

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986
This medicine is dispensed with a doctor's prescription only

IXEL® 25 mg IXEL® 50 mg

Capsules

Composition of the active ingredient and its quantity:

IXEL 25 MG Each capsule contains: Milnacipran Hydrochloride 25 mg

IXEL 50 MG Each capsule contains: Milnacipran Hydrochloride 50 mg

Inactive ingredients and allergens in the medicine: see section 6.

Read this entire leaflet carefully before you start using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to 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 similar.

The medicine is intended for adults over the age of 18 years.

Antidepressants and anti-anxiety medicines increase the risk of suicidal behavior and thoughts in children, adolescents and young adults up to 25 years of age. At the beginning of the treatment with the medicine, patients of all ages and their relatives should follow behavioral changes such as: worsening of depression, suicidal thoughts, aggressiveness, etc. In case changes like these occur, refer to the doctor immediately.

1. What is the medicine intended for?

Treatment of depression in adults over the age of 18 years.

Therapeutic group: Antidepressants of the SNRI group (Serotonin Noradrenaline Reuptake Inhibitors).

2. Before using the medicine

❗ Do not use the medicine:

- if you are hypersensitive (allergic) to the active ingredient milnacipran or to any of the other ingredients the medicine contains - see section 6 "Additional Information".
- in combination with irreversible monoamine oxidase inhibitors (MAOIs) (iproniazid) - see section 2 "Drug interactions".
- if you are breastfeeding.
- if you suffer from uncontrolled high blood pressure or a severe or unstable coronary heart disease.

Special warnings regarding the use of this medicine

- **Suicidal thoughts and worsening of your depression or anxiety disorder.**
 - If you suffer from depression and/or anxiety, you may sometimes consider self-harm or suicide. These symptoms may get worse at the start of antidepressant treatment, as this type of medicine does not act immediately but only after two or more weeks of treatment.
 - You are more likely to experience these kinds of symptoms in the following situations:
 - if you have had suicidal or self-harm thoughts in the past.
 - You are a young adult. Data collected from clinical studies indicates an increase in the risk of suicidal behavior in adults under 25 with mental disorders treated with antidepressants.
- If you have suicidal or self-harm thoughts at any time, refer to the doctor or to a hospital emergency room immediately.
- If you suffer from depression or anxiety, it is recommended to tell a relative or a friend, and ask them to read this leaflet. Ask them whether they think your depression or anxiety is worsening, or whether they are concerned about changes in your behavior.

Medicines like **IXEL** (so-called SSRIs or SNRIs) may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms have continued after stopping the treatment.

❗ Before treatment with IXEL, tell the doctor if you have:

- Insomnia or nervousness at the start of the treatment.
- Jaundice (yellowing of your skin and the whites of your eyes).
- Kidney failure: your doctor may adjust your daily dose.
- Enlarged prostate (prostate adenoma) or difficulty urinating.
- High blood pressure or heart disease.
- Vision disorders with high intraocular fluid pressure (angle-closure glaucoma).
- Epilepsy or a history of epilepsy.

If you have any doubts, consult the doctor or pharmacist.

Children and adolescents under the age of 18 **IXEL** is not usually intended for use in children and adolescents under the age of 18. Patients under the age of 18, who have taken medicines of this group, present a higher risk of

side effects, such as suicide attempts, suicidal thoughts and hostility (predominantly aggression, rebellious behavior and anger). Nevertheless, your doctor can prescribe this medicine to patients under the age of 18 if he believes that it is in the patient's interest. If the doctor has prescribed the medicine to a patient under the age of 18 and you wish to discuss this, refer to the doctor once again. In patients under the age of 18, inform the doctor if any of the symptoms listed above appears or worsens. Furthermore, the long-term effects of **IXEL** have not yet been studied in this age group, concerning growth, maturation and cognitive behavioral development.

❗ Drug interactions

If you are taking, or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. The doctor will decide if **IXEL** can be taken with other medicines.

Do not start or stop taking medicines, including non-prescription medicines, herbal remedies and nutritional supplements without consulting the doctor or pharmacist about their compatibility.

