Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT
ETACIZIN® 50 mg coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION OF THE PRODUCT
Active substance: Aethacizinum (well–established name).
Each coated tablet contains 50 mg of etacizin.
Excipients: the complete list of excipients see in p. 6.1

3. PHARMACEUTICAL FORM
Coated tablets.
Description: round, double convex in yellow coating. Coating and core of almost white colour are seen in a tablet section.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
Extrasystoles (ventricular and supraventricular), supraventricular tachycardia, ventricular tachycardia, atrial flutter and fibrillation.

4.2 Posology and method of administration
Tablets are usually administered orally, independent on meal.
Adults. The dose is adjusted individually. Usually the dose is 50 mg two-three times daily. In case of insufficient clinical effect, the dose can be increased to 50 mg four times daily. Combined therapy of etacizin and adrenoblockers is necessary to achieve the stable antiarrhythmic effect in individual patients.
Elderly. The elderly should use the medicine with caution, it is necessary to decrease the starting dose and cautiously increase the dose.
Children and adolescents (younger than 18 years). Etacizin administration is contraindicated as there are no sufficient data on administration safety and efficacy.
Hepatic failure. Patients with liver disorders should use etacizin for long-term therapy with caution as the hepatotoxic effect is possible (hard disturbances of liver activity if administration is contraindicated).

4.3 Contra-indications
- Hypersensitive to etacizin and/or any other excipients
- Structural heart disturbances:
acute coronary syndrome
acute myocardial infarction and three months after acute myocardial infarction
expressed left ventricular hypertrophy
expressed heart cavity dilation

- Significant disorders of heart functions:
  - serious cardiac insufficiency (Class III and IV according to NYHA)
  - decrease of left ventricular ejection fraction (echocardiography data)

- Expressed disturbances of heart rhythms:
  - class II sinoatrial (SA) blockade or other sinus arrest cases
  - class II and III atrioventricular (AV) blockade
  - intraventricular conduction disturbances (complete block of bundle of His)

- hard liver and/or kidney functions disturbances
- breast-feeding
- children and adolescents (younger than 18 years).

Concomitant use of IC class antiarrhythmic preparations (etacizin) and IA class antiarrhythmics (hinidine, procanamide, disopirnanamide, ajmalin) is contraindicated.
Concomitant use of etacizin and MAO inhibitors is contraindicated.

4.4 Special warnings and precautions for use

Arrhythmia treatment caused by myocardial infarction using etacizin can be started with caution not earlier than 3 months after myocardial infarction.

Etacizin should be used very cautiously in case of sinus node weakness syndrome, Class I AV blockade, incomplete block of bundle of His, severe blood flow disturbances, closed-angle glaucoma, hypertrophy of benign prostate.

Etacizin may have proarrhythmic effect. To avoid it the following terms should be taken into account:

1) administration contra-indications should be strictly observed
2) hypokalemia should be found and prevented in time
3) the treatment course is advisable to start in hospital. After the first and repeated doses of the drug on the 3rd-5th days of administration it is necessary to make ECG control or cardiac activity monitoring.
4) the treatment course should be interrupted immediately, if ectopic ventricular complexes occur more often, blockade or bradycardia develop, if ventricular complexes (QRS) enlarge more than 25 %, their amplitude decreases, ECG P wave extends more than 0.12 seconds or QT intervals >500 ms.

The preparation should be used with caution, if QT intervals >400 ms.

Proarrhythmic effect does not directly depend on the dose. To decrease it concomitant administration of etacizin and a small dose of beta adrenoblockers is advisable.
Patients with liver diseases should be careful as etacizin can have a toxic effect on hepatocytes.

This drug should not be used in patients with rare inherent fructose intolerability, glucose-galactose malabsorption or saccharase isomaltase.

Colouring agent Sunset Yellow in the content of tablets coating can cause allergic reactions.

### 4.5 Interaction with other medicinal products and other forms of interaction

Administration of Etacizin concomitantly with 1A class antiarrhythmics, and with MAO-inhibitors is contraindicated. 

β-adrenoblockers increase antiarrhythmic effect, especially in cases of arrhythmia provoked by physical load or stress. Such combination allows decreasing doses of Etacizin thus reducing frequency of adverse effects. This concomitant administration is advisable in the treatment and for prophylaxis of paroxysmal tachycardia.

Administration of Etacizin concomitantly with Digoxin increases anti-arrhythmic effect of preparations and improves the contractility of myocardium. The concomitant use of these preparations can provoke nausea and decrease appetite that is associated with increasing of Digoxin concentration in the blood. In such cases it is necessary to decrease Digoxin dose.

