Package leaflet: Information for the user

TERIZIDON, 250 mg, capsules, hard

Active substance: Terizidone

For use in adults

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What TERIZIDON is and what it is used for

TERIZIDON is indicated for adults within the scope of an antituberculosis combination therapy for the treatment of tuberculosis, caused by *Mycobacterium tuberculosis*, (see section 2. “What you need to know before you take TERIZIDON").

TERIZIDON may only then be used if insufficient combination partners are available due to verified resistances or incompatibilities.

2. What you need to know before you take TERIZIDON

Do not take TERIZIDON:

- if you are allergic to terizidone and/or cycloserine or any of the other ingredients of this medicine (listed in section 6).

- with severe renal insufficiency (restricted renal function, serum creatinine over 2 mg/dl [laboratory value for the determination of renal function]).
- with severe cerebral sclerosis (severe calcification with circulatory disorder of the brain).
- with alcoholism.
- with psychological disorders (e.g. depression, severe anxiety attacks, psychoses).
- with epilepsy.
- with infections caused by *Mycobacterium bovis* BCG (a certain strain of the tuberculosis pathogen).

Warnings and precautions
Talk to your doctor or pharmacist before taking TERIZIDON.

You should be monitored during the inpatient and outpatient therapy phases due to the possibility of psychological side effects and nervous system side effects (see section 4. "Possible side effects"). Outpatient treatment should not be initiated unless you were free of side effects during the previous inpatient treatment.

If you suffer from severe cerebral sclerosis (severe calcification with circulatory disorder of the brain), alcoholism, psychological disorders (depression, severe anxiety attacks, psychoses) or epilepsy, do not take TERIZIDON, as this drug can itself lead to side effects on the central nervous system (see section 4 "Possible side effects") and can additionally increase the risk of such side effects in the patients listed above.

If you take terizidone, you should also be given pyridoxine (vitamin B_6) to prevent neurological side effects. The recommended dose is 50 mg vitamin B_6/250 mg terizidone.

Terizidone, the active substance in TERIZIDON, can be dialyzed. There are insufficient trials available which indicate that TERIZIDON is still clinically effective in case of continuous forms of dialysis (continuous peritoneal dialysis) (see section 3. "How to take TERIZIDON").

Children and adolescents
There is insufficient data available on the application, dosage and evaluation of the benefit-risk ratio of terizidone in children and adolescents. The application of TERIZIDON in this age group may therefore only be carried out in exceptional situations, if insufficient other active substances are available for therapy due to a severe pathogen resistance and if the risk of a progressive course of the disease is accordingly high. Therapy using TERIZIDON on children and adolescents should take place under supervision and monitoring of the efficacy and side effects. In addition, the application of TERIZIDON in this age group should only then take place if the pathogen has been confirmed susceptible to terizidone or if pathogen susceptibility can be assumed within the scope of the case finding. A specialist experienced in the therapy of tuberculosis must be consulted.

Other medicines and TERIZIDON
Tell your doctor or pharmacist if you are taking/using or have recently taken/used or might take/ use any other medicines, including medicines obtained without a prescription.

The interactive influences when taking TERIZIDON with other medicines/active substances have been summarized in the following table.

In **column 2**, the simultaneous uses are marked with regard to their importance:

Index **1** : Contraindicated

Index **2**: Simultaneous intake not recommended

Index **3**: Simultaneous intake only under monitoring of efficacy and safety

Active substance group/ Active substance	**Index**	**Clinical consequences**
Antituberculotics (medicines against tuberculosis):		
Isoniazide	**3**	Monitoring of side effects on the central nervous system
Ethionamide	**3**	Monitoring of side effects on the central nervous system
Prothionamide	**3**	Monitoring of side effects on the central nervous system
Anticoagulants (medicine for the inhibition of blood coagulation):		
Cumarine	**3**	Monitoring of the side effects and efficacy of the anticoagulants; if applicable dose adjustment of anticoagulants
Antiepileptic drugs (medicine against epilepsy):		
Phenytoine	**3**	Monitoring of the side effects of phenytoine; if applicable dose adjustment of phenytoine
Muscle relaxants (medicine for relaxation of the skeletal muscles):		
Suxamethonium	**3**	Monitoring of the side effects of succinylcholines; if applicable dose adjustment of suxamethonium
Stimulants		
Alcohol	**2**	Avoid simultaneous intake of alcohol (see section 2. “TERIZIDON with food, drink and alcohol”).
	1	TERIZIDON may not be taken if you suffer from chronic alcohol consumption and alcoholism (see section 2. “Do not take TERIZIDON”).
Caffeine	**3**	See section 2. “TERIZIDON with food, drink and alcohol”