Do not take this medicine with:

- Do not take irreversible monoamine oxidase inhibitors such as iproniazid (to treat depression) with **IXEL**. Once you have stopped taking MAOIs, wait at least 14 days before taking **IXEL**. Furthermore, wait at least 7 days after you stop taking **IXEL** before you start taking MAOIs.
- Serotonin syndrome:
 - Taking **IXEL** in combination with other medicines may cause "serotonin syndrome". For information on the symptoms of the potentially life-threatening serotonin syndrome, see section 4 "side effects". This syndrome may occur when **IXEL** is taken with other medicines such as:
 - Irreversible monoamine oxidase inhibitors such as iproniazid.
 - Medicines containing moclobemide - a selective irreversible monoamine oxidase alpha inhibitor (to treat depression)
 - Medicines containing linezolid (an antibiotic to treat infections)
 - Medicines containing tramadol or pethidine (pain relievers)
 - Products containing St John's wort (Hypericum), (an herbal medicine to treat mild depression)
 - Medicines containing methylene blue
 - Other antidepressants

Other medicines may interact with **IXEL**.

Unless the doctor approves it, do not take this medicine with:

Certain medicines that act on the cardiovascular system (injectable alpha and beta adrenergic agonists).

❗ Use of the medicine and food

The medicine must be taken with a glass of water, preferably during a meal.

❗ Use of this medicine and alcohol consumption
The consumption of alcoholic beverages or medicines containing alcohol is not recommended.

❗ Pregnancy, breastfeeding and fertility

Pregnancy

It is not advisable to take this medicine if you are a woman of childbearing age and you do not use contraception, or during pregnancy. Consult the doctor if you discover you are pregnant during treatment, as he can decide whether to continue the treatment with the medicine.

If you take the medicine until you give birth, your baby may immediately or shortly after the birth present reversible symptoms related to the sudden discontinuation of exposure to milnacipran (withdrawal syndrome) or to absorption of milnacipran (the active ingredient). In such a case, medical monitoring is required.

Ask your doctor or pharmacist for advice before taking medicines.

Breastfeeding

The medicine passes into breast milk. Therefore, **do not use** this medicine when you are breastfeeding! Ask your doctor or pharmacist for advice before taking medicines.

Fertility

Milnacipran affects fertility in animals. There is no data available on the impact of milnacipran on human fertility.

❗ Driving and using machines

Special care should be taken when driving a vehicle and operating dangerous machines while using this medicine. There is a possible risk of dizziness, especially at the start of treatment.

3. How should you use this medicine?

Always use the medicine according to the doctor's instructions. You should check with the doctor or pharmacist if you are not sure about the dosage and treatment regimen.

The dosage and treatment will be determined by the doctor only. The usual recommended dosage is:

A dose of 100 mg per day, in two divided doses: 50 mg in the morning and 50 mg in the evening - preferably during a meal.

In patients with kidney problems – start treatment gradually.

Use the get the impression that the effect of **IXEL** 25 mg or **IXEL** 50 mg is too strong or too weak, consult the doctor or pharmacist.

Do not exceed the recommended dose.

Method of administration

Swallow the medicine with a glass of water during a meal.

Opening and dispersing the capsule: there is no information about opening and dispersing the capsule.

Duration of treatment

Even if there is an improvement in your health, do not stop the treatment with the medicine without consulting the doctor or pharmacist. If necessary, stop taking the medicine gradually in accordance with your doctor's instructions (see below "If you stop taking the medicine" and section 4 "Side Effects").

If you have taken an overdose, or if a child or anyone else has accidentally swallowed the medicine, refer immediately to the doctor or to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take this medicine at the scheduled time, do not take a double dose to make up for the forgotten dose.

Continue with the treatment as recommended by the doctor.

If you stop taking this medicine

Do not stop taking the medicine unless your doctor instructed to do so. You may experience withdrawal reactions when the treatment is stopped. Gradually reducing the dose is recommended. Most withdrawal reactions are mild and disappear with time.

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 any further questions regarding the use of the medicine, consult the doctor or pharmacist.

4. Side effects

As with any medicine, the use of **IXEL** may cause side effects in some users. Do not be alarmed while reading the list of side effects. You might not suffer from any of them.

Side effects may particularly occur during the first week or first two weeks of treatment with milnacipran (the active ingredient).

Refer to the doctor immediately if you experience symptoms such as:

- In case of a rash or an allergic reaction such as itching, swollen lips and/or tongue, wheezing and/or shortness of breath - stop treatment with the medicine and refer to the doctor immediately.
- In case of a sudden weakness or numbness of your face, arms or legs, especially on one side, or in cases of speech disorder (stroke symptoms).
- In case of heart problems such as chest pain (contraction, squeezing sensation).
- If you experience symptoms related to an excess of serotonin in the brain (serotonin syndrome) due to a particularly strong effect of the medicine which include: high fever, nausea, excessive sweating, anxiety, hot flushes, muscular contractions or trembling, palpitations and restlessness. This syndrome is observed in particular in patients who are taking additional medicines at the same time.

