SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

NEFOPAM FRILAB 20 mg/2 mL, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Nefopam hydrochloride..... 20 mg
For one 2 mL ampoule.
Excipient with known effect: sodium.
This medicinal product contains 6.79 mg of sodium per ampoule.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear and colourless solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

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

4.2. Posology and method of administration

Posology
As with all analgesic medicinal products, the posology must be adjusted according to the intensity of the pain and the clinical response of each patient.

- **IM route:** NEFOPAM FRILAB must be administered by deep IM injection. The usual recommended dose is 20 mg per injection. If necessary, it may be repeated every 6 hours, without exceeding a total dose of 120 mg/24 hours.
- **IV route:** NEFOPAM FRILAB must be administered by slow IV infusion over more than 15 minutes, with the patient in a recumbent position, in order to avoid the occurrence of adverse effects (nausea, dizziness, sweating). The usual recommended single dose is 20 mg per injection, repeated every 4 hours, if necessary, without exceeding a total dose of 120 mg/24 hours.

Method of administration
NEFOPAM FRILAB can be administered in standard solutions for infusion (isotonic sodium chloride or glucose solution). It is recommended to avoid mixing NEFOPAM FRILAB and other injectable products in the same syringe.

4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Children under 15 years of age, due to the absence of clinical data.
- Convulsions or a history of convulsive disorders.
- Risk of urinary retention

4.4. Special warnings and precautions for use

Special warnings

Drug dependence

The use of nefopam can lead to drug dependence, which may result in abuse, particularly in patients with a history of psychoactive substance use and/or mental health disorders. In these patients, nefopam must be prescribed with caution and signs of dependence must be monitored.

NEFOPAM FRILAB is neither an opioid nor an opioid antagonist. Consequently, discontinuing an opioid in a physically dependent patient treated with NEFOPAM FRILAB risks causing a withdrawal syndrome.

The benefit/risk ratio of NEFOPAM FRILAB treatment must be regularly reassessed.

NEFOPAM FRILAB is not indicated for the treatment of chronic painful conditions.

Precautions for use

Particular caution should be exercised in case of:

- hepatic impairment;
- renal impairment, due to the risk of accumulation and therefore the increased risk of adverse effects;
- all patients with cardiovascular disease, due to the tachycardic effect of the product (see sections 4.5 and 4.8);
- due to these anticholinergic effects, treatment with NEFOPAM FRILAB is not recommended in elderly subjects.

This medicinal product contains less than 1 mmol (23 mg) of sodium per 2 mL ampoule, that is to say essentially 'sodium-free'.

This medicinal product contains 40.74 mg of sodium per maximum dose of 6 ampoules, which is equivalent to 2% of the WHO maximum recommended daily dietary intake of 2 g of sodium for an adult.

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

Account should be taken of the fact that many medicinal products or substances can add up their central nervous system depressant effects and contribute to decreasing alertness. These include opioid derivatives (analgesics, antitussives and replacement therapies), neuroleptics, barbiturates, benzodiazepines, anxiolytics other than benzodiazepines (e.g. meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserin, mirtazapine, trimipramine), sedative H1-antihistamines, central antihypertensives, baclofen and thalidomide.

Concomitant use not recommended

- **Alcohol consumption:**
  Enhancement of the sedative effect of these substances by alcohol.
  Impaired alertness can make driving vehicles and using machines dangerous.
  The intake of alcoholic beverages and medicinal products containing alcohol should be avoided.

Concomitant use to be taken into account

- **Other sedative medicinal products:**
  Opioid derivatives (analgesics, antitussives and replacement therapies), neuroleptics, barbiturates, benzodiazepines, anxiolytics other than benzodiazepines (e.g. meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserin, mirtazapine, trimipramine), sedative H1-antihistamines, central antihypertensives, baclofen and thalidomide.
  Increased central depression. Impaired alertness can make driving vehicles and using machines dangerous.

4.6. Fertility, pregnancy and lactation
In the absence of animal studies and human clinical data, the risk is unknown; therefore, as a precautionary measure, do not prescribe during pregnancy or lactation.

4.7. Effects on ability to drive and use machines
Due to a potential risk of somnolence, alertness may be impaired and make driving vehicles and using machines dangerous.

4.8. Undesirable effects
The adverse reactions that have been reported are listed below by system organ class and by frequency defined as follows: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000) and not known (cannot be estimated from the available data).

