PATIENT INFORMATION LEAFLET

REVAFEN 50 mg/2 ml I.M./I.V. ampoule containing solution for injection and infusion

Administered through intramuscular or intravenous.

- ***Active Ingredient:*** 73,8 mg dexketoprofen trometamol equivalent to 50 mg dexketoprofen
- ***Excipients:*** Ethanol (96%), sodium chloride, sodium hydroxide (for pH adjustment), water for injection

Read all of this leaflet carefully before you start using 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 or pharmacist.*
- *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.*
- *Tell your doctor that you are taking this medicine when you go to the doctor or hospital during the use of this medicine.*
- *Follow exactly what is written in this instruction. Do not use high or low doses other than the recommended dosage*.

What is in this leaflet:

1. What REVAFEN is and what it is used for?

REVAFEN 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.

REVAFEN contains 50 mg dexketoprofen (trometamol) and it is presented in 6x2 ml ampoules each contains clear and colorless solution.

2. What you need to know before you use REVAFEN

DO NOT USE REVAFEN if you;

- are allergic to dexketoprofen or any of the other excipients in the REVAFEN content;
- are allergic to acetylsalicylic acid or to other non-steroidal anti-inflammatory medicines;
- have asthma or 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 acetylsalicylic acid or other non-steroidal anti-inflammatory medicines;

- have a peptic ulcer or if you have suffered in the past from ulceration;
- have or have suffered in the past from stomach or bowel bleeding or perforation, due to previous use of non-steroidal anti-inflammatory drugs (NSAIDs);
- have ongoing digestive problems (such as indigestion, chest burning) or your current inflammatory bowel disease (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;
- are in third trimester of pregnancy or breast feeding.

USE REVAFEN CAREFULLY 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 acetylsalicylic acid or anticoagulants such as warfarin. In such cases, consult your doctor before taking REVAFEN, 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 REVAFEN 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),especially bleeding in particular peptic ulcers and perforation can threaten life. 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 (REVAFEN may impair your fertility, therefore you should not use 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 under 18.
- experience any of the following symptoms during your treatment, stop taking the medicine and seek medical attention immediately: blood in the stool, black tarry stools, blood in the stool, vomiting or coffee grounds;
- have indigestion or heartburn, pain in the abdominal region (stomach pain) or stomach or suffering from other abnormal symptoms, stop taking the medicine and call your doctor.

Please consult your doctor if these warnings are valid for you, even at any time in the past.

Use of REVAFEN with food and drink

No warning is required due to the method of application.

Pregnancy

Consult your doctor or pharmacist before using this medication.

Do not use REVAFEN during the final three months of the pregnancy.

It would be best not to take REVAFEN during the first or second trimester of pregnancy unless

it is very necessary.

Tell your doctor if you are pregnant. It may not be right for you to take REVAFEN if you are planning to become pregnant.

If you notice that you are pregnant during treatment, consult your doctor or pharmacist.

Breast-feeding

Consult your doctor or pharmacist before using this medication.

Do not use REVAFEN when breast-feeding.

Driving and using machines

REVAFEN 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 excipients in REVAFEN

Each ampoule of REVAFEN contains 200 mg 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 1 mmol sodium (23 mg) per dose; however, no adverse side effects are expected in this dose. This should be considered for patients with a controlled sodium diet.

Other medicines and REVAFEN

Tell your doctor or pharmacist if you are taking, have recently taken or might take 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.

Inadvisable combinations:

- Acetylsalicylic 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 (a persistent disease causing pain and deformity in the joints) and cancer
- Hydantoins and phenytoin, used for epilepsy
- Sulfamethoxazole, used for bacterial infections (Inflammation forming infectious diseases)

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
- Chlorpropamide and glibenclamide used for diabetes

Associations to be considered carefully;

- Quinolone antibiotics (e.g. ciprofloxacin, levofloxacin) used for bacterial infections
- Cyclosporine 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

Please inform your doctor or pharmacist if you are currently using any prescription or non-prescription medication or if you have recently used it.

3. How to use REVAFEN

Instructions for proper use and dosage / administration frequency:

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

Your doctor will tell you what is the dose of REVAFEN that you need, according to the type, severity and duration of your symptoms. The recommended dose is generally 1 ampoule (50 mg) of REVAFEN 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 REVAFEN (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.

