SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ACUPAN® 20 mg / 2 ml, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Nefopam (hydrochloride) .....20.00 mg
For one ampoule of 2 mL.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection in ampoule.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

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

4.2. Posology and method of administration

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

Posology

- 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.

4.3. Contraindications

- Hypersensitivity to the active ingredient or to any of the excipients listed in section 6.1.
- Children below 15 years of age 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.

4.4. Special warnings and precautions for use

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

- 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 (see sections 4.5 and 4.8).
- Due to its anticholinergic effects, the treatment with Acupan is not advisable for elderly.

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

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

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.

4.6. Fertility, pregnancy and lactation

In absence of data in animal or data from use in human, the risk is unknown. Consequently as a precautionary measure, do not prescribe Acupan during pregnancy nor during breastfeeding.

4.7. Effects on ability to drive and use machines

There is a possible risk of somnolence, the ability to drive and use machine can be affected.

4.8. Undesirable effects

The side effects which have been reported are classified after by system-organ class and by frequency defined as: very common (≥1/10), common (≥ 1/100, < 1/10), uncommon (≥ 1/1,000, < 1/100), rare (≥ 1/10,000, < 1/1,000) and very rare (< 1/10,000), not known (cannot be estimated from the available data).

System-Organ	Very common	Common	Rare	Not known
Psychiatric disorder			excitability*, irritability*, hallucination, drug abuse, drug addiction	confusional state
Nervous system disorders	somnolence	vertigo*	convulsion*	coma
Cardiac disorders		tachycardia*, palpitation*		
Gastro-intestinal disorders	nausea with or without vomiting	dry mouth*		
Renal and urinary disorders		urinary retention		
General disorders and administration site conditions	hyperhydrose *		malaise	
Immune system disorders			hypersensitivity reaction (urticaria, de Quincke's œdema, anaphylactic shock)	

**Other atropinic effects could appear even if never reported.*

4.9. Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamics properties

Pharmacotherapeutic group: N, Nervous system, ATC code: N02BG06

- 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 an anticholinergic activity.
- It has been observed a moderate and transitory increase of the cardiac frequency and of the blood pressure.

5.2. Pharmacokinetic properties

After administration of a 20 mg dose by IM route, the serum peak (Tmax) is between 0.5 and 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: desmethylnefopam, 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 are present in the urines. Less than 5 % of the dose are eliminated unchanged: the metabolites identified in the urines represent 6, 3 and 36 % respectively of the dose administered by IV route.

5.3. Preclinical safety data

No data

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Disodium phosphate and sodium phosphate, water for injection.

6.2. Incompatibilities

It is recommended to avoid mixing Acupan and other injectable drugs in the same syringe (See section 4.2)

6.3. Shelf life

3 years.
After opening, reconstitution/dilution: the product must be immediately used.

6.4. Special precautions for storage

Store below 30°C.

6.5. Nature and contents of container (and special equipment for use administration or implementation)

2 mL-Glass ampoule, box of 5 or 20.

6.6. Special precautions for disposal (and other handling)

None.

APPLICANT/MANUFACTURER

7. APPLICANT/MANUFACTURER

BIOCODEX
7 avenue Gallieni
94250 GENTILLY
France

8. MARKETING AUTHORISATION NUMBER

H2011/19699/186

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26/05/2011

10. DATE OF REVISION OF THE TEXT

July 2017

CONDITIONS OF PRESCRIPTION AND DISPENSING

Prescription Only Medicine