Rantudil forte is an analgesic and anti-inflammatory drug (nonsteroidal antiphlogistic / analgesic agent). Uses
Symptomatic treatment of pain and inflammation in:
- acute inflammation of the joints (arthritis) including attacks of gout,
- chronic inflammation of the joints (arthritis), in particular in case of rheumatoid arthritis (chronic polyarthritis).
- ankylosing spondylitis (Bechterew’s disease) and other inflammatory rheumatic conditions of the spinal column.
- irritation caused by degenerative disorders of the joints and the spinal column (osteoarthritis, spondylosis).
- inflammatory soft-tissue rheumatism syndrome,
- painful swelling and/or inflammation following injuries.

2. BEFORE YOU TAKE RANTUDIL FORTE
Do not take Rantudil forte
- if you are allergic (hypersensitive) to the active substance acemetacin, to indometacin or any of the other ingredients of this medicinal product.
- if you have blood-formation or blood-clotting disorders of unclear origin.
- if you have gastric or duodenal ulcers.
- if you suffer from gastrointestinal, cerebrovascular or other active bleedings.
- if you are in the final trimester of pregnancy.
- if you are a child or adolescent.

When should you consult a doctor before taking Rantudil forte?
Take Rantudil forte under particular caution (i.e. at longer intervals or reduced dosages) and under medical supervision if you:
- have a history of gastrointestinal bleeding or perforation of the stomach or the intestine in relation with a previous treatment with non-steroidal anti-phlogistic / analgesic agents (NSAIDs).
- have active or a history of recurrent gastric or duodenal ulcers (peptic ulcer) or bleeding (at least two distinct episodes of proven ulceration or bleeding).
- have high blood pressure and/or seriously impaired cardiac output (heart failure).
- have pre-existing kidney damage.
- have severely impaired liver function.
- have certain inherited blood formation disorders (inducible porphyria).
- have just undergone major surgery.

What precautions should be taken for children and elderly patients?
Children and adolescents must not take Rantudil forte as there is insufficient experience with this age group. Particularly careful medical supervision is required for elderly patients.

Take special care with Rantudil forte under the following circumstances:
The following describes when you must take Rantudil forte only under certain conditions (i.e. at longer intervals or reduced dosages and under medical supervision) and only with particular caution. Please ask your doctor about this.
This also applies if you have been affected by these conditions in the past.

Gastrointestinal safety
The use of Rantudil forte with concomitant non-steroidal anti-inflammatory drugs – including so-called COX-2 inhibitors (cyclooxygenase - 2 selective inhibitors) - should be avoided.
Side effects may be reduced by using the lowest effective dose for the shortest duration necessary to control your symptoms.
Elderly patients:
After use of non-steroidal anti-inflammatory drugs, side effects (in particular bleeding and perforation of the stomach and the intestine, which may be life-threatening under certain circumstances) occur more often in elderly patients. For this reason, particular careful medical monitoring will be required when treating elderly patients.

Gastrointestinal bleeding, ulceration and perforation:
Bleeding in the gastrointestinal tract, ulceration or perforation, even with fatal results, has been reported with all NSAIDs. These side effects occurred at anytime during treatment, with or without previous warning symptoms and/or a previous history of serious events in the gastrointestinal tract.

The risk of occurrence of gastrointestinal bleeding, ulceration or perforation is higher with increasing doses of NSAIDs, in patients with a history of ulcer, in particular if complicated with bleeding or perforation (refer to Section 2: “Do not take/use Rantudil forte, if…”), as well as in elderly patients. These patients should commence treatment on the lowest dose available.

For these patients as well as for patients who will need concomitant treatment with low-dosed acetylsalicylic acid (ASS/aspirin) or other medication that may increase the risk of gastrointestinal disease, a combination therapy with products protecting the mucus lining of the stomach (e.g. Misoprostol or proton pump inhibitors) should be considered.

If you have a history of side effects in the gastrointestinal tract, and in particular when you are a senior patient, you should inform your doctor of any unusual symptoms in the abdominal region (in particular gastrointestinal bleeding), especially when treatment is initiated.

Caution is advised if you are treated at the same time with products which may enhance the risk of ulcers and/or bleeding, such as for instance oral corticosteroids, anticoagulant medicines such as warfarin, selective serotonin-reuptake inhibitors which are used for example to treat depressive emotional response, or platelet aggregation inhibitors like ASS (refer to Section 2: “Taking/Using Rantudil forte with Other Medicines”).

