

Patient package insert according to Pharmacists' Regulations (Preparations) -1986

This medicine can be sold with a physician's prescription only

TRITTICO 50 mg

TRITTICO 100 mg

FILM-COATED TABLETS

Active ingredient:

Each film coated tablet of Trittico 50 mg contains:
Trazodone hydrochloride 50 mg equivalent to trazodone 45.5 mg.

Each film coated tablet of Trittico 100 mg contains:
Trazodone hydrochloride 100 mg equivalent to trazodone 91.1 mg.

Inactive ingredients and allergens in the medicine – see section 6 "additional information" and in section 2 "Important information about some of the ingredients of this medicine".

Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask the doctor or pharmacist. This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if you think that their medical condition is the same as yours.

1. What is the medicine intended for?
Treatment of depression with or without anxiety.

Pharmacotherapeutic group: Antidepressants.

2. Before using the medicine:

Do not use the medicine if:

- you are (sensitive) allergic to the active ingredient trazodone hydrochloride or to any of the other ingredients this medicine contains (see section 6, "additional information").
- you consume large quantities of alcohol.
- you are a heavy user of medicines to help you sleep (hypnotics).
- you have recently had a heart attack.
- This medicine is not intended for children and adolescents. See section "Children and Adolescents".

Special warnings regarding the use of this medicine:

Do not switch to a different medicine containing Trazodone (the active ingredient in the medicine) without medical consultation and monitoring.

Talk to your doctor or pharmacist before and during taking Trittico.

In particular, tell your doctor if:

- you or your caregiver notice a change in or worsening of your depression, or your usual behaviour, or if you have thoughts of killing yourself. If this happens, inform your doctor immediately.
- you have or have ever had fits or seizures (**epilepsy**), in which case, your doctor will avoid sudden increases or decreases in dosage.
- you have **reduced liver function**, particularly if severe (liver failure).
- you have **reduced kidney function**, particularly if severe (kidney failure).
- you have **heart or blood vessel disorders**, such as chest pain (angina pectoris), disorders of the heart's electrical conduction system or you have recently had a heart attack. See also "Do not use the medicine if" section.
- you have **hyperthyroidism** (an overactive thyroid gland).
- you have **difficulty urinating**, as in the case of prostate hypertrophy (enlarged prostate).
- you have acute narrow-angle **glaucoma** (increased eye pressure).
- you suffer from **schizophrenia or any other mental disorder**, as using Trittico could make these disorders worse, for example increasing paranoid thoughts (believing something is real or true when it is not). See section 4 "Possible side effects".
- you have **sore throat and fever**. In this case, your doctor may advise you to have a blood test because these could be symptoms of a blood disorder (agranulocytosis).
- you feel **unwell or faint** (in particular when you get out of bed or stand up from a seated position), since this could be a sign of low blood pressure.
- you are male and have a **prolonged and painful erection**. If this occurs, stop the treatment immediately.

Patients from 65 Years of age

Use this medicine with caution, as you may be more likely to get side effects, for example a drop in blood pressure when you stand up (orthostatic hypotension) or sleepiness.

Tell your doctor if you or your caregiver notice these side effects. They will monitor you closely, particularly at the beginning of treatment and before and during dosage increases.

Tell your doctor if you have any diseases or are taking any other medicines (see the section "Drug interactions"). The doctor will take the necessary precautions to avoid an increase in side effects.

Interference with urine tests

If, while you are taking Trittico, you undergo a urine test for drug screening which uses special techniques (immunoassays), you could obtain a false positive result for amphetamines identification. If this happens, talk to your doctor and ask for a confirmatory test based on other techniques.

