PACKAGE LEAFLET: INFORMATION FOR THE USER

Ketesse 50 mg/2 ml
solution for injection or concentrate for solution for infusion

Dexketoprofen

Read all of this leaflet carefully before you start taking this medicine.
- 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. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT KETESSE IS AND WHAT IT IS USED FOR

Ketesse is a pain killer from the group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs). It is used to treat acute moderate to severe pain, when taking tablets is not appropriate, such as post-operative pain, renal colic (severe kidney pain) and low back pain.

2. BEFORE YOU USE KETESSE

Do not take Ketesse and tell your doctor if you:

- are allergic (hypersensitive) to dexketoprofen trometamol or to any of the other ingredients of Ketesse (see section 6);
- are allergic to acetylsalicylic acid or to other non-steroidal anti-inflammatory medicines;
- have suffered attacks of asthma, acute allergic rhinitis (a short period of inflamed lining of the nose), nasal polyps (lumps within 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 aspirin or other non-steroidal anti-inflammatory medicines;
- have or have previously suffered from a peptic ulcer;
- have or have previously suffered in the past from stomach or bowel bleeding, due to previous use of non-steroidal anti-inflammatory drugs (NSAIDs);
- have chronic digestive problems (e.g. indigestion, heartburn) or bowel disease with chronic inflammation (Crohn's disease or ulcerative colitis);
- have serious heart failure, moderate or serious kidney problems or serious liver problems;
- have a bleeding disorder or a blood clotting disorder;
- suffer or have previously suffered from asthma;
- are in third trimester of pregnancy or breast feeding;

Take special care with Ketesse and tell yor doctor if you:

- have suffered in the past from a chronic inflammatory disease of the bowel (ulcerative colitis, Crohn's disease);
- have or have suffered in the past from the other stomach or bowel problems;
- 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), agents that prevent blood clots such as aspirin or anticoagulants such as warfarin. In such cases, consult your doctor before taking Ketesse: he/she may want you to take an additional medicine to protect your stomach (e.g. misoprostol or medicines that block the production of stomach acid);
- 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 or pharmacist; Medicines such as Ketesse 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;
- are elderly: you may be more likely to suffer from side effects (see section 4). If any of these occur, consult your doctor immediately;
- suffer from allergy, or if you have had allergy problems in the past;
- 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;
- are taking diuretics or you suffer from very poor hydration and reduced blood volume due to an excessive loss of fluids (e.g. from excessive urination, diarrhoea or vomiting);
- are a woman with fertility problems (Ketesse may impair your fertility, therefore you should not take it if you are planning to become pregnant or you are doing fertility tests);
- are in the first or second trimester of pregnancy;
- suffer from a disorder in the formation of blood and blood cells;
- have systemic lupus erythematosus or mixed connective tissue disease (immune system disorders that affect connective tissue);
- are less than 18 years of age;

Further warnings about the use of NSAIDs:

- The risk of heart attack or stroke can occur as early as the first weeks of using an NSAID. The risk may increase with longer use of the NSAID.
- The risk appears greater at higher doses.
- It was previously thought that all NSAIDs may have a similar risk. Newer information makes it less clear that the risk for heart attack or stroke is similar for all NSAIDs; however, this newer information is not sufficient for us to determine that the risk of any particular NSAID is definitely higher or lower than that of any other particular NSAID.
- NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease. A large number of studies support this finding, with varying estimates of how much the risk is increased, depending on the drugs and the doses studied.
- In general, patients with heart disease or risk factors for it have a greater likelihood of heart attack or stroke following NSAID use than patients without these risk factors because they have a higher risk at baseline.
- Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to patients who were not treated with NSAIDs after their first heart attack.
- There is an increased risk of heart failure with NSAID use.

Taking other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. There are some medicines that should not be taken together and others that may need their doses to be altered when taken together.

Always inform your doctor, dentist or pharmacist if you are using or receiving any of the following medicines in addition to Ketesse:

Inadvisable combinations:
- Acetylsalycilic acid (aspirin), 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

Combinations requiring precautions:
- ACE inhibitors, diuretics, beta-blockers and angiotensin II antagonists, used for high blood pressure and heart conditions
- Pentoxifylline and oxpentifylline, used to treat chronic venous ulcers
- Zidovudine, used to treat viral infections
- Aminoglycosides antibiotics, used to treat bacterial infections
- Chlorpropamide and glibenclamide used for diabetes

Associations to be considered carefully:
- Quinolone antibiotics (e.g. ciprofloxacin, levofloxacin) used for bacterial infections
- Cyclosporin 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 as an abortifacient (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

If you have any doubt about taking other medicines with Ketesse, consult your doctor or pharmacist.

