SCHEDULING STATUS:

S5

MYTRA 15 & MYTRA 30, film-coated tablets

Mirtazapine

MYTRA 15 contains sugar (lactose monohydrate 102 mg)

MYTRA 30 contains sugar (lactose monohydrate 204 mg)

Read all of this leaflet carefully before you start taking MYTRA

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- MYTRA has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What MYTRA is and what it is used for

MYTRA belongs to a group of medicines called antidepressants.

MYTRA is used to treat major depressive illness (persistently depressed mood or loss of interest in activities, causing significant impairment in daily life).

2. What you need to know before you take MYTRA

Do not take MYTRA:

- If you are hypersensitive (allergic) to mirtazapine or any of the other ingredients of MYTRA (as listed in section 6).
- If you are pregnant or breastfeeding.
- If you are a child and under 18 years old.
- If you are taking or have recently taken (within the last two (2) weeks) medicines called monoamine oxidase inhibitors (MAOIs).

Tell your doctor before taking MYTRA:

If you have ever developed a severe skin rash or skin peeling, blistering and / or mouth sores after taking mirtazapine or other medicinal product(s).

Warnings and precautions

Take special care with MYTRA:

Children and adolescents

MYTRA should not be used for children and adolescents under 18 years. You should know that patients under 18 have an increased risk of side-effects such as suicide attempt, suicidal thoughts and hostility (predominant aggression, oppositional behaviour and anger) when they take antidepressants such as MYTRA.

Thoughts of suicide and worsening of your depression

If you are depressed, you can sometimes have thoughts of harming or killing yourself. These may be increased when first starting antidepressants such as MYTRA, since these medicines all take time to work, usually about two (2) weeks but sometimes longer.

You may be more likely to think like this:

- if you have previously had thoughts about killing or harming yourself.

- if you are a young adult. Information from clinical trials has shown an increased risk of suicidal behaviour in adults aged less than 25 years with psychiatric conditions who were treated with an antidepressant.

If you have thoughts of harming or killing yourself at any time, contact your doctor or go to a hospital straight away.

You may find it helpful to tell a relative or close friend that you are depressed and ask them to read this leaflet. You might ask them to tell you if they think your depression is getting worse, or if they are worried about changes in your behaviour.

Also take special care with MYTRA

If you have, or have ever had one (1) of the following conditions:

- seizures (epilepsy). If you develop seizures or your seizures become more frequent, stop taking MYTRA and contact your doctor immediately;
- serious skin reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported with the use of MYTRA. Stop taking MYTRA and seek medical attention immediately if you notice any of the symptoms described in section 4 in relation to these skin reactions. If you ever developed any severe skin reactions, treatment with MYTRA should not be restarted;
- liver disease, including jaundice. If jaundice occurs, stop taking MYTRA and contact your doctor immediately;
- kidney disease;
- heart disease, or low blood pressure;
- certain kinds of heart conditions that may change your heart rhythm, a recent heart attack, heart failure, or take certain medicines that may affect the heart's rhythm;
- diabetes (you may need to adjust your dose of insulin or other antidiabetic medicines);
- schizophrenia. If psychotic symptoms, such as paranoid thoughts become more frequent or severe, contact your doctor straight away;
- manic depression (alternating periods of feeling elated/overactivity and depressed mood). If you start feeling elated or over-excited, stop taking MYTRA and contact your doctor immediately;
- eye disease, such as increased pressure in the eye (glaucoma);

- difficulty in passing water (urinating), which might be caused by an enlarged prostate;
- if you develop signs of infection such as inexplicable high fever, sore throat and mouth ulcers. Stop taking MYTRA and consult your doctor immediately for a blood test. In rare cases these symptoms can be signs of disturbances in blood cell production in the bone marrow. While rare, these symptoms most commonly appear after four (4) - six (6) weeks of treatment;
- if you are an elderly person. You could be more sensitive to the side-effects of antidepressants such as MYTRA.

Other medicines and MYTRA

Always tell your healthcare provider if you are taking any other medicine (this includes all complementary or traditional medicines).

Do not take MYTRA in combination with:

- monoamine oxidase inhibitors (MAOIs). Also, do not take MYTRA during the two (2) weeks after you have stopped taking MAOIs. If you stop taking MYTRA, do not take MAOIs during the next two (2) weeks either. Examples of MAOIs are moclobemide, tranylcypromine (both antidepressants) and selegiline (used for Parkinson's disease).

