PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

This medicine can be sold under doctor's prescription only

REMERON® 30 mg

Tablets

Each tablet contains:
Mirtazapine 30 mg
For a list of inactive ingredients see section 6.1, "**What REMERON contains**".

Read all of this leaflet carefully before you start using this medicine.

- This leaflet contains concise information about **REMERON**. If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.
- This medicine is not intended for use in children and adolescents below 18 years of age.
    - It will take 1-2 weeks until **Remeron** will start working. After 2-4 weeks you may start to feel better. If after 2-4 weeks you do not feel better or if you feel worse you should speak with your doctor. Additional information appears in section 3 under "When can you expect to start feeling better"**.**

Anti-anxiety and anti-depression drugs, elevate the risk of suicidal behavior and suicidal thoughts in children, adolescents and young adults up to age 25.

When starting the treatment with the medicine, patients in all ages and their relatives, must monitor after behavioral changes e.g.: worsening of the depression, suicidal thoughts, and aggressiveness.

1. WHAT IS THE MEDICINE INTENDED FOR?

REMERON is used to treat depression.

Therapeutic group: An SNRI preparation.

2. BEFORE YOU TAKE REMERON

2.1 Do not use REMERON if you:

- are allergic to mirtazapine or any of the other ingredients of this medicine (listed in section 6). If so, you must talk to your doctor as soon as you can before taking **REMERON**.
- are taking or have recently taken (within the last two weeks) medicines called monoamine oxidase inhibitors (MAO-Is).

2.2 Special warnings concerning use of REMERON

Before starting treatment with REMERON, talk to your doctor or pharmacist.

Children and adolescents
REMERON is not intended for use in children and adolescents under 18 years because efficacy was not demonstrated. Also, you should know that patients under 18 have an increased risk of side-effects such as suicide attempt, suicidal thoughts and hostility (predominantly aggression, oppositional behaviour and anger) when they take this class of medicines. If your doctor has prescribed **REMERON** for a patient under 18 and you want to discuss this, please go back to your doctor. You should inform your doctor if any of the symptoms listed above develop or worsen when patients under 18 are taking **REMERON**. Also, the long-term safety effects concerning growth, maturation and cognitive and behavioural development of **REMERON** in this age group have not yet been demonstrated. In addition, significant weight gain has been observed in this age category more often when treated with **REMERON** compared with adults.

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, since these medicines all take time to work, usually about two 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 straightaway.

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 **REMERON**
- if you have, or have ever had one of the following conditions.

→ Tell your doctor about these conditions before taking **REMERON**, if not done previously
  - **seizures** (epilepsy). If you develop seizures or your seizures become more frequent, stop taking **REMERON** and contact your doctor immediately;
  - **liver disease**, including jaundice. If jaundice occurs, stop taking **REMERON** and contact your doctor immediately;
  - **kidney disease**;
  - **heart disease**, or **low blood pressure**;
  - **schizophrenia**. If psychotic symptoms, such as paranoid thoughts become more frequent or severe, contact your doctor straightaway;
  - **manic depression** (alternating periods of feeling elated/over activity and depressed mood). If you start feeling elated or over-excited, stop taking **REMERON** and contact your doctor immediately;
  - **diabetes** (you may need to adjust your dose of insulin or other antidiabetic medicines);
  - **eye disease**, such as increased pressure in the eye (glaucoma);
  - **difficulty in passing water** (urinating), which might be caused by an enlarged prostate.
  - **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.
- if you develop signs of infection such as inexplicable high fever, sore throat and mouth ulcers.

→ Stop taking **REMERON** 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 4-6 weeks of treatment.
- if you are an elderly person. You could be more sensitive to the side-effects of antidepressants.

2.3 Taking other medicines
If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, you should tell the attending doctor or pharmacist.
Do not take REMERON in combination with:
- **monoamine oxidase inhibitors** (MAO inhibitors). Also, do not take **REMERON** during the two weeks after you have stopped taking MAO inhibitors. If you stop taking **REMERON**, do not take MAO inhibitors during the next two weeks either.
  Examples of MAO inhibitors are moclobemide, tranylcypromine (both are antidepressants) and selegiline (used for Parkinson's disease).

Take care when taking **REMERON** in combination with:
- **antidepressants such as SSRIs, venlafaxine and L-tryptophan or triptans** (used to treat migraine), **tramadol** (a pain-killer), **linezolid** (an antibiotic), **lithium** (used to treat some psychiatric conditions), **methylene blue** (used to treat high levels of methemoglobin in the blood) **and St. Johns Wort – Hypericum perforatum preparations** (a herbal remedy for depression). In very rare cases **REMERON** alone or the combination of **REMERON** 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.
- **the antidepressant nefazodone.** It can increase the amount of **REMERON** in your blood. Inform your doctor if you are using this medicine. It might be needed to lower the dose of **REMERON**, or when use of nefazodone is stopped, to increase the dose of **REMERON** again.
- **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.
  In combination with these medicines **REMERON** 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) and medicines for HIV/AIDS (such as HIV-protease inhibitors) and **drugs for stomach ulcers** (such as cimetidine).

