Package leaflet: Information for the user

Skudexa 75 mg/25 mg granules for oral solution in sachet

tramadol hydrochloride/dexketoprofen

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.
- 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. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Skudexa is and what it is used for

Skudexa contains the active substances tramadol hydrochloride and dexketoprofen.
Tramadol hydrochloride is a pain killer belonging to a group of medicines called opioids that act on the central nervous system. It relieves pain by acting on specific nerve cells of the brain and spinal cord.
Dexketoprofen is a pain killer and it belongs to a group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs).

Skudexa is used for the symptomatic short term treatment of moderate to severe acute pain in adults.

2. What you need to know before you take Skudexa

Do not take Skudexa:
- if you are allergic to dexketoprofen, to tramadol hydrochloride or any of the other ingredients of this medicine (listed in section 6)
- if you are allergic to acetylsalicylic acid or to other NSAID
- if you have asthma or have suffered attacks of asthma, acute allergic rhinitis (a short period of inflamed lining of the nose), nasal polyps (lumps in the nose due to allergy), urticaria (skin rash), angioedema (swollen face, eyes, lips, or tongue, or respiratory distress) or wheezing in the chest after taking acetylsalicylic acid or other non-steroidal anti-inflammatory medicines
- if you have had photoallergic or phototoxic reactions (reddening and/or blistering of the skin exposed to sunlight) while taking ketoprofen (a NSAID) or fibrates (drugs used to lower the level of fats in the blood)
- if you have a peptic ulcer, stomach or bowel bleeding or if you have suffered in the past from stomach or bowel bleeding, ulceration or perforation, including that due to previous use of NSAIDs
- if you have chronic digestive problems (e.g. indigestion, heartburn)
- if you have bowel disease with chronic inflammation (Crohn's disease or ulcerative colitis)
- if you have serious heart failure, moderate or serious kidney problems or serious liver problems
- if you have a bleeding disorder, a blood clotting disorder or other active bleedings.
- if you are severely dehydrated (have lost a lot of body fluids) due to vomiting, diarrhoea or insufficient intake of fluids

- if you have acute poisoning with alcohol, sleeping pills, pain relievers, or medicines that affect mood and emotions
- if you are also taking monoamine oxidase inhibitors (MAOIs) (certain medicines used for the treatment of depression) or have taken them in the last 14 days before treatment with this medicine (see "Other medicines and Skudexa")
- if you have epilepsy or suffer from fits, because the risk of a fit may increase
- if you are breathing with difficulty
- if you are pregnant or breast feeding.

Warnings and precautions
Talk to your doctor before taking Skudexa:
- if you have an allergy, or if you have had allergy problems in the past
- if you have kidney, liver or heart problems (hypertension and/or heart failure) as well as fluid retention, or have suffered from any of these problems in the past
- if you are taking diuretics (substances that increase production of urine)
- if you have heart problems, previous stroke or think that you might be at risk of these conditions (for example if you have high blood pressure, diabetes or high cholesterol or are a smoker) you should discuss your treatment with your doctor; medicines such as this medicine may be associated with a small increased risk of heart attack (myocardial infarction) or stroke. Any risk is more likely with high doses and prolonged treatment. Do not exceed the recommended dose or duration of treatment
- if you are elderly: you may be more likely to suffer from side effects (see section 4). If any of these occur, consult your doctor immediately
- if you are a woman with fertility problems: this medicine may affect your fertility, therefore you should not take it if you are planning to become pregnant or you are having fertility tests
- have a disorder affecting the formation of blood and blood cells
- if you have systemic lupus erythematosus or mixed connective tissue disease (immune system disorders that affect connective tissue)
- if you have suffered in the past from a chronic inflammatory disease of the bowel (ulcerative colitis, Crohn's disease)
- if you have or have suffered in the past from other stomach or bowel problems
- if you have an infection - please see heading "Infections" below
- if you are taking other medicines that increase the risk of peptic ulcer or bleeding, e.g. oral steroids, some antidepressants (those of the SSRI type, i.e. Selective Serotonin Reuptake Inhibitors), drugs that prevent blood clots such as acetylsalicylic acid or anticoagulants such as warfarin. In such cases, consult your doctor before taking this medicine: he/she may want you to take an additional medicine to protect your stomach
- if you suffer from depression and you are taking antidepressant as some of them may interact with tramadol (see "Other medicines and Skudexa")
- if you are taking other medicines containing the same active substances in this medicine, do not exceed the maximum daily doses of dexketoprofen or tramadol
- if you think that you are addicted to other pain relievers (opioids)
- if you have consciousness disorders (if you feel that you are going to faint)
- if you are in a state of shock (cold sweat may be a sign of this)
- if you have increased pressure in the brain (possibly after a head injury or brain disease)
- if you have difficulty in breathing
- if you have porphyria (a disease in which there is an abnormal metabolism of heme).