TERIZIDON with food, drink and alcohol

During treatment with TERIZIDON, do not drink **alcohol**. The simultaneous intake of alcohol and terizidone increases the risk of the occurrence of side effects on the central nervous system (see section 2. "Other medicines and TERIZIDON").

There are indications that the simultaneous intake of terizidone and **caffeine** may increase the risk of side effects on the nervous system. Due to a current lack of knowledge on this subject, the simultaneous intake of caffeine in the form of food and drink should be undertaken with caution. The intake of certain beverages or stimulants with very high caffeine levels should be avoided as a precautionary measure.

Pregnancy and breast feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

It can be assumed that on taking TERIZIDON, cycloserine (cycloserine is released from the active substance terizidone) passes into the embryonic blood circulation and into a mother's milk.

The application of TERIZIDON during pregnancy should only be carried out after a careful benefit-risk assessment by your doctor.

The risk of sensitisation, diarrhoea and yeast-like fungi on the mucous membranes cannot be excluded on breast-fed babies.

Your doctor must make a decision on whether breast-feeding should be interrupted or treatment with TERIZIDON should be terminated.
Here both the benefits of breast-feeding for the child and the benefits of the therapy for the mother should be taken into account.

Driving and using machines
Do not drive cars or other vehicles. Do not operate electrical tools or machines. Do not work where you cannot hold on to something!

Commonly, side effects on the central nervous system have been reported. Due to central nervous side effects, TERIZIDON can also alter reaction capabilities when used according to the intended purpose; so much so that the ability for active participation in road traffic or the operation of machines, or working without being able to hold on to something, is restricted. This is in particular the case in interaction with alcohol. You will not be able to react quickly enough and in a targeted manner to unexpected and sudden events.

TERIZIDON contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take TERIZIDON?

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is
Adults are generally administered 3 or 4 TERIZIDON capsules, hard per day (meaning 750-1000 mg terizidone). These should be taken in 3 or 4 individual doses (one TERIZIDON capsule, hard every 8 or 6 hours). The maximum daily dose is 1000 mg terizidone, which is 4 TERIZIDON capsules, hard.

Dosage for patients with renal impairments:
There are no recommendations for the application of terizidone for patients with renal insufficiency. Because the active substance terizidone releases cycloserine, the recommendations for cycloserine can be used as a basis:

- Patients with a creatinine clearance (laboratory value for the determination of renal function) of less than 30 ml/min should be given 250 mg terizidone (equals 1 TERIZIDON capsule, hard) daily or intermittently 500 mg terizidone (equals 2 TERIZIDON capsules, hard) 3 days per week, for example Monday, Wednesday and Friday.

- Please observe that terizidone can be dialyzed. Terizidone should therefore be administered to dialysis patients immediately after dialysis. For dialysis patients who have a continuous form of dialysis, please observe the guidelines in section 2. "What you need to know before you take TERIZIDON".

- TERIZIDON is contraindicated with serum creatinine over 2 mg/dl due to severe renal insufficiency (see section 2. “What you need to know before you take TERIZIDON").

Mode of administration
For oral administration
The capsules, hard are to be taken over the course of the day unchewed with sufficient fluids (e.g. a glass of water) at regular intervals (one capsule, hard every 6 or 8 hours) during mealtimes.
In order to avoid compatibility disorders, your doctor can gradually increase the dose to the optimum quantity.

Duration of use
The duration of therapy generally totals 18-24 months from the time point when no more pathogens can be found in the sputum (after conversion has taken place).
The duration of the application of terizidone in a combination therapy with other antimycobacterial substances is dependent on the clinical progression, in particular on the time point of conversion and the severity of the illness, as well as the therapy regimen applied based on the resistance test.

Please consult your doctor or pharmacist if you have the impression that the effects of TERIZIDON are too severe or too weak.