Should you experience gastrointestinal bleeding or ulceration under treatment with Rantudil forte, therapy must be stopped immediately.

In patients with a history of gastrointestinal disease (ulcerative colitis, Crohn’s disease) NSAIDs should be used with care, as their state may aggravate (refer to Section 4).

Effects on the cardiovascular system
Medicinal products like Rantudil forte may be associated with a slightly increased risk of heart attack (“cardiac infarction”) or stroke. Any risk becomes greater with high doses and prolonged treatment. Therefore, do not exceed the recommended dose and/or the period of treatment.

If you have heart problems or if you have experienced a stroke already, or if you believe you could be at risk for such diseases (for instance: if you have high blood pressure, diabetes mellitus or high cholesterol values, or if you smoke), you should discuss your therapy with your doctor or your pharmacist.

Skin reactions
Under treatment with NSAIDs, very rare cases of serious skin reactions accompanied with reddening of the skin and formation of blisters – some with fatal results – were reported (exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis / Lyell’s syndrome. refer to Section 4). The risk to develop such reactions seems to be especially high when therapy is initiated, as the majority of these cases occurred during the first month of treatment.

Upon the first appearance of skin rash, lesions of the mucous membranes or any other signs of an allergic reaction, you must stop taking Rantudil forte and you should consult your doctor immediately.

Further information
Patients with hay fever or swelling of the nasal mucous membranes (so-called nasal polyps), chronic obstructive airway disease (e.g. asthma) or chronic infections of the airway as well as patients who react hypersensitive (allergic) to other pain-relievers
Using Rantudil forte with other medicines:
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without prescription.

What other medicinal products influence the effects of Rantudil forte or what do you have to consider when taking Rantudil forte?
Please be aware that the following applies also for medicines used recently.

Concomitant administration of Rantudil forte and digoxin (a medicine used to increase cardiac output), phenytoin (a medicine used to treat convulsions) or lithium (a medicine for treatment of psychiatric disorders) can increase the plasma concentrations of these substances.

Rantudil forte can weaken the effect of diuretics and antihypertensive agents (blood pressure-lowering medication).

Rantudil forte can weaken the effect of ACE inhibitors (medicines used to treat heart failure and to lower blood pressure). In addition, concomitant use of these products increases the risk of impaired kidney function.

Concomitant administration of Rantudil forte and potassium-sparing diuretics (a class of substances to eliminate water from the body) can lead to increased levels of potassium in plasma.

Furosemide accelerates the excretion of the active ingredient of Rantudil forte.

Concomitant administration of Rantudil forte and glucocorticoids or other anti-inflammatory and analgesic substances of this type (non-steroidal anti-inflammatory agents) increase the risk of side effects in the gastrointestinal tract (see “Possible Side Effects”).

Administration of Rantudil forte within 24 hours before or after administration of methotrexate can lead to elevated concentrations of methotrexate and may increase its unwanted side effects.

Medicines containing probenecid or sulphinpyrazone (anti-gout medicines) can delay elimination of Rantudil forte.

The combination of Rantudil forte and coagulation-inhibiting agents can increase the risk of bleeding.
The patient’s coagulation status must therefore be monitored if concomitant therapy with these substances is required.

Non-steroidal anti-inflammatory agents may enhance the effects of anticoagulant agents such as warfarin.

Non-steroidal anti-inflammatory agents (e.g. acemetacin) can increase renal toxicity of ciclosporin. In clinical investigations interactions of non-steroidal anti-inflammatory agents and sulfonylurea (a medicine used to lower blood glucose levels) were reported. Up to date, no interactions between acemetacin, the active substance of Rantudil forte, and sulfonylurea have been reported. Nonetheless, monitoring of blood glucose levels is recommended in case of concomitantly use.

Particular caution is advised when Rantudil forte is administered concomitantly with other medicines that affect the central nervous system or together with alcohol.

Rantudil forte should not be taken concomitantly with triamterene since in combination with indometacin, the main metabolite of acemetacin, there is a risk of acute kidney failure.

Rantudil forte should also not be taken concomitantly with diflunisal as a marked increase in the concentration of indometacin, the main metabolite of acemetacin, is likely (fatal gastrointestinal haemorrhages / gastrointestinal bleeding leading to death have been described).

Acemetacin can delay excretion of penicillin antibiotics.