Tramadol may lead to physical and psychological addiction. When this medicine is taken for a long time, its effect may decrease, so that higher doses have to be taken (tolerance development). In patients with a tendency to abuse medicines or who are dependent on medicines, treatment with Skudexa should only be carried out for short periods and under strict medical supervision.
Tell your doctor if any of these problems occurs during Skudexa treatment or if they applied in the past.

Talk to your doctor if you experience any of the following symptoms while taking Skudexa: extreme fatigue, lack of appetite, severe abdominal pain, nausea, vomiting or low blood pressure. This may

indicate that you have adrenal insufficiency (low cortisol levels). If you have these symptoms, contact your doctor, who will decide if you need to take hormone supplement.

Tramadol is transformed in the liver by an enzyme. Some people have a variation of this enzyme and this can affect people in different ways. In some people, they may not get enough pain relief but other people are more likely to get serious side effects. If you notice any of the following side effects, you must stop taking this medicine and seek immediate medical advice: slow or shallow breathing, confusion, sleepiness, small pupils, feeling or being sick, constipation, lack of appetite.

There is a small risk that you may experience a so-called serotonin syndrome that can occur after having taken tramadol in combination with certain antidepressants or tramadol alone. Seek medical advice immediately if you have any of the symptoms related to this serious syndrome (see section 4 "Possible side effects").

Sleep-related breathing disorders
Skudexa can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.

Infections
Skudexa may hide signs of infections such as fever and pain. It is therefore possible that Skudexa may delay appropriate treatment of infection, which may lead to an increased risk of complications. This has been observed in pneumonia caused by bacteria and bacterial skin infections related to chickenpox. If you take this medicine while you have an infection and your symptoms of the infection persist or worsen, consult a doctor without delay.
During chicken pox it is advisable to avoid use of this medicine.

Children and adolescents
This medicine has not been studied in children and adolescents. Therefore, safety and efficacy have not been established and the product should not be used in children and adolescents.
Use in children with breathing problems
Tramadol is not recommended in children with breathing problems, since the symptoms of tramadol toxicity may be worse in these children.

Other medicines and Skudexa
Tell your doctor if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. Some medicines should not be taken together and others may need their doses to be altered when taken together.

Always inform your doctor if you are using or receiving any of the following medicines in addition to Skudexa:

Use with Skudexa is not recommended:
- Acetylsalicylic acid, corticosteroids or other anti-inflammatory drugs
- Warfarin, heparin or other medicines used to prevent blood clots
- Lithium, used to treat certain mood disorders
- Methotrexate, used for rheumatoid arthritis and cancer
- Hydantoins and phenytoin, used for epilepsy
- Sulfamethoxazole, used for bacterial infections and other sulphonamides
- Monoamine oxidase inhibitors (MAOIs) (medicines for the treatment of depression).