Children and adolescents

Trittico is not intended for children and adolescents under 18 years of age.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. In particular if you are taking:

Medicines that could increase the possible side effects of Trittico

- Medicines that modify the way the liver functions, such as:
 - erythromycin (an antibiotic).
 - ketoconazole, itraconazole (medicines used to treat fungal infections).
 - ritonavir, indinavir (medicines used to treat HIV infection).
- nefazodone (medicine used to treat various forms of depression).
Avoid taking Trittico with these medicines. If necessary, your doctor will reduce the dose of Trittico.
- Tricyclic antidepressants (medicines used to treat depression). Avoid taking these medicines at the same time with trazodone.
- Fluoxetine (a medicine used to treat anxiety and depression).
- Neuroleptics (medicines used to treat mental disorders such as schizophrenia).
- Phenothiazine (medicines used to treat mental disorders such as schizophrenia), such as chlorpromazine, fluphenazine, levomepromazine, perphenazine.
- Medicines that might prolong the QT interval (medicines that cause changes in the electrocardiogram).
- Preparations containing Hypericum perforatum (St. John's Wort, a plant used as an antidepressant).

Medicines that reduce the effect of Trittico

- Oral contraceptives (birth control pill).
- Phenytoin (medicine used to treat epilepsy).
- Carbamazepine (medicine used to treat epilepsy). Your doctor will monitor you to determine whether the dosage of Trittico needs to be increased.
- Barbiturates medicines used as sedatives (tranquillisers), anaesthetics, anti-epileptics, hypnotics (sleep medicines).

Medicines that increase the effect of Trittico

- Cimetidine (medicine used for stomach ulcers).

Other medicines that interfere with Trittico

- Antipsychotics (medicines used to treat certain mental illnesses), hypnotics (sleep medicines), sedatives (tranquillisers), anxiolytics (medicines for anxiety) and antihistamines (medicines used to treat allergies), since their

sedative effect may be increased (reduces alertness). In this case, your doctor may reduce the dose of these medicines.

- MAOI's: monoamine oxidase inhibitors (medicines used to treat anxiety and depression). Do not take trazodone with MAOI's or in the two weeks following discontinuation of MAOI's treatment. Likewise, do not use MAOI's in the week following discontinuation of trazodone treatment.
- Anaesthetics. If you need to have surgery requiring the use of inhaled anaesthetics, tell your anaesthetist that you are taking Trittico. Trittico may increase the effect of the anaesthetic.
- Muscle relaxants (medicines that cause muscle relaxation). If you need to have surgery requiring the use of muscle relaxants, tell your anaesthetist that you are taking Trittico. Trittico may increase the effect of these medicines.
- Levodopa (medicine used to treat Parkinson's disease), as the effect of levodopa may decrease.
- Clonidine (medicine used to lower high blood pressure) as trazodone can decrease the effect of clonidine.
- Warfarin (medicine used to thin the blood).
- Antihypertensives (medicines used to treat high blood pressure), as the doctor may reduce the dose of the antihypertensive if necessary.
- Digoxin (medicine used to treat heart problems).

Use of this medicine and food

If possible, take the tablets on a full stomach. Taking Trittico after meals reduces the chances of side effects.

Use of this medicine and alcohol consumption

Do not take Trittico if you consume large quantities of alcohol (see section 2 "Do not use the medicine if").

Trittico increases the sedative effects (reduces alertness) of alcohol. You should therefore avoid drinking alcohol during treatment with Trittico.

Pregnancy, breast-feeding and Fertility

The information regarding taking Trittico during pregnancy is limited.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, talk to your doctor or pharmacist before taking this medicine.

If you are pregnant or breast-feeding, only take Trittico in case of real need and under the close supervision of your doctor.

If the doctor instructs to take Trittico until delivery, newborns should be monitored for withdrawal symptoms.

Driving and using machines

Trittico has minor or moderate influence on the ability to drive and use machines. Therefore, take special care if you need to drive or use machines. Do not drive or use machines if you get any side effects such as drowsiness, sedation (reduces alertness), vertigo, confusion or blurred vision.

Important information about some of the ingredients of this medicine:

Trittico 50 mg film-coated tablets and Trittico 100 mg film-coated tablets contain:

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.

Castor oil - may cause stomach upset and diarrhoea.

Sodium - this medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially "sodium-free".

