ACUPAN®20 mg/2 mL, solution for injection

1. QUALITATIVE AND QUANTITATIVE COMPOSITION

Nefopam (hydrochloride).....20 mg
Disodium phosphate and sodium phosphate, water for injection q.s 2ml.

2. PHARMACEUTICAL FORM

Solution for injection in ampoule.

3. PHARMACOLOGICAL PROPERTIES

Acupan is a non-narcotic central analgesic. It is not structurally related to other known analgesics. *In vitro*, on synapstosomes of rats, an inhibition of catecholamine and serotonine recapture is evoked. *In vivo*, in animal, nefopam has shown antinociceptive properties. An antihyperalgesic actions has also been demonstrated by a mechanism not yet completely demonstrated. Through clinical studies, Acupan has shown a positive effect against the post-operative shivering. Acupan has no anti-inflammatory activity or antipyretic activity. It does not lead to a respiratory depression and does not slow the intestinal transit. Acupan has a anticholinergic activity. It has been observed a moderate and transitory increase of the cardiac frequency and of the blood pressure.

4. PHARMACOKINETIC PROPERTIES

After administration of a 20 mg dose by IM route, the serum peak (Tmax) is between 0.5 et 1 hour and the maximal concentration (Cmax) is 25 ng/ml in average. The serum half life is 5 hours in average. After IV administration of a same dose the serum half life is 4 hours in average. The link ratio to plasmatic proteins is 71-76 %.
The biotransformation is important and 3 main metabolites have been identified: desmethyl nefopam, nefopam N-oxide and N-glucuronide. The two first which are not conjugated did not show any analgesic activity in animal.
The elimination is mainly urinary: 87 % of the administered dose is present in the urine. Less than 5 % of the dose is eliminated unchanged; the metabolites identified in the urines represent 6, 3 and 36 % respectively of the dose administered by IV route.

5. THERAPEUTIC INDICATIONS:

Symptomatic treatment of acute painful conditions, specially post-operative pains.

6. DOSAGE AND ADMINISTRATION:

As for any antipain treatment, the dosage must be adapted to pain intensity and patient response.

Dosage

- IM route: Acupan should be administered by deep intramuscular route. The usual recommended dose is 20 mg per injection. If necessary, it can be repeated every 6 hours without exceeding the total dose of 120 mg/day.
- IV route: Acupan should be administered by slow intravenous infusion in more than 15 minutes, the patient laying down in order to avoid some side effects such as nausea, dizziness, sweat. The usual recommended unique dose is 20 mg per injection. If necessary, it can be repeated every 4 hours, without exceeding 120 mg/day.

Method of administration

Acupan can be administered in the usual solutions for perfusion (isotonic solution of sodium chloride or glucose solution). It is recommended to avoid mixing Acupan and other injectable drugs in the same syringe.

7. CONTRAINDICATIONS:

- Hypersensitivity to nefopam or to one of the components of Acupan.
- Children below 15 years in of the absence of clinical studies.
- Convulsions or previous history of convulsions.
- Risk of urinary retention linked to uretroprostatic disorders.
- Risk of acute angle glaucoma.

8. PRECAUTIONS:

Special warnings

It exists a risk of drug addiction with Acupan.
Acupan is nor a morphinic agent, neither an antagonist of morphinic drugs. Thus, stopping a treatment by a morphinic drug for an addicted patient already treated by Acupan risks to lead to a withdrawal syndrome.
The benefit/risk ratio of the treatment by Acupan must be regularly re-evaluated.
Acupan is not indicated for the treatment of chronic painful conditions.

Precautions for use

It has to be particularly prudent in case of:
- hepatic insufficiency
- renal insufficiency, due to the risk of accumulation and then the increased risk of side effect.
- For patients who have a cardio-vascular pathology due to the tachycardiac effect of the product.
- Due to its anticholinergic effects, the treatment with Acupan is not advisable for elderly.

Use in pregnancy: In the absence of study in animals and human clinical data, the risk is unknown. Consequently, by precaution, do not prescribe during pregnancy, neither in case of lactation.
- Due to the possible risk of somnolence, the vigilance can be altered and makes dangerous the drive of vehicles or the use of machines.

ACUPAN 20 mg/2 mL, injectable solution contains sodium.

This medicine contains less than 1mmol sodium (23mg) per ampoule, that is to say essentially "sodium-free".
This medicinal product contains 40.74mg sodium (main component of cooking/table salt) per maximum dose of 6 ampoules. This is equivalent to 2% of the recommended maximum daily dietary intake of sodium for an adult.

Overdose

These are anticholinergic the symptoms: tachycardia, coma, convulsions and hallucinations (see section 4.4).
Treatment: symptomatic treatment with cardiac and respiratory monitoring in hospital.

9. ADVERSE REACTIONS:

The very common side effects are: somnolence, nausea with or without vomiting, hyperhydrose* The common side effects are: vertigo*, tachycardia*, palpitation*, dry mouth*, urinary retention. The rare side effects are: excitability*, irritability*, hallucination, drug abuse, drug addiction, convulsion*, malaise, hypersensitivity reaction (urticaria, de Quincke's œdema, anaphylactic shock). The side effects with unknown frequency are: coma, confusion, paint at the injection site
*- *Other atropinic effects could appear even if never reported*

10. DRUG INTERACTIONS:

It has to be taken into consideration that many drugs or substances can increase the depress of central nervous system, by addition of each effect and can lead to the decrease of vigilance. The drugs concerned are: Morphinics (analgesic, cough medicine and substituted treatment for addictions), neuroleptics, barbiturates, benzodiazepine, non benzodiazepine anxiolytic (like meprobamate), hypnotics, sedative antidepressant drugs (amitriptyline, doxepine, mianserine, mirtazapine, trimipramine), sedative antihistaminic H1, central antihypertensive, baclofene, thalidomide. Unadvisable association: Consumption of alcohol (Increase of the sedative effect by alcohol consumption). This may affect the ability to drive vehicles or use of machines. Absorption of alcohol or of medicine containing alcohol must be avoided. Association to take into account: Other sedative

drugs such as morphinics (analgesic, cough medicine and substituted treatment for addictions), neuroleptics, barbiturates, benzodiazepine, non benzodiazepine anxiolytic (like meprobamate), hypnotics, sedative antidepressant drugs (amitriptyline, doxepine, mianserine, mirtazapine, trimipramine), sedative antihistaminic H1, central antihypertensive, baclofene, thalidomide (majoration of the central depress). This may affect the ability to drive vehicles or use of machines.

11. PRESENTATION OF THE DRUG:
ACUPAN is a clear, colorless solution. The solution is marketed in a 2 ml-glass ampoule containing 20.0 mg of nefopam hydrochloride, packed in boxes containing 5 or 20 ampoules.

12. STORAGE INSTRUCTIONS:
ACUPAN should be stored at a temperature below 30 °C.
KEEP OUT OF REACH OF CHILDREN.

13. ADDRESS OF MANUFACTURER:
DELPHARM TOURS
Rue Paul Langevin
37170 Chambray-Lès-Tours - France

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