System Organ Class	Very common	Common	Rare	Not known
Psychiatric disorders			**Excitability*, irritability*, hallucination, abuse, drug dependence**	**Confusional state**
Nervous system disorders	**Somnolence**	**Dizziness***	**Convulsion***	**Coma**
Cardiac disorders		**Tachycardia*, palpitations***		
Gastrointestinal disorders	**Nausea with or without vomiting**	**Dry mouth***		
Renal and urinary disorders		**Urinary retention**		
General disorders and administration site conditions	**Hyperhidrosis***		**Malaise**	**Injection site pain**
Immune system disorders			**Hypersensitivity reaction (urticaria, angioedema, anaphylactic shock)**	

***Although never reported, atropine-like effects other than those described may potentially occur**

Drug dependence
The use of NEFOPAM FRILAB 20 mg/2 mL, solution for injection can lead to drug dependence. The risk of dependence may vary depending on the patient's individual risk factors (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system: Agence nationale de sécurité du médicament et des produits de santé (ANSM) and network of Regional Pharmacovigilance Centres - Website: https://signalement.social-sante.gouv.fr/.

4.9. Overdose
These are anticholinergic-type manifestations: tachycardia, coma, convulsions, and hallucinations (see section 4.4).
Symptomatic treatment with cardiac and respiratory monitoring, in a hospital setting.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties
Pharmacotherapeutic group: OTHER ANALGESICS AND ANTIPYRETICS, N: Central Nervous System, ATC code: N02BG06

- A non-opioid central analgesic, nefopam has a chemical structure unrelated to that of currently known analgesics.
- *In vitro*, on rat synaptosomes, an inhibition of catecholamine and serotonin reuptake is suggested.
- *In vivo*, in animals, nefopam has shown anti-nociceptive properties. An antihyperalgesic activity has also been demonstrated by a mechanism that is not fully elucidated.
- Nefopam has shown an effect on post-operative shivering in clinical studies.
- Nefopam has no anti-inflammatory or antipyretic action. It does not cause respiratory depression and does not slow down intestinal transit.
- Nefopam possesses anticholinergic activity.
- From a haemodynamic standpoint, a moderate and transient increase in heart rate and blood pressure has been observed.

5.2. Pharmacokinetic properties

Absorption
Following administration of a 20 mg dose by the IM route, the peak plasma concentration (Tmax) is reached between 0.5 and 1 hour and maximum concentrations (Cmax) average 25 ng/mL. The mean plasma half-life is 5 hours.
When the same dose is administered by the IV route, the mean plasma half-life is 4 hours.

Distribution
Plasma protein binding is 71-76%.

Biotransformation
Biotransformation is extensive and 3 major metabolites have been identified: desmethyl-nefopam, nefopam N-oxide, and nefopam N-glucuronide. The first two unconjugated metabolites have not shown analgesic activity in animals.

Elimination
Elimination is mainly urinary: 87% of the administered dose is recovered in the urine.
Less than 5% of the dose is excreted unchanged; the metabolites identified in the urine represent 6%, 3%, and 36% of the IV administered dose, respectively.

5.3. Preclinical safety data
Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Sodium dihydrogen phosphate dihydrate, disodium phosphate dodecahydrate, water for injections.

6.2. Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section 4.2.

6.3. Shelf life
3 years.
After first opening/dilution: Do not refrigerate.
In-use physico-chemical stability has been demonstrated for 24 hours at 25°C.
From a microbiological point of view, unless the method of opening and dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4. Special precautions for storage
This medicinal product does not require any special storage conditions.

6.5. Nature and contents of container
2 mL ampoule (type I glass).
Box of 5, 10, 20, 50 or 100.
Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER
LABORATOIRES FRILAB
104 BOULEVARD AUGUSTE BLANQUI
75013 PARIS

8. MARKETING AUTHORISATION NUMBER(S)
- 34009 303 317 6 7: 2 mL in ampoule. Box of 5.
- 34009 303 317 7 4: 2 mL in ampoule. Box of 10.
- 34009 303 317 8 1: 2 mL in ampoule. Box of 20.
- 34009 303 317 9 8: 2 mL in ampoule. Box of 50.
- 34009 303 318 0 4: 2 mL in ampoule. Box of 100.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
[To be completed later by the holder]

10. DATE OF REVISION OF THE TEXT
[To be completed later by the holder]

11. DOSIMETRY
Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS
Not applicable.

CONDITIONS FOR PRESCRIPTION AND SUPPLY
List I (Prescription only medicine).