Method of administration

REVAFEN can be administered either by intramuscular or by intravenous route (technical details for the intravenous injection are given in the section "The following information is for healthcare professionals who will apply this medication").

When REVAFEN is given intramuscularly, the solution should be injected immediately after its removal from the colored ampoule, by slow injection deep into the muscle.

Only a clear and colorless solution should be used.

Different age groups

Use in children and adolescents:

This medicine should not be used in children and adolescents (under age 18).

Use in the elderly:

Elderly people with renal failure should not exceed 50 mg REVAFEN daily (1 ampoule) daily.

Special cases for use

Liver/renal failure

The elderly with renal dysfunction and patients with kidney or liver problems should not exceed a total daily dose of 50 mg of REVAFEN (1 ampoule).

If you have an impression that the effect of REVAFEN is too strong or too weak, talk to your doctor or pharmacist

If you use more REVAFEN than you should

Talk to a doctor or pharmacist if you have used more than you should use from REVAFEN.

Please do not forget to take the package or instructions for use.

If you forget to use REVAFEN

Do not use a double dose to make up for a forgotten dose. Use the next regular dose when it is due (according to section 3 "How to use REVAFEN").

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

4. Possible side effects

Like all medicines REVAFEN can cause side effects, although not everybody gets them, in addition, side effects may occur in people who are sensitive to the substances in the content of REVAFEN.

The possible side effects are listed below depending on how often they occur. This table shows how often can these side effects occur:

Common	More than 1 in 100 patient and less than 1 in 10 patient
Uncommon	More than 1 in 1000 patient and less than 1 in 100 patient
Rare	More than 1 in 10000 patient and less than 1 in 1000 patient
Very Rare	Less than 1 in 10,000 patients, including isolated reports

Common side effects:

- Nausea and/or vomiting
- Injection site pain
- Injection site reactions, e.g. inflammation, bruising or hemorrhage

Uncommon side effects:

- Vomiting blood
- Low blood pressure
- Fever
- Blurred vision
- Dizziness
- Sleepiness
- Sleep disturbances
- Headache
- Anemia
- Abdominal pain
- Constipation
- Digestive problems
- Diarrhea
- Dry mouth
- Flushing
- Rash
- Dermatitis,
- Itching
- Sweating increased
- Tiredness
- Pain

- Feeling cold

Rare side effects:

- Peptic ulcer, peptic ulcer hemorrhage 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 (extra systole)
- Fast heartbeat
- Peripheral edema(swelling of the legs and arms)
- Abnormal sensation
- Feeling feverish
- 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 (hyperglycemia), decreased blood sugar level (hypoglycemia), increased triglyceride fats concentration in blood (hypertriglyceridemia), ketone bodies in the urine (ketonuria), proteins in the urine (proteinuria).

Very rare side effects:

- 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
- Liver cell injury (hepatitis),
- 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 REVAFEN 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 REVAFEN may be associated with a small increased risk of heart attack ("myocardial infarction") or stroke.

In patients with systemic lupus erythematous 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 REVAFEN.

Please consult your doctor or pharmacist if the side effects get worse or you notice any side effects not listed in these instructions.

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

5. How to store REVAFEN

Keep REVAFEN out of the reach and sight of children. Store at room temperature below 25°C, protect from light. Keep the ampoule in the outer carton.

Use REVAFEN in accordance with the expiry date.

Do not use this medicine after the expiry date which is stated on the package. Do not use

REVAFEN if you notice any defects in the product and / or its packaging.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use and how to properly dispose of your used needles and syringes. These measures will help to protect the environment.

Do not use this medicine if you notice that the solution is not clear and colorless, but shows signs of deterioration (e.g. particles). REVAFEN is for single use only and should be used immediately once opened. Discard any unused quantity of the product.

Marketing Authorization Holder:
HAVER FARMA Ilac A.S.
Acarlar Mah. 74. Sok. Acarkent Sitesi B742 No.:17/1
Beykoz / İstanbul /Turkey

Manufactured By:
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THE FOLLOWING INFORMATION IS INTENDED FOR HEALTHCARE PROFESSIONALS ONLY:

Intravenous use:

Intravenous infusion: the contents of one ampoule (2 ml) of REVAFEN 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) REVAFEN can be given in a slow intravenous bolus over no less than 15 seconds.

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

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

Compatibilities:

REVAFEN 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. REVAFEN 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 of REVAFEN 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).