Taking Rantudil forte with food and drink
Consumption of alcohol should be avoided as far as possible during therapy with Rantudil forte.

Pregnancy
You must inform your doctor if you discover that you are pregnant while taking Rantudil forte over an extended period of time. Rantudil forte must not be taken during the first and second trimesters of pregnancy without consulting your doctor. Rantudil forte must not be taken during the last three months of pregnancy due to the increased risk of serious complications for both mother and child.

Breast-feeding period
Small quantities of acemetacin, the active ingredient of Rantudil forte, and its metabolites pass into breast milk. If long-term use of high doses is prescribed, you should consider weaning your baby prematurely.

Fertility
Rantudil forte may make it more difficult for you to become pregnant.
You should therefore inform your doctor if you plan to become pregnant or if you have problems to become pregnant.

Driving and using machines:
Rantudil forte can cause side effects involving the central nervous system, such as fatigue and dizziness. The ability to drive and/or operate machinery may be impaired in isolated cases. You may then not be able to react rapidly and appropriately in the event of sudden, unexpected incidents.

Do not attempt to drive automobiles or other motor vehicles in these circumstances. Do not operate power tools or machinery. Do not work without a secure foothold.

3. HOW TO TAKE RANTUDIL FORTE
Always take Rantudil forte exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.
Please follow the directions carefully as otherwise Rantudil forte cannot work properly.
Unless otherwise prescribed by your doctor, the usual dose is:

How much Rantudil forte should you take and how often?
The correct dose of acemetacin depends on the severity of the disorder being treated. The recommended dose range for adults is between 30 and 180 mg of acemetacin per day, spread over 1 -3 individual doses. Rantudil forte is not recommended for children and adolescents as there is not sufficient experience in these age groups.
If you forget to take Rantudil forte.
If you forget to take a dose, do not take more than the normal recommended quantity next time.

4. POSSIBLE SIDE EFFECTS
Like all medicines, Rantudil forte can cause side effects, although not everybody gets them.
Evaluation of the side effects is based on the following frequency information:

<table>
<thead>
<tr>
<th>Category</th>
<th>Frequency Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very common</td>
<td>More than 1 of 10 treated patients</td>
</tr>
<tr>
<td>Common</td>
<td>Less than 1 of 10, however more than 1 of 100 treated patients</td>
</tr>
<tr>
<td>Uncommon</td>
<td>Less than 1 of 100, however more than 1 of 1,000 treated patients</td>
</tr>
<tr>
<td>Rare</td>
<td>Less than 1 of 1,000, however more than 1 of 10,000 treated patients</td>
</tr>
<tr>
<td>Very rare</td>
<td>Less than 1 of 10,000 treated patients, including isolated reports</td>
</tr>
</tbody>
</table>

Significant side effects and/or symptoms you should pay attention to and actions to be taken if you should develop any of these side effects:
It must be considered that the following side effects are mainly dose-dependent and can vary from patient to patient.
The most commonly seen side effects affect the digestive tract.
Stomach/duodenal ulceration (peptic ulcers), as well as perforation and/or bleeding of the stomach or the intestine - sometimes fatal – may occur, in particular in elderly patients (refer to Section 2: “Take special care with Rantudil forte under the following circumstances”).
Nausea, vomiting, diarrhoea, flatulence, constipation, digestive trouble, abdominal pain, tarry stool, blood vomiting, ulcerative stomatitis, aggravation of inflammation of the colon and Crohn’s disease were reported following administration of Rantudil forte (refer to Section 2: “Take special care with Rantudil forte under the following circumstances”). Less frequently, inflammation of the stomach has been seen. In particular, the risk of gastrointestinal bleeding is dependent on the dose range and the duration of use.
Oedema, high blood pressure and heart failure have been reported in association with NSAID treatment.
Medicinal products like Rantudil forte may be asso-
associated with a slightly increased risk of heart attack (“cardiac infarction”) or stroke.

**Heart disorders**
In very rare cases palpitations, pain in the chest, high blood pressure and collapse of the circulation was reported. Sensation of tightness in the chest (angina pectoris symptoms) may occur as well.
In very rare cases, heart failure (insufficiency of the heart) can occur.