Take care when taking MYTRA in combination with:

- antidepressants such as selective serotonin reuptake inhibitors (SSRIs), venlafaxine and L-tryptophan, or triptans (used to treat migraine), tramadol (a pain-killer), linezolid (an antibiotic), venlafaxine (used to treat depression), lithium (used to treat some psychiatric conditions), methylene blue (used to treat high levels of methaemoglobin in the blood and St. John's Wort - *Hypericum perforatum* preparations (a herbal remedy for depression). In very rare cases MYTRA alone or the combination of MYTRA with these medicines, can lead to a so-called serotonin syndrome. Some of the symptoms of this syndrome are: inexplicable fever, sweating, increased heart rate, diarrhoea, (uncontrollable) muscle contractions, shivering, overactive reflexes, restlessness, mood changes, and unconsciousness. If you get a combination of these symptoms, talk to your doctor immediately.
- warfarin - medicines to prevent blood clotting. MYTRA can increase the effects of warfarin on the blood. In case of combination it is advised that your doctor monitors your blood carefully.

- medicines for anxiety or insomnia such as benzodiazepines; medicines for schizophrenia such as olanzapine; medicines for allergies such as cetirizine; medicines for severe pain such as morphine; alcohol.

In combination with these medicines MYTRA can increase the drowsiness caused by these medicines.

- medicines for infections; medicines for bacterial infections (such as erythromycin); medicines for fungal infections (such as ketoconazole); medicines for HIV / AIDS (such as HIV protease inhibitors) and medicines for stomach ulcers (such as cimetidine).

In combination with MYTRA, these medicines can increase the amount of MYTRA in your blood. Inform your doctor if you are using these medicines. It might be needed to lower the dose of MYTRA, or when these medicines are stopped, to increase the dose of MYTRA again.

- medicines for epilepsy such as carbamazepine and phenytoin;
- medicines for tuberculosis such as rifampicin.

In combination with MYTRA, these medicines can reduce the amount of MYTRA in your blood. Inform your doctor if you are using these medicines. It might be needed to increase the dose of MYTRA, or when these medicines are stopped, to lower the dose of MYTRA again.

- medicines that may affect the heart's rhythm such as certain antibiotics and some anti-psychotics.

MYTRA with food, drink and alcohol

You may get drowsy if you drink alcohol while you are taking MYTRA. You are advised not to drink any alcohol when taking MYTRA.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking MYTRA.

You should not take MYTRA if you are pregnant or breastfeeding your baby (refer to 'Do not take MYTRA').

Driving and using machines

MYTRA may decrease your concentration, alertness, judgment and thinking.

It is not always possible to predict to what extent MYTRA may interfere with your daily activities. You should ensure that you do not engage in driving a vehicle or use machinery until you are aware of the measure to which MYTRA affects you.

MYTRA contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take MYTRA

Do not share medicines prescribed for you with any other person.

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

The usual starting dose is 15 mg every day. Your doctor may advise you to increase your dose after a few days to the amount that is best for you (between 15 mg and 45 mg per day).

Take MYTRA at the same time each day. It is best to take MYTRA as a single dose before you go to bed. However, your doctor may suggest you split your dose of MYTRA, once in the morning and once at night, before you go to bed. The higher dose should be taken before you go to bed.

However, if you are an elderly person or if you have renal or liver disease, your doctor may adapt the dose.

Take your tablets orally. Swallow your prescribed dose of MYTRA without chewing, with some water.

It is important that during the first few weeks of the treatment, you talk with your doctor if you have any thoughts about harming yourself.

Your doctor will tell you how long your treatment with MYTRA will last.

If you have the impression that the effect of MYTRA is too strong or too weak, tell your doctor or pharmacist.

If you take more MYTRA than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available contact the nearest hospital or poison centre.

If you forget to take MYTRA

Do not take a double dose to make up for forgotten individual doses.

If you stop taking MYTRA

Your doctor will tell you how long to take the treatment. Do not stop earlier than you are told, even if you feel better.

Do not suddenly stop taking MYTRA, even when your depression has lifted. If you suddenly stop taking MYTRA you may feel sick, dizzy, agitated or anxious, and have headaches. These symptoms can be avoided by stopping gradually. Your doctor will tell you how to decrease the dose gradually.

4. Possible side effects

MYTRA can have side effects.

Not all side effects reported for MYTRA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking MYTRA, please consult your healthcare provider for advice.

