrochloride tablets may make your sleepiness or dizziness worse if you take it with alcohol or other medicines • Trazodone hydrochloride tablets should be taken shortly after a meal or

### Trazodone hydrochloride tablets can cause serious side effects or death

See "What is the most important information I should know about tr

### Serious side effects include:

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

much energy, feeling like you have to keep talking or do not sleep (mania) Irregular or fast heartbeat or faint (QT prolongation).

Erection lasting for more than 6 hours (priapism).

include: headache, feeling weak, feeling confused, trouble concentratin memory problems and feeling unsteady when you walk.

tablets without talking to your healthcare provider

behaviors, thoughts, or feelings. This is very important when an antidepressant Constination

 Keen all follow-up visits with your healthcare provider as scheduled. Call your. that does not go away. These are not all the possible side effects of trazodone hydrochloride tablets. For

Call your doctor for medical advice about side effects. You may report side

For more information, call 1-888-838-2872

sodium starch glycolate

4. Trazodone hydrochloride tablets are not approved for use in children. Talk

### to vour healthcare provider for more in What are trazodone hydrochloride tablets?

tablets are a prescription medicine used to treat major

depressive disorder in adults. What should I tell my healthcare provider before taking trazodon

hydrochloride tablets? Before you take trazodone hydrochloride tablets tell your healthcare provide

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

- · have ever had a heart attack
- have liver or kidney problems · have other serious medical conditions
- pregnant or plan to become pregnant.
- hydrochloride passes into your breast milk. You and your healthcare provider should decide if you will take trazodone hydrochloride or

taking an MAOI in the last 2 weeks.

neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or Using trazodone hydrochloride tablets with certain other medicines can affect

### Know the medicines you take. Keep a list of them and show it to your healthcar • There is a potential for hypotension, including orthostatic hypotension provider and pharmacist when you get a new medicine

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

Do not stop taking trazodone hydrochloride tablets without talking to you

half along the score line. Do not chew or crush trazodone hydrochloride tablets. Tell your healthcare provider if you cannot swallow trazodone eithe

# until you know how trazodone hydrochloride tablets affect you. Trazodone

that cause sleepiness or dizziness. What are the possible side effects of trazodone hydrochloride tablets?

- Low blood pressure. You feel dizzy or faint when you change positions (go from sitting to standing)
- Low sodium in your blood (hyponatremia). Symptoms of hyponatremia
- Withdrawal symptoms Symptoms of withdrawal can include anxiety 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
- · Pay close attention to any changes, especially sudden changes in mood Dizziness
  - Tell your healthcare provider if you have any side effect that bothers you o
- more information, ask your healthcare provider or pharmacist. Call a healthcare provider right away if you have any of the following
  - How should I store trazodone hydrochloride tablets?
  - . Keep in tight container
  - . Keep out of the light Safely throw away medicine that is out of date or no longer needed.

## General information about the safe and effective use of trazodon nydrochloride tablets.

our healthcare provider. You can ask your pharmacist or healthcare provide or information about trazodone hydrochloride tablets that is written for health

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 Active ingredient: trazodone hydrochloride Inactive ingredients: colloidal silicon dioxide. magnesium stearati

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- have bipolar disorder
- are pregnant or plan to become pregnant. Trazodone hydrochloride tablets may harm your unborn baby. Talk to your healthcare provider if you are
- · are breastfeeding or plan to breastfeed. It is not known if trazodone

Tell your healthcare provider about all the medicines you take, including

gastrointestinal symptoms (e.g., nausea, vomiting, and diarrhea). · Trazodone hydrochloride has been associated with the occurrence of each other causing serious side effects.

## How should I take trazodone hydrochloride tablets?

Take trazodone hydrochloride tablets exactly as your healthcare provide

- 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.
- healthcare provider. Trazodone hydrochloride tablets should be swallowed whole or broken
- If you take too much trazodone hydrochloride, call your doctor 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

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## hydrochloride tablets

Feeling high or in a very good mood, then becoming irritable, or having too

- Unusual bruising or bleeding.
- some children, teenagers, and young adults within the first few months
  - medical help right away, if you have any of the symptoms listed above
- Blurry vision • Call your healthcare provider right away to report new or sudden changes in

  - Store trazodone hydrochloride tablets between 20° to 25°C (68° to 77°F)

# Keep trazodone hydrochloride tablets and all medicines out of the reach

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 This Medication Guide summarizes the most important information about trazodone hydrochloride tablets. If you would like more information, talk with

# What are the ingredients in trazodone hydrochloride tablets?

Antidepressant medicines have other side effects. Talk to your healthcare microcrystalline cellulose, pregelatinized corn starch, sodium lauryl sulfate and provider about the side effects of your medicines. Antidepressant medicines can interact with other medicines. Know all of the This Medication Guide has been approved by the U.S. Food and Drug 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

### **MEDICATION GUIDE**

Trazodone Hydrochloride (traz' oh done hye" droe klor' ide) Tablets USP

Read the Medication Guide that comes with trazodone hydrochloride tablets before you start taking it and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. Talk to your healthcare provider or pharmacist if there is something you do not understand or you want to learn about trazodone hydrochloride tablets.

# 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.

4. Trazodone hydrochloride tablets **are not approved for use in children.** Talk to your healthcare provider for more information.

What are trazodone hydrochloride tablets? Trazodone hydrochloride tablets are a prescription medicine used to treat major depressive disorder in adults.

# What should I tell my healthcare provider before taking trazodone hydrochloride tablets?

Before you take trazodone hydrochloride tablets tell your healthcare provider if you:

- have heart problems, including Q1 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 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 non-prescription medicines, vitamins, and herbal supplements.

Using trazodone hydrochloride tablets with certain other medicines can affect each other causing serious side effects.

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, call your doctor 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 affect 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. See "What is the most important information I should know about trazodone hydrochloride tablets?"

### Serious side effects include:

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

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

# The most common side effects of trazodone hydrochloride tablets include:

- Sleepiness
- Dizziness
- Constipation
- Blurry vision

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of trazodone hydrochloride tablets. For more information, ask your healthcare provider or pharmacist.

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

This Medication Guide summarizes the most important information about trazodone hydrochloride tablets. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about trazodone hydrochloride tablets that is written for health professionals.

For more information, call 1-888-838-2872.

# What are the ingredients in trazodone hydrochloride tablets?

Active ingredient: trazodone hydrochloride Inactive ingredients: colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, pregelatinized corn starch, sodium lauryl sulfate and sodium starch glycolate.

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

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