In combination with **REMERON** these medicines can increase the amount of **REMERON** in your blood. Inform your doctor if you are using these medicines. It might be needed to lower the dose of **REMERON**, or when these medicines are stopped, to increase the dose of **REMERON** again.
- **medicines for epilepsy** such as carbamazepine and phenytoin;
  medicines for tuberculosis such as rifampicin.
  In combination with **REMERON** these medicines can reduce the amount of **REMERON** in your blood. Inform your doctor if you are using these medicines. It might be needed to increase the dose of **REMERON**, or when these medicines are stopped to lower the dose of **REMERON** again.
- **medicines to prevent blood clotting** such as warfarin.
  REMERON can increase the effects of warfarin on the blood. Inform your doctor if you are using this medicine. In case of combination it is advised that a doctor monitors your coagulation functions carefully.

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

2.4 Taking REMERON with food and alcohol
You may get drowsy if you drink alcohol while you are taking **REMERON**.
You are advised not to drink any alcohol.
You can take **REMERON** with or without food.

2.5 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.

Limited experience with **REMERON** administration to pregnant women does not indicate an increased risk. However, caution should be exercised when used during pregnancy.
If you use **REMERON** until, or shortly before birth, your baby should be supervised for possible adverse effects.
When taken during pregnancy, similar drugs (SSRIs) may increase the risk of a serious condition in babies, called persistent pulmonary hypertension of the new-born (PPHN), making the baby breathe faster and appear bluish. These symptoms usually begin during the first 24 hours after the baby is born. If this happens to your baby you should contact your midwife and/or doctor immediately.

2.6 Driving and using machines
REMERON can affect your concentration or alertness. Make sure these abilities are not affected before you drive or operate machinery. **2.7 Important information about some of the ingredients of REMERON**
REMERON tablets contain lactose. If you have been told by your doctor that you have an intolerance for some sugars, contact your doctor before taking this medicinal product (see also section 6.1, "What **REMERON** contains?").

3. HOW TO TAKE REMERON?
Always take **REMERON** as instructed by the doctor. You should check with your doctor or pharmacist if you are not sure.
The dosage and duration of treatment will be determined by the doctor only.

The usually recommended dose is:
The recommended starting dose is 15 or 30 mg every day. Your doctor may advise you to after a few days to the amount that is best for you (between 15 and 45 mg per day). The dose is usually the same for all ages. However, if you are an elderly person or if you have renal or liver disease, your doctor may adapt the dose.
The tablet can be halved.
Do not exceed the recommended dose.

When to take REMERON
Take **REMERON** at the same time each day. It is best to take **REMERON** as a single dose before you go to bed. However your doctor may suggest you to split your dose of **REMERON** – once in the morning and once at night-time before you go to bed. The higher dose should be taken before you go to bed.
Take your tablets orally. Swallow your prescribed dose of **REMERON** without chewing or crushing, with some water or juice.

When can you expect to start feeling better

Usually **REMERON** will start working after 1 to 2 weeks and after 2 to 4 weeks you may start to feel better.
It is important that, during the first few weeks of the treatment, you talk with your doctor about the effects of **REMERON**:
2 to 4 weeks after you have started taking **REMERON**, talk to your doctor about how this medicine has affected you.
If you still don't feel better, your doctor may prescribe a higher dose. In that case, talk to your doctor again after another 2 to 4 weeks.
Usually you will need to take **REMERON** until your symptoms of depression have disappeared for 4 to 6 months.

If you take more REMERON than you should
If you or someone else has taken too much **REMERON**, call a doctor straightaway.
The most likely signs of an overdose of **REMERON** (without other medicines or alcohol) are **drowsiness, disorientation and increased heart rate**. The symptoms of a possible overdose may include changes to your heart rhythm (fast, irregular heartbeat) and/or fainting which could be symptoms of a life-threatening condition known as Torsade de Pointes.
If you have taken an overdose, or if a child has accidentally swallowed the medicine, proceed immediately to a hospital emergency room and bring the package of the medicine with you.

If you forget to take REMERON
If you are supposed to take your dose **once a day**
- Do not take a double dose to make up for a forgotten dose. Take your next dose at the normal time.

If you are supposed to take your dose **twice a day**
- if you have forgotten to take your morning dose, simply take it together with your evening dose.
- if you have forgotten to take your evening dose, do not take it with the next morning dose; just skip it and continue with your normal morning and evening doses.
- if you have forgotten to take both doses, do not attempt to make up for the missed doses. Skip both doses and continue the next day with your normal morning and evening doses.

If you stop taking REMERON
Only stop taking **REMERON** in consultation with your doctor.
If you stop too early, your depression might come back. Once you are feeling better, talk to your doctor. Your doctor will decide when treatment can be stopped.
Do not suddenly stop taking **REMERON**, even when your depression has lifted. If you suddenly stop taking **REMERON** 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.

