When should you consult a doctor before taking Rantudil retard?

Take Rantudil retard under particular caution (i.e. at longer intervals or reduced dosages) and under medical supervision if you:
- have a history of gastrointestinal disorders or suspected gastric or duodenal ulcers or enteritis (e.g. ulcerative colitis, Crohn’s disease),
- have high blood pressure and/or impaired cardiac output (heart failure),
- have pre-existing kidney damage,
- have severely impaired liver function,
- have certain inherited blood formation disorders (induceable porphyria),
- have just undergone major surgery.

What precautions should be taken for children and elderly patients?

Children and adolescents must not take Rantudil retard as there is insufficient experience with this age group.

Particularly careful medical supervision is required for elderly patients.

Take special care with Rantudil retard under the following circumstances:

Patients with hay fever or swelling of the nasal mucous membranes (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 or rheumatism cures from the group of the non-steroidal anti-inflammatory agents should take Rantudil retard only when certain precautions are taken and only under direct medical supervision.

These patients are rather at risk to suffer from hypersensitivity reactions (allergic reactions) when taking Rantudil retard.

The symptoms may be asthma attacks (so called analgesic intolerance / analgesic asthma), local swelling of the skin or mucous membranes (angioedema) or nettle rash (urticaria).
The same applies for patients who react hypersensitive (allergic) to other substances. These patients are also at risk to suffer from hypersensitivity reactions. Acemetacin can cause temporary inhibition of platelet aggregation. Patients with coagulation disorders should therefore be monitored carefully. Long-term administration of Rantudil retard requires regular monitoring of the patient’s liver values, kidney function and blood count. Consult/inform your doctor or dentist if you take Rantudil retard before surgery. This pharmaceutical product contains lactose. Therefore, please consult your doctor first before using Rantudil retard if you know that you have lactose intolerance.

What other precautions must be taken?
Long-term use of high doses of analgesic medicines taken contrary to instructions can cause headaches which must not be treated by even higher doses of the medicine.
In general, habitual consumption of analgesic medicines, particularly combinations of several analgesic active substances, can lead to permanent kidney damage with the risk of kidney failure (analgesic nephropathy).

Using Rantudil retard 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 retard or what do you have to consider when taking Rantudil retard?
Please be aware that the following applies also for medicines used recently.
Concomitant administration of Rantudil retard 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 retard can weaken the effect of diuretics and antihypertensive agents (blood pressure-lowering medication).
Rantudil retard 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 retard 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 retard.
Concomitant administration of Rantudil retard and glucocorticoids or other antiinflammatory 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 retard 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 retard.
The combination of Rantudil retard 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 (e.g. acemetacin) can increase renal toxicity of cyclosporin.
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 and sulfonylurea have been reported. Nonetheless, monitoring of blood glucose levels is recommended in case of concomitantly use.
Particular caution is advised when Rantudil retard is administered concomitantly with other medicines that affect the central nervous system or together with alcohol.
Rantudil retard should not be taken concomitantly with triamterene since in combination with indomethacin, the main metabolite of acemetacin, there is a risk of acute kidney failure.

Rantudil retard should also not be taken concomitantly with diflunisal as a marked increase in the concentration of indomethacin, the main metabolite of acemetacin, is likely (fatal gastrointestinal haemorrhages have been described).

Acemetacin can delay excretion of penicillin antibiotics.

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

**Pregnancy and breast-feeding**
You must inform your doctor if you discover that you are pregnant while taking Rantudil retard over an extended period of time.

Rantudil retard must not be taken during the first and second trimesters of pregnancy without consulting your doctor. Rantudil retard must not be taken during the last three months of pregnancy due to the increased risk of serious complications for both mother and child (including potentially life-threatening kidney and intestinal damage) during birth.

Small quantities of the active ingredient acemetacin and its metabolites pass into breast milk. You should therefore avoid taking Rantudil retard while you are breast-feeding.

If long-term use of high doses is prescribed, you should consider weaning your baby prematurely.

**Driving and using machines:**
Rantudil retard 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 RETARD
Always take Rantudil retard 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 retard cannot work properly.

Unless otherwise prescribed by your doctor, the usual dose is:

**How much Rantudil retard 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 retard is not recommended for children and adolescents as there is not sufficient experience in these age groups.

<table>
<thead>
<tr>
<th>Age</th>
<th>Single dose: (Capsules)</th>
<th>Total daily dose: (Capsules)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>1 (equivalent to 90 mg of acemetacin)</td>
<td>1 – 2 (equivalent to 90 – 180 mg of acemetacin)</td>
</tr>
</tbody>
</table>

**How and when should you take Rantudil retard?**
Rantudil retard should be swallowed whole with sufficient liquid not on an empty stomach. If you suffer from gastric impairment it is recommended to take Rantudil retard during meals.

**For how long should you continue taking Rantudil retard?**
Your doctor will decide how long you should continue taking Rantudil retard.

Patients with rheumatic disorders may have to take Rantudil retard over an extended period of time.