Use of alcohol should be avoided during therapy.

### 4.6 Pregnancy and lactation

Clinical data of etacizin use during pregnancy are not available. Animal studies did not show any direct or indirect effect on pregnancy, embryonal/foetus development. When the drug is used in women during pregnancy, it is necessary to take into account the consequences of cardiac disease’s non-treatment for mother and possible risk for a newborn. Etacizin penetrates into breast milk, therefore the preparation must not be used in breast-feeding women.

### 4.7 Effects on ability to drive and use machines

Preparation use may cause dizziness, vision disturbances. In these cases it is necessary to avoid driving and operate any tools or machines.

### 4.8 Undesirable effects

<table>
<thead>
<tr>
<th>Very common</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very rare</th>
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<td>&gt; 1/10</td>
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Like all medicines, etacizin can cause side effects, although not everybody gets them.
Using Etacizin® 50 mg Tablets undesirable effects may occur, especially when the high doses of the drug are used.

**Cardiovascular system disturbances:** rare – AV blockade, intraventricular conduction disturbances, worsening of myocardial contractility. In single cases – proarrhythmic effect with an unexpected death risk.

ECG changes: PQ interval, P wave and QRS complex elongation.

**Nerve system disturbances:** common – dizziness, accommodation disturbances (in the beginning of treatment), ataxia, rare – headache.

**Gastrointestinal tract disturbances:** rare – nausea, ache in epigastria.

### 4.9 Overdose

*Symptoms:* inhibition in cardiovascular system, proarrhythmic risk increases.

*Treatment:* gastric lavage and symptomatic therapy. Blood pressure and ECG should be carefully controlled in patients (monitoring at least 6 hours till all ECG changes disappear).

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antiarrhythmics, IC class.

**ATC code:** C01BC.

According to Vaughan Williams antiarrhythmic agents’ classification, Etacizin is IC class antiarrhythmic (membranes stabilizers). Etacizin inhibits “fast” sodium ions current through cell membranes of sodium channels. It has an effect on sodium channels, which are on the surface of cell membranes, and on this part of channels that are on the inner surface of cell membranes. These additional places of binding provide etacizin long-term activity. To a less extent etacizin inhibits calcium ions current through “slow” calcium channels. Negative nootropic activity of etacizin is connected with blockade of “slow” calcium channels.

Etacizin has moderate antiischemic activity.

Etacizin slows down distribution of excitation in the conduction system of myocardium. Electrocardiogram (ECG) shows prolongation of the P-Q, P-R interval and QRS complex.

Etacizin inhibits increase of activity potential speed (Vmax), does not change the potential of rest.

Etacizin has cholinolytic characteristics, therefore it is very effective in the treatment of arrhythmia, which is connected with n. Vagus activation.

Etacizin has also local anesthetic activity.

#### 5.2 Pharmacokinetic properties

*Absorption / distribution.* After peroral administration the preparation is rapidly absorbed from gastrointestinal tract. Food intake does not influence on etacizin absorption. Preparation
bioavailability is 40 %. Maximal plasma concentration of the active substance is achieved during 2.5 hours after administration of single oral 100 mg dose. About 90 % of etacizin are bound with plasma proteins. Etacizin has big distribution volume, approximately 400 l. Preparation activity continues 6-8 hours. Etacizin crosses placental barrier, penetrates into breast milk. 

*Biotransformation / excretion.* Etacizin has an expressed first pass metabolism, some metabolites have antiarrhythmic activity. Elimination half-life is at average 2.5 hours. Etacizin is excreted from the body in the form of urine metabolites. After prolonged preparation of the drug accumulation is not observed.

5.3. Preclinical safety study. 
In animal studies the received data on pharmacological safety, repeated dose toxicity, mutagenicity and effect on reproductivity do not certify of any risk to people.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Tablet core: potato starch, sucrose, methylcellulose, calcium stearate. 
Tablet coating: sucrose, povidone, calcium carbonate, magnesium carbonate, silica, carnauba wax, colouring agents: Quinoline Yellow (E 104), Sunset Yellow (E110), titanium dioxide (E171).

6.2. Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Do not store above 25 °C. Protect from light and moisture.
Store in the original package.

6.5 Nature and contents of container
10 tables in blister from transparent PVC film and aluminium foil; 
1, 2, 3 or 5 blisters (10, 20, 30 or 50 tablets) with patient’s leaflet in the carton pack.

6.6 Instructions for use and handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER
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8. MARKETING AUTHORISATION NUMBER
98-0371

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16.06.1998. / 18.12.2003. /03.03.200

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