State Agency of Medicines, Director
I.Adoviča *__/signature/__*
Registered No.*10843-300708*

Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

ADAPTOL® 300 mg Tablets
ADAPTOL® 500 mg Tabletes
ADAPTOL® 300 mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION OF THE PRODUCT

Active substance: mebicar (Mebicarum) – well known name.

Each ADAPTOL® 300 mg tablet contains 300 mg mebicar.
Each ADAPTOL® 500 mg tablet contains 500 mg mebicar.
Each ADAPTOL® 300 mg **c**apsule contains 300 mg mebicar

Excipients: the complete list of excipients see in p. 6.1

3. PHARMACEUTICAL FORM

Tablets.
Description: White or almost white, round flat tablets with bevelled edge and break line on one side of the tablet.

Capsules.
Description: gelatine capsules No. 0 filled with white or almost white granules.

4. CLINICAL DESCRIPTION

4.1. Indications

Neuroses and neurotic disturbances (irritability, emotional excitability, anxiety, fear).

Cardialgias of different genesis, which are not connected with ischemic heart disease.

To improve tolerability of neuroleptics and tranquilizers.

Complex therapy to decrease addiction to smoking.

4.2 Administration and dosage

The drugs are administered orally independently of meals.

Adults use 300-500 mg 2-3 times a day. The highest single dose is 3 g, the highest daily dose - 10 g. The course of treatment - from a few days up to 2-3 months.

Complex therapy to decrease the addiction to smoking – 600-1000 mg a day for 5-6 weeks.

Elderly should not adjust the dose.

Patients with liver impairment should not diminish the dose.

Dose adjustment is not studied in *patients with kidneys deficiency*. These patients should use the drugs with caution.

4.3 Contra-indications

Hypersensitive to mebicar and/or any other excipients.

4.4 Special warnings and special precautions for use

No special requirements.

4.5 Interaction with other medicinal products and other forms of interaction

Adaptol® can be used concomitantly with neuroleptics, tranquilizers (benzodiazepines), soporifics, antidepressants and psychostimulants.

4.6 Pregnancy and lactation

Active substance penetrates well into all tissues and liquids of organism. There is not sufficient quantity of adequate and well-controlled studies on safety use of the preparation in pregnant and breast-feeding women, therefore the use of the drug in pregnancy and breast-feeding is not recommended.

4.7 Effects on ability to drive and use machines

The drug may cause hypotension and weakness that may have an effect on the ability to drive a motor vehicle and use machines.

4.8 Undesirable effects

Classification of frequency of side effects is given in the table.

Very common > 1/10	Common > 1/100, < 1/10	Uncommon > 1/1 000, < 1/100	Rare > 1/10 000,< 1/1 000	Very rare < 1/10 000

Like all medicines, *Adaptol*® can cause side effects, although not everybody gets them.

Nerve system disturbances: rare– dizziness.

Cardiovascular system disturbances: rare – hypotension.

Gastrointestinal tract disturbances: rare – digestive disturbances.

Skin and subcutaneous tissues disturbances: rare – after administration of high dose allergic reactions are possible (skin rash). In case of allergic reactions the use of the drug should be interrupted.

General disorders: rare – hipotermia, weakness.

In cases when low blood pressure and/or decreased body temperature occurs (body temperature may decrease for 1-1.5 °C), the drug administration should not be interrupted. Blood pressure and body temperature are normalized after the end of treatment.

4.9 Overdose

The drug has low toxicity. There is information of two cases of overdose when intending to make suicide 30 g single dose was taken. The mentioned dose did not cause the death and also did not leave the effect on health.

Treatment: Generally used detoxication procedures and symptomatic therapy should be performed. Specific antidote is not known.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: anxiolytic (medicinal preparation of different chemical groups).

ATC code: N05BX

5.1 Pharmacodynamics

Medicinal preparation *Adaptol*® active substance *mebicar* refer to a pharmacotherapeutic group, which is called anxiolytics. According to their chemical structure *Adaptol*® active substance *mebicar* is similar to organism natural metabolites - its molecule consists of two methylated fragments of urea included in bicyclic system. It is freely soluble in water and organic solvents. Mebicar is chemically inert and stable substance, does not interact with acids, alkali, oxidants or reducers, different drugs or food components

Mebicar is proved to have anxiolytic and nootropic characteristics, it decreases unfavourable side effects caused by other tranquilizers of neuroleptic and benzodiazepine group (emotional despondency, excessive calming effect, muscles weakness), it has antialcoholic effect.

