

PACKAGE LEAFLET

Package leaflet: Information for the patient

Metyrapone Esteve 250mg soft capsules

Metyrapone

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 Metyrapone Esteve is and what it is used for
2. What you need to know before you take Metyrapone Esteve
3. How to take Metyrapone Esteve
4. Possible side effects
5. How to store Metyrapone Esteve
6. Contents of the pack and other information

1. What Metyrapone Esteve is and what it is used for

Metyrapone Esteve belongs to a group of medicines called endocrine medicines. It works by decreasing the production of certain types of steroids.

Metyrapone Esteve contains 250 mg of metyrapone. Metyrapone belongs to a group of medicines known as tests for pituitary function evaluation. Metyrapone is used as a diagnostic test to identify if you have an insufficient level of ACTH, a hormone secreted by the pituitary gland which controls cortisol secretion; or metyrapone may be used to help diagnose a specific type of Cushing's syndrome (a condition when the body produces too much cortisol which is a type of steroid).

The medicine can also be used to treat the signs and symptoms of endogenous Cushing's syndrome by lowering the elevated levels of cortisol (a hormone produced by the adrenal glands). Cushing's syndrome is a set of symptoms resulting from high levels of the hormone cortisol produced in your body by the adrenals.

It is also used to treat some types of water retention in patients suffering from certain kidney problems, cirrhosis of the liver, or heart failure.

2. What you need to know before you take Metyrapone Esteve

Do not take Metyrapone Esteve as a diagnostic test for ACTH insufficiency:

- If you suffer from a condition whereby your adrenal glands do not produce enough steroid hormones, cortisol or aldosterone, known as Addison's disease.

Do not take Metyrapone Esteve:

- If you are allergic (hypersensitive) to metyrapone or any of the other ingredients of this medicine (listed in section 6)

Warnings and precautions

Talk to your doctor before taking Metyrapone Esteve if:

- you have, or think you may have, a condition in which your hormone levels are low (e.g. reduced adrenal gland production of cortisol or severe hypopituitarism). Your doctor will need to perform a test to make sure Metyrapone Esteve is right for you.
- you have cirrhosis of the liver, liver disease or damage to the liver, as this may cause the medicine to work more slowly.
- you are taking any medicines such as glucocorticoids as your doctor may decide to not do the Metyrapone Esteve test as you will need to stop taking these.

During treatment with Metyrapone Esteve

Metyrapone Esteve may temporarily lower the amount of hormones produced by your adrenal gland but your doctor will correct this using appropriate steroid medication.

If you have Cushing's syndrome, your doctor may also give you medicine to prevent infections developing. But if you develop shortness of breath and fever over hours or days contact your doctor as soon as possible as you may be developing a serious lung infection.

Tests before and during treatment with Metyrapone Esteve

Your doctor will test your blood before you start the treatment and regularly during the treatment. This is to detect any possible abnormalities in your potassium levels and also to measure the levels of cortisol. Depending on the results, your doctor may adapt the dosage and/or prescribe a corrective treatment.

Depending on your cardiac risk factors, your doctor may decide to perform an ECG before the initiation or during treatment with Metyrapone Esteve.

Talk to your doctor if you experience any of the following symptoms: weakness, fatigue, dizziness, loss of appetite, nausea or vomiting, diarrhoea, abdominal pain. These symptoms and also low blood pressure, high levels of potassium, low levels of sodium or low levels of glucose in the blood may be signs of hypocortisolism (insufficient levels of cortisol in the blood).

Your doctor will therefore check your blood pressure and perform a blood test. If you are diagnosed with hypocortisolism, your doctor may decide to temporarily administer a steroid (glucocorticoid) replacement therapy and/or reduce the dose or interrupt the treatment with Metyrapone Esteve.

If you take Metyrapone Esteve for a long time

Your blood pressure may increase when taking this medicine.