Children and adolescents
Do not take Ketesse if you are less than 18 years of age.

Pregnancy and breast-feeding
Do not use Ketesse during pregnancy or when breast feeding.
Ask your doctor or pharmacist for advice before taking any medicine:
- tell your doctor if you are pregnant, or if you are planning to become pregnant, as Ketesse may not be right for you.
- you must not take Ketesse if you are breast-feeding. Ask your doctor for advice.

Driving and using machines
Ketesse may slightly affect your ability to drive and handle machines, due to the possibility of dizziness or drowsiness as side effects of treatment. If you notice such effects, do not drive or use machines until the symptoms wear off. Ask your doctor for advice.

Important information about some of the ingredients of Ketesse
Each ampoule of Ketesse contains 200mg of ethanol, equivalent to 5 ml beer or 2.08 ml wine per dose.
Harmful for those suffering from alcoholism.
To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease, or epilepsy.
This medicinal product contains less than 1 mmol sodium (23mg) per dose, i.e. essentially “sodium-free”.

3. HOW TO TAKE KETESSE

Always take Ketesse exactly as your doctor has told you. You should check with your doctor if you are not sure.
Your doctor will tell you what is the dose of Ketesse that you need, according to the type, severity and duration of your symptoms. The recommended dosage is generally 1 ampoule (50 mg) of Ketesse every 8 - 12 hours. If needed, the injection can be repeated after only 6 hours. Do not exceed a total daily dose of 150 mg of Ketesse (3 ampoules) in any case.
Use the injection treatment only in the acute period (i.e. no longer than two days). Switch to an oral pain killer when possible.
The elderly with renal dysfunction and patients with kidney or liver problems should not exceed a total daily dose of 50 mg of Ketesse (1 ampoule).

Method of administration:
Ketesse can be administered either by intramuscular or by intravenous route (technical details for the intravenous injection are given in the section 7):

When Ketesse is given intramuscularly, the solution should be injected immediately after its removal from the coloured ampoule, by slow injection deep into the muscle.
Only a clear and colourless solution should be used.

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

If you forget to use Ketesse
Do not take a double dose to make up for a forgotten dose. Take the next regular dose when it is due (according to section 3 "How to use Ketesse**"**).

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Ketesse, can cause side effects, although not everybody gets them.
Possible side effects are listed below according to how likely they are to occur. This table tells you how many patients might get these side effects:

Common	more than 1 out of 100 persons and less than 1 out of 10 persons
Uncommon	more than 1 out of 1,000 persons and less than 1 out of 100 persons
Rare	more than 1 out of 10,000 persons and less than 1 out of 1,000 persons
Very rare	less than 1 out of 10,000 persons, including isolated reports

Common side effects:
Nausea and/or vomiting, injection site pain, injection site reactions, e.g. inflammation, bruising or haemorrhage.

Uncommon side effects:
Vomiting blood, low blood pressure, fever, blurred vision, dizziness, sleepiness, sleep disturbances, headache, anaemia, abdominal pain, constipation, digestive problems, diarrhoea, dry mouth, flushing, rash, dermatitis, itching, sweating increased, tiredness, pain, feeling cold.

Rare side effects:
Peptic ulcer, peptic ulcer haemorrhage or peptic ulcer perforation, high blood pressure, fainting, too-slow breathing, inflammation of a superficial vein due to a blood clot (superficial thrombophlebitis), isolated heart skip (extrasystole), fast heartbeat, peripheral oedema, laryngeal oedema, abnormal sensation, feeling feverish and shivering, ringing in the ears (tinnitus), itchy rash, jaundice, acne, back pain, renal pain, passing water frequently, menstrual disorders, prostate problems, muscle stiffness, joint stiffness, muscle cramp,

abnormal liver tests (blood tests), increased blood sugar level (hyperglyceaemia), decreased blood sugar level (hypogliceaemia), increased triglyceride fats concentration in blood (hypertriglyceridaemia), ketone bodies in the urine (ketonuria), proteins in the urine (proteinuria), liver cell injury (hepatitis), acute renal failure.