Use with Skudexa requires precautions:
- ACE inhibitors, diuretics and angiotensin II antagonists, used for high blood pressure and heart problems
- Pentoxifylline, used to treat chronic venous ulcers

- Zidovudine, used to treat viral infections
- Sulfonylureas such us chlorpropamide and glibenclamide, used for diabetes
- Aminoglycoside antibiotics, used to treat bacterial infections.
- Concomitant use of Skudexa and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However if your doctor does prescribe Skudexa together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor. Please tell your doctor about all sedative medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

Use with Skudexa requires care:
- Quinolone antibiotics (e.g. ciprofloxacin, levofloxacin) used for bacterial infections
- Ciclosporin or tacrolimus, used to treat immune system diseases and in organ transplant
- Streptokinase and other thrombolytic or fibrinolytic medicines, i.e. medicines used to break up blood clots
- Probenecid, used in gout
- Digoxin, used to treat chronic heart failure
- Mifepristone, used to terminate a pregnancy
- Antidepressants of the selective serotonin reuptake inhibitors type (SSRIs)
- Anti-platelet agents used to reduce platelet aggregation and the formation of blood clots
- Tenofovir, deferasirox, pemetrexed
- Beta blockers used for high blood pressure and heart problems.

The pain-relieving effect of tramadol may be reduced, and the length of time it acts may be shortened, if you also take medicines containing:
- Carbamazepine (for epileptic fits)
- Buprenorphine, nalbuphine, or pentazocine (pain relievers)
- Ondansetron (prevents nausea).

The risk of side effects increases
- if you take tranquillizers, sleeping pills, other pain relievers such as morphine and codeine (also as cough medicine), or alcohol while you are taking Skudexa. You might feel drowsier or feel that you might faint. If this happens tell your doctor
- if you are taking medicines which may cause convulsions (fits), such as certain antidepressants or antipsychotics. The risk of having a fit may increase if you take Skudexa at the same time. Your doctor will tell you whether Skudexa is suitable for you
- if you are taking certain antidepressants. Skudexa may interact with these medicines and you may experience serotonin syndrome (see section 4 "Possible side effects")
- if you take anticoagulants (medicines for blood thinning), e.g. warfarin, together with this medicine. The effect of these medicines on blood clotting may be affected and bleeding may occur.

Skudexa with alcohol
Do not drink alcohol during treatment with Skudexa as it may increase the effect of the medication. For the instruction how to take Skudexa see section 3.

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

Dexketoprofen can cause kidney and heart problems in your unborn baby. It may affect your and your baby's tendency to bleed and cause labour to be later or longer than expected. From 20 weeks of pregnancy, dexketoprofen can cause kidney problems in your unborn baby, that may lead to low levels of amniotic fluid that surrounds the baby (oligohydramnios) or narrowing of a blood vessel (ductus arteriosus) in the heart of the baby.
Tramadol is excreted into breast milk.
Skudexa must not be used in pregnancy or during breast-feeding.

Driving and using machines
The medicine can affect your ability to drive as it may make you sleepy or dizzy.
Do not drive while taking this medicine until you know how it affects you.
It is an offence to drive if this medicine affects your ability to drive.
However, you would not be committing an offence if:

- The medicine has been prescribed to treat a medical or dental problem and
- You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
- It was not affecting your ability to drive safely. Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

Skudexa may affect your ability to drive and handle machines, due to the possibility of dizziness, blurred vision or drowsiness as side effects of treatment. This applies particularly when Skudexa is taken with medicines that affect mood and emotions, or alcohol.
If you are affected, do not drive or use machines until the symptoms wear off.

Skudexa contains sucrose
Skudexa contains 2.7 g of sucrose per dose. This should be taken into account in patients with diabetes mellitus. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Skudexa

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

The lowest effective dose should be used for the shortest duration necessary to relieve symptoms. If you have an infection, consult a doctor without delay if symptoms (such as fever and pain) persist or worsen (see section 2).

The dose of Skudexa that you need depends on the type, severity and duration of your pain. Your doctor will tell you how many sachets you must take daily, and for how long.

The recommended dose is generally 1 sachet (corresponding to 75 mg of tramadol hydrochloride and 25 mg of dexketoprofen) every 8 hours, with no more than 3 sachet daily (corresponding to 225 mg of tramadol hydrochloride and 75 mg of dexketoprofen) and not exceeding 5 days of treatment.

Use in children and adolescents
Skudexa is not suitable for children and adolescents.