How can you contribute to the success of the treatment?
Do not take medicines in the dark! Check the label and the dose each time you take your medicine.
Wear glasses if you need them.

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

4. SIDE EFFECTS
Like all medicines, **REMERON** can cause side effects, in some of the users.
Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

If you experience any of the following serious side effects, stop taking mirtazapine and tell your doctor immediately.

Uncommon side effects (may affect up to 1 in 100 people):
- feeling elated or emotionally 'high' (mania)

Rare side effects (may affect up to 1 in 1,000 people):
- yellow colouring of eyes or skin; this may suggest disturbance in liver function (jaundice)

Not known side effects (frequency cannot be estimated from the available data):
- signs of infection such as sudden unexplainable high fever, sore throat and mouth ulcers (agranulocytosis). In rare cases mirtazapine can cause disturbances in the production of blood cells (bone marrow depression). Some people become less resistant to infection because mirtazapine can cause a temporary shortage of white blood cells (granulocytopenia). In rare cases mirtazapine 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).
- epileptic attack (convulsions)
- 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. In very rare cases these can be signs of serotonin syndrome.
- thoughts of harming or killing yourself
- severe skin reactions (Stevens-Johnson Syndrome, toxic epidermal necrolysis)

Other possible side effects with mirtazapine are:

Very common (may affect more than 1 in 10 people)**:**
- increase in appetite and weight gain
- drowsiness or sleepiness
- headache
- dry mouth

Common (may affect up to 1 in 10 people)**:**
- lethargy
- dizziness
- shakiness or tremor
- nausea
- diarrhoea
- vomiting
- constipation
- rash or skin eruptions (exanthema)
- pain in your joints (arthralgia) or muscles (myalgia)
- back pain
- feeling dizzy or faint when you stand up suddenly (orthostatic hypotension)
- swelling (typically in ankles or feet) caused by fluid retention (oedema)
- tiredness
- vivid dreams
- confusion

- feeling anxious
- sleeping problems

Uncommon (may affect up to 1 in 100 people):
- abnormal sensation in the skin e.g. burning, stinging, tickling or tingling (paraesthesia)
- restless legs
- fainting (syncope)
- sensations of numbness in the mouth (oral hypoaesthesia)
- low blood pressure
- nightmares
- feeling agitated
- hallucinations
- urge to move

Rare (may affect up to 1 in 1,000 people)**:**
- muscle twitching or contractions (myoclonus)
- aggression
- abdominal pain and nausea; this may suggest inflammation of the pancreas (pancreatitis)

Not known (frequency cannot be estimated from the available data)**:**
- abnormal sensations in the mouth (oral paraesthesia)
- swelling in the mouth (mouth oedema)
- swelling throughout the body (generalized oedema)
- localized swelling
- hyponatraemia
- inappropriate anti-diuretic hormone secretion
- severe skin reactions (dermatitis bullous, erythema multiforme).
- sleep walking (somnambulism)
- speech disorder
- increased creatine kinase blood levels
- difficulty in passing urine (urinary retention)
- muscle pain, stiffness and/or weakness, darkening or discolouration of the urine (rhabdomyolysis)

Additional side effects in children and adolescents
In children under 18 years the following adverse events were observed commonly in clinical trials: significant weight gain, hives and increased blood triglycerides.

Reporting of side effects
Side effects can be reported to the Ministry of Health by using the link "Reporting side effects due to medicinal treatment" at the home page of the Ministry of Health's web site (**www.health.gov.il**) which refers to the online side effects reporting form, or by using the link:
https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. HOW TO STORE REMERON?
- Avoid Poisoning! This medicine, as all other medicines, must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor!

- Do not use **REMERON** after the expiry date (exp. date) which is stated on the pack. The expiry date refers to the last day of the indicated month.
- **Storage conditions:** Do not store above 30°C. Store in the original package in order to protect from light and moisture.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

6.1 What REMERON contains?

- The active substance is: mirtazapine. Each tablet contains mirtazapine 30 mg.
- In addition to the active ingredient the medicine also contains inactive ingredients: Maize starch, hydroxypropyl cellulose, magnesium stearate, silica colloidal anhydrous, lactose monohydrate, hydroxypropylmethylcellulose, polyethylene glycol 8000, titanium dioxide (E 171), ferric oxide yellow, ferric oxide red.
- Each tablet contains 217 mg lactose.

6.2 What REMERON looks like and contents of the pack

REMERON are film-coated tablets.
REMERON film-coated tablets are oval, biconvex, red-brown, scored and coded with ‘Organon’ on one side and with ‘TZ5’ on the other side on both sides of the score.

Pack size:
REMERON 30 mg is marketed in pack size of 30 tablets.

Marketing authorization holder:
Merck Sharp & Dohme (Israel-1996) Company Ltd., P.O.Box 7121, Petah-Tikva 49170.

Manufacturer:
N.V. Organon, Oss, The Netherlands.

This Leaflet was checked and approved by the Ministry of Health on February 2018

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108.28.28503.00