Trittico 50 mg film-coated tablets contain also sunset yellow (E110):

Sunset yellow (E110): may cause allergic reactions.

3. How to use this medicine?

Always use this medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine. The dosage and manner of treatment will be determined by the doctor only.

Adults

- The starting dose varies from 75 mg (one and a half 50 mg Trittico tablets) to 150 mg (three 50 mg Trittico tablets or one and a half 100 mg Trittico tablets) per day, to be taken in divided doses.
- During treatment, your doctor may increase the dose to up to 300 mg (six 50 mg Trittico tablets or three 100 mg Trittico tablets) per day, to be taken in divided doses. If you are a hospitalized patient, the dose may be as high as 600 mg per day.

Patients from 65 Years of age

Your doctor will adjust the dose according to your general health and tolerance to the medicinal product. In general, the recommended starting dose is 100 mg per day, given in divided doses or as one single dose, to be taken at night. Single doses above 100 mg should be avoided in these patients. Doses above 300 mg per day are unlikely to be required.

Manner of administration

If possible, take the tablets on a full stomach. Taking Trittico after meals lowers the chances of side effects. Take the night-time dose before going to bed.

The tablet can be divided into equal parts. This allows you to spread the doses out throughout the day, as prescribed by your doctor.

The tablets cannot be chewed or crushed – as they are film coated.

Do not exceed the recommended dose.

Treatment duration

Take this medicine for the amount of time prescribed by your doctor.

If you have accidentally taken a higher dosage

In the event of accidental ingestion or intake of an overdose of Trittico, contact a doctor immediately or go to the nearest hospital. Take this package leaflet with you.

If you take an overdose of this medicine, the following symptoms may appear:

- Drowsiness
- Vertigo
- Nausea
- Vomiting

In the most severe cases, the following symptoms may occur:

- Coma
- Tachycardia (increased number of heartbeats)
- Hypotension (low blood pressure)
- Hyponatraemia (decrease of sodium in the blood which causes a general malaise)
- Convulsions
- Severe difficulty breathing
- Heart disorders including bradycardia (reduced heart rate), arrhythmia (heart rhythm problems).

The doctor will prescribe the most suitable supportive treatment according to the nature and severity of your symptoms.

Symptoms may appear within 24 hours or more after overdose.

If you forget to take the medicine

Do not take a double dose to make up for a forgotten dose. Take the next dose at the usual time and consult your doctor.

If you stop taking the medicine

Do not suddenly stop taking the medicine, particularly in prolonged treatment. Treatment with this medicine must be stopped gradually and under medical supervision so as to minimise the onset of withdrawal symptoms such as nausea, headache and malaise.

Continue with the treatment as recommended by the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions on the use of this medicine, consult the doctor or pharmacist.

4. Side effects

Like any medicine, the use of Trittico may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

If any of the following side effects arise or if noticed by your caregiver, **STOP treatment with this medicine and contact your doctor immediately:**

- Jaundice (yellowing of the skin and white of the eyes).
- Worsening of depression characterised by manic behaviour (obsessive behaviour and/or ideas).
- Priapism (abnormal erection that will not go away).

If any of the following side effects occur or if noticed by your caregiver, contact your doctor immediately:

- suicidal thoughts or suicidal behaviour or any other change in behaviour. These effects could appear both during treatment and in the early stages following the withdrawal of treatment. Your doctor will therefore monitor these symptoms.