Elderly patients
If you are aged 75 years or over, your doctor may recommend prolonging the dosage interval because your body may handle the drug more slowly.

Severe liver or kidney disease (insufficiency)/dialysis patients:
If you have severe liver and/or moderate to severe kidney insufficiency should not take Skudexa.
If you have renal dysfunction, if in your case the insufficiency is mild, your doctor may recommend prolonging the dosage interval.

If you have hepatic dysfunction, if in your case the insufficiency is mild or moderate, your doctor may recommend prolonging the dosage interval.

Dissolve the whole contents of each sachet in a glass of water; shake/ stir well to help to dissolve. The obtained solution should be immediately taken after reconstitution.
Food delays the absorption of Skudexa, so for a faster effect take the granules for oral solution in sachet at least 30 minutes before meals.

If you take more Skudexa than you should
If you use too much of this medicine, tell your doctor immediately or go to the emergency department of your nearest hospital. Please remember to take this medicine pack or this leaflet with you.

The symptoms of an overdose of this medicine are:
- vomiting, loss of appetite, stomach pain, drowsiness, dizziness/spinning sensation, disorientation, headache (for dexketoprofen);
- contraction of the pupil, vomiting, heart failure, loss of consciousness, convulsions and difficulty in breathing (for tramadol).

If you forget to take Skudexa
Do not take a double dose to make up for a forgotten dose. Take the next regular dose when it is due (see section 3 “How to take Skudexa”).

If you stop taking Skudexa
Generally there will be no after-effects when treatment with Skudexa is stopped.
However, on rare occasions, patients who have been taking Skudexa granules for oral solution in sachet for some time may feel unwell if they stop taking them abruptly. They may feel agitated, anxious, nervous or shaky, be confused, hyperactive, have difficulty sleeping and have stomach or bowel disorders. Rarely, people may get panic attacks, hallucinations, delusions, paranoia or feel a loss of identity. They may experience unusual perceptions such as itching, tingling and numbness, and ringing in the ears (tinnitus). Further unusual symptoms, i.e. confusion, delusions, feeling as though you are detached from yourself (depersonalization), and change in perception of reality (derealisation) and delusion of persecution (paranoia) have been seen very rarely. If you experience any of these complaints after stopping Skudexa, please consult your doctor.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Possible side effects are listed below according to how likely they are to occur.

You should see a doctor immediately if you experience symptoms of an allergic reaction such as swollen face, tongue and/or throat, and/or difficulty swallowing or hives together with difficulties in breathing.

Stop using Skudexa as soon as you notice the appearance of a skin rash, or any lesion inside the mouth or on mucous membranes, or any sign of an allergy.

Very common (may affect more than 1 in 10 people):
- nausea/feeling sick
- dizziness.

Common side effects (may affect up to 1 in 10 people)**:**
- vomiting
- stomach pain
- diarrhoea

- digestive problems
- headaches
- drowsiness, fatigue
- constipation
- dry mouth
- increased sweating.

Uncommon side effects (may affect up to 1 in 100 people):
- increase in the number of blood platelets
- effects on the heart and blood circulation (pounding of the heart, fast heart beat, feeling faint or collapse), low blood pressure. These adverse effects may occur particularly when patients are in an upright position or under physical strain.
- high or very high blood pressure
- swelling in the voice-box (laryngeal oedema)
- reduced potassium in the blood
- psychotic disorder
- swelling next to the eye
- shallow or slow breathing
- discomfort, abnormal feeling
- blood in urine
- spinning sensation
- sleeplessness or difficulty falling asleep
- nervousness/anxiety
- flushing
- flatulence
- tiredness
- pain
- feeling feverish and shivering, generally feeling unwell
- abnormal blood tests
- urge to vomit (retching)
- feeling of pressure in the stomach, bloating
- inflammation of the stomach
- skin reactions (e.g. itching, rash)
- amnesia
- facial swelling