If you take more TERIZIDON than you should
Should you inadvertently have taken a larger quantity of TERIZIDON than prescribed, the consequences of an overdose are increased severity of the side effect symptoms listed in section 4. "Possible side effects", in particular those referring to side effects on the nervous system such as headaches, dizziness, confusion, drowsiness, excitability, paraesthesia (sensation disorders such as "ants running along the skin", tingling of the skin), dysarthria (speech disorders), psychoses, paresis (paralysis), trembling, cramps and comas.

If you suspect that you have taken an overdose, please consult your doctor immediately so that he can decide whether measures must be taken according to the degree of severity.

If you forget to take TERIZIDON
Do not take a double dose to make up for a forgotten dose.

If you stop taking TERIZIDON
Tuberculosis pathogens can become resistant against medicines through irregular intake and/or premature termination of treatment. By doing this, you place your chances of healing at risk and decrease the possibilities for later treatment.

If you have any further questions on the use of the medicine, ask your doctor or pharmacist.

4. Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them.

The incidence rates of side effects are based on the following categories:

Very common:	may effect more than 1 in 10 people
Common:	may affect up to 1 in 10 people
Uncommon:	may affect up to 1 in 100 people
Rare:	may affect up to 1 in 1,000 people
Very rare:	may affect up to 1 in 10,000 people
Unknown:	frequency cannot be estimated from the available data

Nervous system disorders
Commonly, central nervous disorder side effects such as headaches, dizziness, excitability, shivering, insomnia and feeling drunk can occur.
Rarely to uncommonly, epilepsy-like seizures, depressive and manic reactions and anxiety attacks may occur.

Gastrointestinal disorders
Rarely to uncommonly, gastrointestinal disorders in the form of nausea, stomach pain, meteorism, digestive disorders, diarrhoea or constipation occur.

The following side effects have occurred on administration of cycloserine (the active substance terizidone releases cycloserine):
Congestive cardiac failure (heart complaints), Stevens-Johnson syndrome (allergic skin disorder), rashes, megaloblastic anaemia (blood formation disorder), liver toxicity (damage to the liver through cycloserine), hypersensitivity reactions, central nervous system disorders (drowsiness, somnolence, comas, headaches, shivering, dysarthria [speaking disorders], dizziness, confusion and disorientation with memory loss, nervousness, excitability, psychoses [possibly with self-damaging behaviour], paranoia [delusions], catatonia [body spasms], convulsions, hyperreflexia [increased reflex receptivity], vision impairments, paresis [paralysis], epilepsy-like seizures and absence [impaired consciousness] and encephalopathy [pathological changes to the brain]).
It can be expected that these side effects also occur on application of terizidone.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

Bundesinstitut für Arzneimittel und Medizinprodukte
(Federal Institute for Drugs and Medical Devices)
Abt. Pharmakovigilanz
(Department of Pharmacovigilance)
Kurt-Georg-Kiesinger-Allee 3
53175 Bonn
Website: www.bfarm.de

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store TERIZIDON

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton or container after "Expiry date:". The expiry date refers to the last day of that month.

Storage conditions
Do not store above 30 °C.
Do not throw away any medicines via wastewater (e.g. do not use the toilet or washbasin). Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment. Further information can be found under www.bfarm.de/arzneimittelentsorgung.

6. Contents of the pack and other information

What TERIZIDON contains

- The active substance is terizidone.
  One capsule, hard contains 250 mg terizidone.

- The other ingredients are: lactose monohydrate, gelatine, talcum, purified water, magnesium stearate (Ph. Eur.) [vegetable], copovidone, titan dioxide (E171), iron(III) hydroxide-oxide x H_2O (E172), indigo carmine (E132).

What TERIZIDON looks like and contents of the pack

TERIZIDON is a green, opaque capsule, hard.
Original pack containing 50 capsules, hard

Marketing Authorization Holder and Manufacturer

Marketing Authorization Holder

Esteve Pharmaceuticals GmbH
Hohenzollerndamm 150-151
14199 Berlin
Germany
phone +49 30 338427-0
e-mail info.germany@esteve.com

*formerly RIEMSER Pharma GmbH

Manufacturer

SW Pharma GmbH
Robert-Koch-Straße 1
66578 Schiffweiler
Germany

This leaflet was last revised in November 2021.