**Blood disorders**
Uncommonly, blood cell production can be impaired (anaemia, leucopenia, agranulocytosis, thrombocytopenia). The initial symptoms include: fever, sore throat, superficial lesions in the mouth, flu-like symptoms, severe weariness, nosebleeds and bleeding of the skin.
In these cases, use of the medicinal product must be discontinued immediately and a doctor must be consulted (see “Precautions for use and warnings”). You should not use any analgesic and fever lowering medicines to treat these symptoms yourself. The blood picture of patients undergoing long-term therapy should be monitored at regular intervals.
In very rare cases, haemolytic anaemia (anaemia caused by accelerated decomposition of red blood cells) has occurred. It is possible that the substance affects blood coagulation and causes an increased tendency to bleed.

**Central nervous system and sensory organs**
Central nervous disorders such as headache, excitation, irritability, fatigue, drowsiness, dizziness, depression and vertigo may occur commonly. Very rare cases of impaired sensitivity, muscular weakness, increased perspiration, impaired taste perception, ringing in the ear and temporary impaired hearing, impaired memory, psychiatric disorders, sleeping disorders, disorientation, convulsions, anxiety, nightmares, tremor and temporary loss of consciousness extending up to coma were reported.
Intensification of the symptoms of epilepsy, Parkinson’s disease and pre-existing psychiatric disorders is possible during therapy with Rantudil forte.

**Eye disorders**
In very rare cases, impaired vision (blurred eyesight and/or double vision, occurrence of coloured spots in your vision) and inflammation of the cornea may occur.
Uncommonly, changes (degeneration of the retinal pigment) in the retina and corneal clouding were observed during long-term treatment with indometacin, the main metabolite of acemetacin.
A significant symptom may be blurred eyesight. This requires a thoroughly ophthalmologic check. Since these changes may occur also without symptoms a regular ophthalmologic check is recommended during long-term treatment. If these changes occur discontinuation of treatment is recommended.
Uncommonly, vision of double images is reported.

**Gastrointestinal tract disorders**
Very common side effects include gastrointestinal disorders such as nausea, vomiting, diarrhoea and minor loss of blood from the gastrointestinal tract which, in exceptional cases, can cause anaemia.
Commonly, impaired digestion, flatulence, abdominal cramps, loss of appetite and gastric or duodenal ulcers (sometimes accompanied by bleeding and perforation) can occur and occasionally, blood can appear in vomit, faeces or diarrhoea.
If stronger pains in the upper abdomen and / or black stools occur the use of Rantudil forte has to be discontinued at once and a doctor should be consulted.
Very rare cases of inflammation of the oral mucosa, inflammation of the tongue, lesions on the oesophagus (damage of the gullet lining), complaints in the lower abdomen (e.g. non-specific, bleeding inflammation of the colon, deterioration of Crohn’s disease or ulcerative inflammation of the colon) and constipation have been reported.
Very rare cases of intestinal stricture were reported.

**Disorders of the kidney and the urinary tract**
In very rare cases, acute dysfunction of the kidneys (kidney insufficiency), protein in the urine (proteinuria), blood in the urine (haematuria) or kidney damage (interstitial nephritis, nephrotic syndrome, papillary necrosis) can occur.
Reduced urine excretion, accumulation of fluid in the body (oedema) and general malaise may be symp-
caused by infection (e.g. development of necrotising fasciitis) was observed at the same time as the administration of certain anti-inflammatory agents (non-steroidal anti-inflammatory agents, a category of medicines that includes Rantudil forte). You should therefore consult your doctor immediately if you develop symptoms of infection (e.g. redness, swelling, heat, pain, fever), or your existing symptoms deteriorate, while taking Rantudil forte.

Note the guidelines for behaviour listed for certain side effects mentioned above.

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

5. HOW TO STORE RANTUDIL FORTE
Keep out of the reach and sight of children.
Do not use Rantudil forte after the expiry date which is stated on the carton and on the container after <Use before>.

Storage conditions: Do not store above 30°C.

6. FURTHER INFORMATION
What Rantudil forte contains:
The active substance is: Acemetacin
The other ingredients are: Ferric oxide hydrate, ferric(III) oxide, gelatine, lactose monohydrate, magnesium stearate (Ph. Eur.), sodium dodecylsulfate, colloidal anhydrous silica, talcum, titanium dioxide.

What Rantudil forte looks like and contents of the pack:
Rantudil forte is available in packs containing 20 (N1), 50 (N2) and 100 (N3) hard capsules each. The blister pack is made of child-proof, rigid composite foil. The capsules are most easily removed by pressing on the blister end.

This leaflet was last approved in April 2007.