Very rare:
Anaphylactic reaction (hypersensitive reaction which may also lead to a collapse), ulceration of the skin, mouth, eyes and genital areas (Stevens Johnson and Lyell's syndromes), facial swelling or swelling of the lips and throat (angioedema), breathlessness due to contraction of the muscles around the airways (bronchospasm), shortness of breath, pancreatitis, skin sensitivity reactions and skin over-sensitivity to light, renal damage, reduced white blood cell count (neutropenia), reduced platelet count (thrombocytopenia).

Tell your doctor immediately if you notice any 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.

Stop using Ketesse as soon as you notice the appearance of a skin rash, or any lesion on the mucous surfaces (e.g. the surface along the inside of the mouth), or any sign of allergy.

During treatment with non-steroidal anti-inflammatory drugs, fluid retention and swelling (especially in the ankles and legs), a raise in blood pressure and heart failure have been reported.

Medicines such as Ketesse may be associated with a small increased risk of heart attack ("myocardial infarction") or stroke.

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

Tell your doctor immediately if signs of infection occur or get worse whilst using Ketesse.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE KETESSE

Keep out of the reach and sight of children.

Do not use Ketesse after the expiry date which is stated on the carton and on the ampoule. The expiry date refers to the last day of that month.

Store below 30°C.
Keep the ampoule in the outer carton in order to protect it from light.

Do not use Ketesse if you notice that the solution is not clear and colourless, but shows signs of deterioration (e.g. particles). Ketesse solution for injection or concentrate for solution for infusion is for single use only and should be used immediately once opened. Discard any unused quantity of the product (please see "disposal" subsection below).

Disposal
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required and how to properly dispose of your used needles and syringes. These measures will help to protect the environment.

6. FURTHER INFORMATION

What each 2 ml ampoule of KETESSE contains
The active substance is dexketoprofen trometamol (73,80 mg) corresponding to dexketoprofen (INN) 50 mg.
The other ingredients are alcohol (ethanol), sodium chloride, sodium hydroxide and water for injections.

What KETESSE looks like and contents of the pack
Ketesse is a solution for injection or a concentrate for solution for infusion. It is supplied in packs containing 1,5,6,10,20,50 and 100 type I glass coloured ampoules each one with 2 ml of a clear and colourless solution . 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:

A. Menarini Manufacturing Logistics and Services S.r.l.
via Sette Santi, 3
50131 Florence
Italy

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7. INFORMATION FOR THE HEALTH PROFESSIONAL

Intravenous use:

Intravenous infusion: the content of one ampoule (2 ml) of Ketesse should be diluted in a volume of 30 to 100 ml of Normal Saline, 5% glucose or ringer lactate solution. The diluted solution should be given as a slow intravenous infusion, lasting 10 to 30 min. The solution must be always protected from natural daylight.
Intravenous bolus: if necessary, the content of one ampoule (2 ml) Ketesse can be given in a slow intravenous bolus over no less than 15 seconds.

Ketesse is contraindicated for neuraxial (intrathecal or epidural) administration due to its ethanol content.

Instructions on handling the product:
When Ketesse is given as intravenous bolus the solution should be injected immediately after its removal from the coloured ampoule.
For administration as intravenous infusion, the solution should be diluted aseptically and protected from natural daylight.
Only a clear and colourless solution should be used.

Compatibilities:
Ketesse has shown to be compatible when **mixed in small volumes** (e.g. in a syringe) with injectable solutions of heparin, lidocaine, morphine and theophylline.
The solution for injection diluted as indicated is a clear solution. Ketesse diluted **in a volume of 100 ml** of normal saline or glucose solution has been shown to be compatible with the following solutions for injection: dopamine, heparin, hydroxyzine, lidocaine, morphine, pethidine and theophylline.
No absorption of the active ingredient has been found when diluted solutions Ketesse have been stored in plastic bags or administration devices made of Ethyl Vinyl Acetate (EVA), Cellulose Propionate (CP), Low Density Polyethylene (LDPE) and Polyvinyl Chloride (PVC).