Other medicines and Metyrapone Esteve

Tell your doctor or pharmacist if you are taking, have recently taken/used or might take any of the following medicines as they may influence the results of the test with this medicine. The following medicines may affect the results of the Metyrapone Esteve test:

- Anticonvulsants used to control epilepsy (e.g. phenytoin, barbiturates)
- Anti-depressants and neuroleptics used to treat anxiety, depression or psychiatric problems (e.g. amitriptyline, chlorpromazine, alprazolam)
- Hormones that affect the hypothalamo-pituitary axis which regulate many body

processes such as stress, emotions, energy levels, digestion and the immune system (e.g. cortisol, hydrocortisone, ACTH, tetracosactin)

- Corticosteroids
- Antithyroid agents used to treat thyroid conditions (e.g. thyroxine, liothyroxine, carbimazole)
- Cyproheptadine used to treat allergies (e.g. Periactin)

Metyrapone Esteve should not be taken with paracetamol without consulting your doctor.

Please tell your doctor or pharmacist if you are taking or have recently taken/used any other medicines, including medicines obtained without a prescription.

Metyrapone Esteve with food and drink

Metyrapone Esteve should be swallowed whole with a drink of milk or after a meal. This will reduce the chance of the capsules making you feel sick.

Pregnancy and breast-feeding

Use in pregnancy

Metyrapone Esteve is not recommended in women of childbearing potential who are not using contraception.

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

If you have to take the medicine during pregnancy, your doctor will need to monitor your baby's cortisol levels for the first week of its life.

Use in breast-feeding

Breast-feeding should be discontinued during treatment with Metyrapone Esteve as there is a possibility that metyrapone may be passed to your baby in breast milk.

Driving and using machines

Taking Metyrapone Esteve may make you feel dizzy or tired. If you are affected you should not drive or work with machinery until this effect has worn off.

Metyrapone Esteve contains sodium ethylparahydroxybenzoates (E215) and sodium propylparahydroxybenzoate (E217) which may cause allergic reactions (possibly delayed).

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium free'.

Monitoring and supervision

When used as a diagnostic test, you should only be given this medicine when a healthcare professional is present, as they will need to monitor your body's responses to the medicine.

3. How to take Metyrapone Esteve

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. If you are being given Metyrapone Esteve to diagnose Cushing's Syndrome, you will need to go into hospital for some tests.

Metyrapone Esteve should be swallowed whole with a drink of milk or after a meal. Do not chew the capsules.

The recommended dose for each condition is given below.

If you are having a short single-dose test (to test pituitary function):

You will be asked to swallow the capsule(s) with yoghurt or milk at about midnight. You will then have a blood sample taken in the morning which will be reviewed by the doctor. The recommended dose is 30 mg/kg. The same dose is used in children.

If you are having a multiple-dose test (to test pituitary function and to help diagnose a specific type of Cushing's syndrome):

To determine if you have Cushing's syndrome you will be kept in hospital for 4 days. Your urine will be tested each day. Your doctor will start taking samples of your urine 24 hours before you are given this medicine. You will then be given 2-3 capsules (500 – 750 mg) every 4 hours for the next 24 hours. You should take the capsules with milk or after a meal. Your doctor will then take more urine samples over the next 24 hours. The fourth day of your hospital stay will give the results of your test. You will then be told by your doctor whether or not you have Cushing's syndrome.

Treatment of signs and symptoms of endogenous Cushing's syndrome

The usual dose is between one (250 mg) and 24 capsules (6 g) each day in three or four divided doses. The Metyrapone Esteve dose may be periodically adjusted by your doctor with the aim to restore normal cortisol levels. You should always follow the doctors' instructions closely and never change your dose unless your doctor tells you to.

Treatment of water retention

The usual dose is 12 capsules (3 g) a day, divided throughout the day. You will also be given a steroid medicine at the same time.

If you are elderly, you will receive the same doses as above.

Use in children

For the multiple-dose test children should be given 15 mg/kg with a minimum dose of 250 mg every 4 hours.

For management of Cushing's syndrome, the dose should be adjusted on an individual basis as a function of cortisol levels and tolerability

If you are not sure how many capsules to take, ask your doctor or pharmacist.