In addition, the following side effects could occur for which the frequency is not known:

Side effects with unknown frequency (effects for which a frequency has not yet been determined):

- agranulocytosis/leukopenia (reduced white blood cell count)
- eosinophilia (increased white blood cell count)
- thrombocytopenia (reduced blood platelet count)
- anaemia (reduced haemoglobin - substance that transports oxygen in the blood)
- allergic reactions
- syndrome of inappropriate antidiuretic hormone secretion (disease characterised by decreased blood sodium levels)
- reduced blood sodium levels
- weight loss, loss of appetite with serious weight loss, increased appetite
- confusion, insomnia, disorientation, anxiety, nervousness and agitation (occasionally worsening to delirium)
- delirium, aggressiveness, hallucinations (seeing things that are not really there), nightmares
- reduced sexual desire
- withdrawal syndrome (onset of withdrawal symptoms with such symptoms as nausea, headache, malaise)
- serotonin syndrome (disease characterised by an excessive increase in the effect of a substance called "serotonin", which causes a series of effects including headache, agitation, mental confusion, hallucinations and coma)
- convulsions
- malignant neuroleptic syndrome (severe nervous system disease)
- dizziness, vertigo, headache
- drowsiness, restlessness, decreased alertness
- tremor (shaking)
- blurred vision
- memory disturbance
- muscle twitching (myoclonus)
- language disorders (expressive aphasia)
- altered sensitivity (paraesthesia)
- altered muscle tone (dystonia)
- altered taste
- cardiac arrhythmias (heart rhythm problems), bradycardia (reduced number of heartbeats), tachycardia (increased number of heartbeats), electrocardiogram changes.
- hypotension (low blood pressure), including orthostatic hypotension (severe reduction in blood pressure when rising to a standing position)
- syncope (fainting)
- hypertension (high blood pressure)
- nasal congestion (stuffy nose), dyspnoea (difficulty breathing)
- nausea, vomiting, dry mouth, constipation, diarrhoea, digestion problems, stomach pain, gastroenteritis (inflammation involving the stomach and initial portion of the intestine), increased salivation, paralytic ileus (intestinal obstruction)
- altered liver function (including liver damage and cholestasis)
- rash, itching, excessive sweating (hyperhidrosis)
- pain in the legs and arms, back pain, myalgia (muscle pain), arthralgia (joint pain)
- urinary disorders
- weakness, oedema (swelling due to fluid accumulation), influenza-like symptoms, fatigue, chest pain, fever
- increased liver enzymes (substances present in the liver and which, when increased, indicate the presence of liver damage).

If a side effect appears, if one of the side effects worsens or if you suffer from a side effect which is not mentioned in this leaflet, consult the doctor.

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking the link "report side effects due to medication" that can be found on the homepage of the Ministry of Health website (www.health.gov.il) directing to an online form for reporting side effects, or by clicking the link: <https://sideeffects.health.gov.il>.

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. Date) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** This medicinal product does not require any special storage conditions, but it is recommended to be stored in room temperature.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

TRITTICO 50 mg film-coated tablets:
Lactose monohydrate, Calcium hydrogen phosphate *2H2O, Microcrystalline cellulose, Maize starch, Sodium starch glycolate type A, Povidone, Magnesium stearate, Ethylcellulose, Sunset yellow (E110) Lake, Castor oil (virgin), E wax, Talc.

TRITTICO 100 mg film-coated tablets:
Lactose monohydrate, Calcium hydrogen phosphate *2H2O, Microcrystalline cellulose, Maize starch, Sodium starch glycolate type A, Povidone, Magnesium stearate, Ethylcellulose, Talc, Castor oil (virgin), E wax.

What does the medicine look like and what does the package contain:

Trittico 50 mg Tablets:
Trittico 50 mg is Pale orange yellow, round, smooth, glossy, biconvex film-coated tablets with one sided central score line.

Trittico 100 mg Tablets:
Trittico 100 mg is white to off-white, round, smooth, glossy, biconvex film-coated tablets with one sided central score line.

The tablets are packaged in blisters, in a box containing 30 tablets (2 blisters of 15 tablets, 50 mg or 100 mg each).

Marketing authorization holder and importer
RAZ pharmaceuticals LTD., 31 GESHER HAETZ ST., INDUSTRIAL PARK, EMEK HEFER, 3877701, ISRAEL

Registration numbers of the medicines in the national drug registry of the ministry of health:

TRITTICO 50 MG: 173-30-36297-00
TRITTICO 100 MG: 173-31-36296-00

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