If any of the following happens, stop taking MYTRA and tell your doctor immediately or go to the casualty department of your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat (angioedema), which may cause difficulty in swallowing or breathing,
- skin rash or itching,
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to MYTRA. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

Frequent

- skin rash with fever

Less frequent

- signs of infection such as sudden unexplainable high fever, sore throat and mouth ulcers (agranulocytosis);
- feeling elated or emotionally ‘high’ (mania)
- hallucinations
- convulsions (fits)
- inability to sit or keep still
- muscle twitching or contractions
- abnormal physical weakness or lack of energy
- inflammation of the pancreas which may cause abdominal pain and nausea
- aggression

Frequency unknown

- thoughts of harming or killing yourself;
- a skin reaction known as ‘erythema multiforme (itchy reddish purple patches on the skin, especially on the palms of the hands or soles of the feet, ‘hive-like’ raised swollen areas on the skin, tender areas on the surfaces of the mouth, eyes and genitals, which may be accompanied by fever and tiredness);
- reddish patches on the torso which are target-like macules or circular, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome, toxic epidermal necrolysis);
- widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome);
- jaundice (yellowing of skin and / or eyes)

- MYTRA can cause disturbances in the production of blood cells (bone marrow depression). Some people become less resistant to infection because MYTRA can cause a temporary shortage of white blood cells (granulocytopenia). MYTRA can also cause a shortage of red and white blood cells, as well as blood platelets (aplastic anaemia), a shortage of blood platelets (thrombocytopenia) or an increase in the number of white blood cells (eosinophilia)

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects

- abnormal dreams;
- confusion;
- anxiety;
- trouble falling or staying asleep (insomnia);
- nightmares;
- drowsiness, sleepiness;
- dizziness;
- headache;
- involuntary shaking (tremor);
- lack of energy and enthusiasm;
- memory loss;
- increase in appetite and weight gain;
- dry mouth;
- constipation;
- nausea, vomiting;
- diarrhoea;
- thirst;
- low blood pressure when you stand up from a sitting or lying position;

- joint pain, muscle pain, back pain.

Less frequent side effects

- increased sweating;
- tiredness;
- moving or spinning sensation (vertigo);
- abnormal sensation in the skin e.g. burning, stinging, tickling or tingling (paraesthesia);
- sensations of numbness in the mouth (oral hypoaesthesia);
- fluid retention (swollen ankles, feet or legs);
- elevated levels of certain enzymes as revealed by blood tests.

Unknown frequency

- a bitter or bad taste in the mouth;
- increase in liver enzymes;
- condition that occurs when the level of sodium in the blood is too low (hyponatraemia);
- sleepwalking;
- a combination of symptoms such as inexplicable fever, sweating, increased heart rate, diarrhoea, (uncontrollable) muscle contractions, shivering, overactive reflexes, restlessness, mood changes, unconsciousness and increased salivation. These can be signs of serotonin syndrome.
- slowed or slurred speech;
- your salivary glands produce more saliva than usual;
- general swelling throughout the body;
- difficulty urinating and completely emptying the bladder;
- a breakdown of muscle tissue that releases a damaging protein into the blood (rhabdomyolysis);
- increased prolactin hormone levels in blood (hyperprolactinemia, including symptoms of enlarged breasts and/or milky nipple discharge).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of MYTRA.

5. How to store MYTRA

Store at or below 25 °C.

Protect from light and moisture.

Store blisters in the original carton until required for use.

Store all medicines out of reach of children.

Do not use after the expiry date stated on the label and carton.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What MYTRA contains

Each film-coated tablet contains 15 or 30 mg mirtazapine.

The other ingredients are lactose monohydrate, hydroxypropyl cellulose, maize starch, silica colloidal anhydrous (Aerosil 200), low-substituted hydroxypropyl cellulose (Grade LH-11), magnesium stearate.

Film-coating

MYTRA 15: Opadry Yellow 20A52560 consisting of: hydroxypropyl cellulose, hypromellose titanium dioxide, iron oxide yellow.

MYTRA 30: Opadry Brown 20A56788 consisting of: hydroxypropyl cellulose, hypromellose titanium dioxide, iron oxide yellow, iron oxide red, iron oxide black.

What MYTRA looks like and contents of the pack

MYTRA 15: Yellow, biconvex, capsule shaped, film-coated tablets with a score line in between ‘1’ and ‘5’ on one side and ‘MI’ debossed on the other side.

MYTRA 30: Reddish brown, biconvex, capsule shaped, film-coated tablets with a score line in between ‘3’ and ‘0’ on one side and ‘MI’ debossed on the other side.

Tablets are packed in white opaque PVC (250 microns) coated with PVdC (60 g/m^2) as the forming material and aluminium foil (25 microns) as the lidding material, in the following pack sizes:

MYTRA 15: 30's

MYTRA 30: 30's

Holder of Certificate of Registration

Novagen Pharma (Pty) Ltd.

Office 2, 100 Sovereign Drive, Route 21 Corporate Park

Nellmapius Drive, Irene, Pretoria

Tel no. 012 345 3175

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Registration number

MYTRA 15: A40/1.2/0652

MYTRA 30: A40/1.2/0653

Professional Information for MYTRA tablets available on the Novagen Pharma website:

http://www.novagenpharma.co.za/products/central-nervous-system/