Rare side effects (may affect up to 1 in 1,000 people)**:**
- swelling of the lips and throat
- peptic ulcer, peptic ulcer perforation or bleeding, which may be seen as vomiting blood or black stools
- prostate problems
- liver inflammation (hepatitis), liver damage
- acute kidney failure
- slow heartbeat
- epileptic fits
- allergic/anaphylactic reactions (e.g. difficulty breathing, wheezing, swelling of the skin) and shock (sudden circulatory failure)
- transient loss of consciousness (syncope)
- hallucinations
- water retention or swollen ankles
- loss of appetite, changes in appetite
- acne
- back pain
- passing urine frequently, or less than normal, with difficulty or pain
- menstrual disorders
- abnormal sensations (e.g. itching, tingling, numbness)

- trembling, muscle twitches, uncoordinated movement, weak muscles
- confusion
- sleep disorders and nightmares
- disturbed perception
- blurred vision, contraction of the pupil
- shortness of breath.

Psychological side effects may occur after treatment with Skudexa. Their intensity and nature may vary (according to the patient's personality and length of therapy):
- change in mood (mostly high spirits, occasionally irritation)
- changes in activity (slowing down but sometimes an increase in activity)
- being less aware
- less able to make decisions, which may lead to errors in judgement.

Worsening of asthma has been reported.

When treatment is stopped abruptly signs of withdrawal may appear (see "If you stop taking Skudexa").

Epileptic fits have occurred mainly at high doses of tramadol or when tramadol was taken at the same time as other medicines which may induce fits.

Very rare (may affect up to 1 in 10,000 people)**:**
- inflammation of the pancreas
- kidney problems
- reduced white blood cell count (neutropenia)
- fewer platelets in the blood (thrombocytopenia)
- open sores on skin, mouth, eyes and genital areas (Stevens Johnson and Lyell's syndromes)
- breathlessness due to narrowing of the airways
- ringing in the ears (tinnitus)
- sensitive skin
- sensitivity to light.

Not known (frequency cannot be estimated from the available data):
- serotonin syndrome, that can manifest as mental status changes (e.g. agitation, hallucinations, coma), and other effects, such as fever, increase in heart rate, unstable blood pressure, involuntary twitching, muscular rigidity, lack of coordination and/or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea) (see section 2 "What you need to know before you take Skudexa")
- speech disorders
- extreme pupil dilatation
- decrease in blood sugar levels
- hiccups.

Tell your doctor immediately if you experience stomach/bowel side effects at the start of treatment (e.g. stomach pain, heartburn or bleeding), if you have previously suffered from any such side effects due to long-term use of anti-inflammatory drugs, and especially if you are elderly.

The most common side effects during treatment with Skudexa are nausea and dizziness, which occur in more than 1 out of 10 patients.

During treatment with NSAIDs, fluid retention and swelling (especially in the ankles and legs), increased blood pressure and heart failure have been reported.

Medicines such as Skudexa may be associated with a small increased risk of heart attack or stroke.

In patients with immune system disorders that affect connective tissue (systemic lupus erythematosus or mixed connective tissue disease), anti-inflammatory medicines may rarely cause fever, headache and neck stiffness.

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Skudexa

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 on the sachet after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions.
Store in the original package in order to protect from light.

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. Contents of the pack and other information

What Skudexa contains
- The active substances are tramadol hydrochloride and dexketoprofen. Each sachet contains: 75 mg of tramadol hydrochloride and 25 mg dexketoprofen (as dexketoprofen trometamol).
- The other ingredients are the following: Sucrose, Lemon Flavour, Acesulfame potassium (E-950).

What Skudexa looks like and contents of the pack
White to almost white granules for oral solution, provided in sachets formed by thermo-sealed Paper/Aluminium/Polyethylene multilayer foil (as copolymer with vinylacetate) in a carton box.

Skudexa is supplied in packs containing 2, 3, 10, 15, 20, 50, 100 and 500 sachets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
Menarini International Operations Luxembourg S.A.
1 Avenue de La Gare
L-1611 Luxembourg

Manufacturer:
E-Pharma Trento S.p.A.
Frazione Ravina – Via Provina, 2
Trento, 38123
Italy

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France: Skudexum

Italy: Lenizak
Spain: Enanplus

This leaflet was last revised in 09/2024