Mebicar has an effect on the structure of limbic-reticular activity, particularly on hypothalamus emotional zone, as well as on all 4 basic neuromediator systems – γ aminobutyric acid (GASS), choline -, serotonin- and adrenergic activity.

The preparation has moderate tranquilizing (anxiolytic) activity, eliminates or weakens anxiety, anxious hypochondria, fear, an internal emotional pressure and irritability. Tranquilizing effect

of the preparation is not accompanied by myorelaxation and infringement of coordination of movements, it does not disturb mental or physical activity, therefore ***Adaptol*** can be administered not interrupting work or study. The preparation has no direct hypnotic effect, but it increases activity of hypnotics and normalizes duration of the disturbed night dream.

Mebicar relieves or takes off nicotine abstinence.

Alcoholic patients have a decreased level of endogen ethyl alcohol in the blood, and this is one of the reasons of inclination towards alcohol. Mebicar increases endogen alcohol level more than other tranquilizers diminishing inclination towards alcohol.

Mebicar does not cause increase of the mood or euphoria, no drug dependence or syndrome of withdrawal has been observed during its administration.

Besides nootropic activity mebicar has also nootropic characteristics. It was observed in the clinical studies that mebicar increases logic, associative thinking, improves attention and ability to work and productivity not stimulating productive symptomatics – delirium and pathologic emotional activity.

5.2 Phamacokinetics

Administered perorally the preparation is well absorbed (77-80 %) from gastrointestinal tract, about 40 % of active substance bind to erythrocytes. Other part of active substance is in blood plasma in an unbound form with proteins, freely distributed in the body and crosses cells' membranes. Distribution volume is 0.9 l/kg. Maximal plasma concentration of the active substance is achieved during 0.5 hour after administration, the high level of concentration is kept for 3-4 hours, and then the concentration is decreased. Mebicar does not metabolize in the body, 55-70 % of the administrated dose is excreted unchanged in the urine, others - in the faeces during the first day.

5.3. Preclinical safety study.

The preparation has low toxicity. In the studies of acute toxicity in animals, which were administered mebicar perorally, LD_{50} was 3800 mg/kg of body weight, in rats – 3450 mg/kg of body weight. The administration of the preparation very rarely causes side effects. In the studies of chronic toxicity, which were administered mebicar perorally at a dose of 750 mg/kg and

500 mg/kg of body weight, all animals remained alive, increase of body weight was the same as in a control group, blood content and biochemical characteristics remained within the norm limits, no histological changes were observed in the inner organs.

No carcinogenic, teratogenic or embryotoxic activity was observed in the animal studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablets: methylcellulose, calcium stearate.
Capsules: methylcellulose, calcium stearate.

6.2 Incompatibilities:

Not applicable.

6.3 Shelf life:

Tablets: 4 years.
Capsules: 3 years.

6.4 Special precautions for storage:

Tablets:
Do not store above 25 °C.
Protect from light and moisture.

Capsules:
Do not store above 25 °C.
Protect from light and moisture.

6.5 Nature and contents of container::

Tablets:
10 tables in blister from PVC film and aluminium foil,
2 blisters (20 tablets) with patient's leaflet in the carton pack.

Capsules:
10 capsules in blister from PVC film and aluminium foil;
2 blisters (20 capsules) with patient's leaflet in the carton pack..

6.6. Instructions for use and handling:

No special requirements. Any unused product or waste should be disposed of in accordance with local requirements

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER:

ADAPTOL® 300 mg Tablets: No. 98-0373
ADAPTOL® 500 mg Tablets: 03-0002
ADAPTOL® 300 mg Capsules: 03 – 0001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

ADAPTOL® 300 mg Tablets:
1998. / 24.10.2003. / 20.06.2008.

ADAPTOL® 500 mg Tablets and ADAPTOL® 300 mg Capsules:
12.02.2003 ./ 12.05.2008.

10. DATE OF REVISION OF THE TEXT:

02.2008.