If you take more Metyrapone Esteve than you should

If you accidentally take too many Metyrapone Esteve capsules, or someone else takes any of this medicine, you should tell your doctor or nurse immediately or contact your nearest accident and emergency department. You may feel sick and have stomachache and/or diarrhoea. You may also feel dizzy, tired, have a headache, begin sweating and your blood pressure increases. You may need to take activated charcoal and be given hydrocortisone. Show any left over medicines or the empty packet to the doctor.

If you forget to take Metyrapone Esteve

If you forget to take a dose, take it as soon as possible, unless it is almost time to take the next dose. Do not take a double dose to make up for a forgotten capsule. Then go on as before.

If you stop taking Metyrapone Esteve

Do not stop taking Metyrapone Esteve suddenly as this can make your condition worse.

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

4. Possible side effects

Like all medicines, Metyrapone Esteve can cause side effects, although not everyone gets them.

Some side effects may be serious:

- Tell your doctor immediately if you have two or more of these symptoms: weakness, light-headedness, fatigue, lack of appetite, nausea, vomiting, abdominal pain, diarrhea. This may indicate that you have adrenal insufficiency (low cortisol levels). Adrenal insufficiency occurs when metyrapone lowers the amount of cortisol too much. It is more likely to occur during periods of metyrapone dosage increase or increased stress. Your doctor will correct this by using a hormone medicine to compensate lack of cortisol and/or by adjusting the dose of metyrapone.
- Tell your doctor immediately if you have bleeding or bruising lasting longer than normal, blood seen in the gums, nose or skin and feeling tired most of the time. This may indicate that you have a decrease of amount of red blood cells and/or white blood cells and/or platelets in blood.

See also Section 2 “During treatment with Metyrapone Esteve”.

Side effects (by frequency):

Very common (may affect more than 1 in 10 people):

- Adrenal insufficiency (low cortisol levels)
- Loss of appetite
- Headache
- Dizziness (light-headedness)
- High blood pressure (hypertension)
- Nausea (feeling sick)
- Abdominal (stomach) pain
- Diarrhoea
- Skin allergic reaction (urticaria, rash (skin redness), itching)
- Joint pain
- Swelling of limbs, hands or feet
- Asthenic conditions (tiredness, fatigue)

Common (may affect up to 1 in 10 people):

- Low level of potassium(hypokalaemia)
- Feeling tired or sleepy
- Vomiting
- Low blood pressure (hypotension).
- Acne
- Excessive hair growth in unusual area (hirsutism)
- Muscular pain

Not known (frequency cannot be estimated from the available data):

- Abnormal liver function (hepatic enzymes increased)
- Leukopenia, anaemia, thrombocytopenia (decrease of amount of red blood cells, white blood cells or platelets in blood)
- Alopecia (hair loss)

- Pulmonary infection

Reporting side effects

If you get any side effects, tell your doctor or pharmacist.

This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see below). By reporting side effects, you can help provide more information on the safety of this medicine.

United Kingdom

Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

5. How to store Metyrapone Esteve

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 and bottle. The expiry date refers to the last day of that month.

Store below 25°C. Keep the bottle tightly closed in order to protect from moisture. Do not take Metyrapone Esteve if you notice any change in the colour of the capsules.

Medicines should not be disposed of 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. Contents of the pack and other information

What Metyrapone Esteve contains

- The active substance is metyrapone. Each capsule contains 250 mg of metyrapone.
- The other ingredients are
 - capsule core: glycerin, polyethylene glycol 400, polyethylene glycol 4000 and water
 - capsule shell: sodium ethyl parahydroxybenzoate (E215), ethyl vanillin, gelatin, p- methoxy acetophenone, sodium propyl parahydroxybenzoate (E217) and titanium dioxide (E171).

What Metyrapone Esteve looks like and contents of the pack

Each plastic bottles contains 100 soft capsules.

Each oblong capsule is yellowish-white. Each capsule has 'HRA' printed on one side. The printing is in red ink.

Marketing Authorization Holder

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