Additional side effects

Very common side effects (appear in more than one user out of 10): nausea, headache.

Common side effects (appear in 1-10 users out of 100):

- Restlessness, anxiety, eating disorders, sleep disorders, suicidal behavior.
- Migraine, trembling, dizziness, modified sensitivity, drowsiness.
- Palpitations, rapid heart rate (tachycardia), increased blood pressure, hot flushes.
- Abdominal pain, diarrhea, constipation, dry mouth, indigestion, vomiting.
- Itching, rash, excessive sweating.
- Muscular pain.
- Urinary retention, frequent urination.
- Erectile dysfunction, ejaculation disorders, testicular pain.
- Fatigue.

Uncommon side effects (appear in 1 and 10 users out of 1,000):

- Increased lipid levels in the blood, weight loss.
- Feelings of panic, confusion, delirium, strange visions or sounds, hyperactive behavior or thoughts (mania), reduced libido, abnormal dreams, suicidal thoughts.
- Memory impairment, sensation of restlessness, balance disorders, change in the sense of taste, loss of consciousness (syncope).
- Blurred vision, dry eyes, eye pain, reduced visual acuity, dilated pupils.
- Sensation of dizziness (vertigo), ringing or noises in the ears.
- Heart problems such as: low blood pressure, conduction disorders.
- Low blood pressure, poor blood circulation causing numbness and pallor of the fingers and toes (Raynaud's syndrome), orthostatic hypotension.
- Breathing difficulties, cough, nasal dryness, swallowing disorders.
- Gastrointestinal disorders such as: gastritis, stomatitis, abdominal discomfort, ulcers, hemorrhoids.

- Liver function impairment.
- Skin diseases (dermatosis), skin allergies (hives), skin inflammation (dermatitis).
- Muscular pain or stiffness.
- Urinary disorders such as: trouble urinating, urinary retention, incontinence, urine color changing to red is possible.
- Some women may suffer from irregular heavy menstrual bleeding, or the absence of menstruation.
- Prostate problems.
- Malaise, fever, pain

Rare side effects (appear in 1-10 users out of 10,000):

- Unregulated secretion of the hormone controlling the volume of urine (antidiuretic hormone).
- Psychotic disorder.
- Involuntary body movements (dyskinesia), Parkinsonism (a medical term that can include a large number of symptoms such as: increased saliva secretion, musculoskeletal stiffness, reduced or abnormal body movements, lack of facial expression, muscular contractions and trembling).
- Angina pectoris.
- Hepatitis, liver damage.
- Sensitivity to sunlight (photosensitivity).

Side effects of unknown frequency (side effects whose frequency has not been determined yet):

- Reduced sodium levels in the blood (hyponatremia).
- Bleeding of the skin and mucous membranes.
- Convulsions (especially in patients with a history of epilepsy).
- Aggression.
- Hepatitis (cytolytic hepatitis).
- Stevens-Johnson syndrome (a serious generalized disease which includes blisters in the skin and mucous membranes).
- Broken heart syndrome (Takotsubo cardiomyopathy).

Some symptoms may also be caused by your depression.

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

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting Side Effects from Drug Treatment " that can be found on the home page of the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

Additionally, you can report to Perrigo via the following address: www.perrigo-pharma.co.il

5. How to store the medicine?

Avoid poisoning! This medicine, and any other medicine, must be kept in a closed 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 the doctor. Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month. Store below 25°C.

6. Additional Information

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

Capsule contents:

Calcium hydrogen phosphate dihydrate, Carmellose calcium, Povidone K30, Magnesium stearate, Talc, Anhydrous colloidal silica

Capsule composition:

Titanium dioxide (E171), yellow iron oxide (E172) red iron oxide (E172), gelatin

What the medicine looks like and contents of the package

IXEL 25 mg: Capsule cap in pink color with "Ixel" imprinted in black, capsule body in pink color with "25" imprinted in black.

IXEL 50 mg: Capsule cap in pink color with "Ixel" imprinted in black, capsule body in rust color with "50" imprinted in black.

Quantity of capsules in package: 14, 28, 56 or 112.

Not all package sizes may be marketed.

Manufacturer and address: Pierre Fabre Medicament, Boulogne, France.
Registration Holder and address: Perrigo Israel Agencies Ltd., 29 Lehi St., Bnei-Brak.

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Drug registration number at the National Drug Registry of the Ministry of Health:

IXEL 25 mg: 112-55-29468

IXEL 50 mg: 112-56-29469

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