**Dosage in acute attacks of gout:**
The usual recommended dose to treat acute attacks of gout - until the symptoms subside - is 180 mg of acemetacin per day. Higher doses may be indicated if specifically prescribed by the doctor.

Patients without pre-existing gastrointestinal damage can take 120 mg of acemetacin at the start of therapy followed by 60 mg of acemetacin every 6 hours; a maximum dose range of 300 mg of acemetacin per 24 hours is permitted. On the second day of therapy, the same dose may be taken if necessary; otherwise, the dose should be reduced.

Please contact your doctor or pharmacist if you
have the impression that the activity of Rantudil retard is too strong or too weak.

**If you take more Rantudil retard than you should**

Symptoms of overdose include central nervous disturbances such as headache, dizziness, confusion, lack of drive, drowsiness and loss of consciousness and also abdominal pain, nausea and vomiting. In addition, bleeding in the gastrointestinal tract, perspiration, high blood pressure, accumulation of fluid in the body, decreased excretion of urine, blood in the urine and impaired liver and kidney function can occur. No specific antidote is known.

If you suspect that you are experiencing an overdose, consult a doctor so that he/she can decide on the further procedure depending on the severity of the intoxication.

**If you forget to take Rantudil retard**

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 retard 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>Frequency</th>
<th>Definition</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. In particular, the risk of gastrointestinal bleeding (ulcers, mucous membrane defects, inflammation of the gastric mucous membrane) is dependent on the dose range and the duration of use.

**Gastrointestinal tract**

Very common side effects include gastrointestinal disorders such as nausea, vomiting, diarrhea and minor loss of blood from the gastrointestinal tract which, in exceptional cases, can cause anemia. 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 retard 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, complaints in the lower abdomen (e.g. non-specific, bleeding inflammation of the colon, deterioration of Cohn’s disease or Colitis ulcerosa) and constipation have been reported.

Very rare cases of intestinal stricture were reported.

**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 retard.

**Skin**

Hypersensitivity reactions such as skin rash and itching have been commonly reported.

Nettle rash or hair loss has been observed occasionally.

In very rare cases, skin rash with blistering, eczema, erythema, light-sensitivity, minor and extensive cutaneous bleeding (also allergy-related) and serious forms of skin reactions (Stevens-Johnson syndrome, Lyell’s syndrome) can occur.
Kidney
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 symptoms of a kidney disease or even kidney failure. In very rare cases vaginal bleeding and problems with urination can occur.
If any of the above symptoms occur or worsen, stop using Rantudil retard and contact your doctor.

Liver
Commonly, elevated liver enzyme levels in the blood may occur (serum transaminases).
Uncommonly, liver damage is possible (hepatitis with or without jaundice, taking a fulminant course in very rare cases and at times without prior symptoms). The patient's liver values should therefore be monitored at regular intervals.

Pancreas
Inflammation of the pancreas, elevated blood glucose levels and glucose in the urine have been reported in very rare cases.

Blood
Uncommonly, blood cell production can be impaired (anemia, 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 feverlowering 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, hemolytic anemia (anemia 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.

Cardiovascular system
In very rare cases palpitations, pain in the chest and high blood pressure can occur.
Sensation of tightness in the chest (angina pectoris symptoms) has been reported.
In very rare cases, heart failure (insufficiency of the heart) can occur.

Systemic reactions and other organ systems
Severe hypersensitivity reactions are possible and can manifest themselves as: oedema of the face and eyelids, swollen tongue, swollen larynx (voice box) with constriction of the airways, shortness of breath ranging up to asthma attacks, tachycardia, a drop in blood pressure ranging up to potentially fatal shock.
Medical assistance must be obtained immediately if any of these symptoms occur, a reaction that can occur the first time this product is used.
In very rare cases, allergy-related inflammation of the blood vessels (vasculitis) and the lungs (pneumonitis) have been observed.
Uncommonly, oedema (e.g. peripheral oedema) can occur, particularly in patients with high blood pressure or impaired kidney function.
Uncommonly, degeneration of the retinal pigment and corneal clouding were observed during long-term treatment with indomethacin, the main metabolite of acemetacin. A significant symptom may be blurred vision. 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, double vision is reported. In very rare cases, deterioration of inflammation caused by infection (e.g. development of necrotising fasciitis) was observed at the same time as the administration of certain antiinflammatory agents (non-steroidal anti-inflammatory agents, a category of medicines that includes Rantudil retard).
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 retard. 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 RETARD
Keep out of the reach and sight of children.
Do not use Rantudil retard 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 retard contains:
The active substance is:
Acemetacin

The other ingredients are:
Cellacefat, gelatine, lactose monohydrate, magnesium stearate (Ph. Eur.), sodium dodecylsulfate, Povidon 25, crospovidon, colloidal anhydrous silica, talcum, triacetin, ferric oxide hydrate, ferric(III) oxide, ferric(II,III) oxide, titanium dioxide

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

This leaflet was last approved in November 2006.