SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG

PROPOFAN capsules

2. Qualitative and quantitative composition

Paracetamol .... 400.0 mg
Caffeine .... 62.5 mg
Phosphate hemihydrate codeine .... 20.0 mg

For a capsule.

excipients:
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule.

4. CLINICAL DATA

4.1. Therapeutic indications

Symptomatic treatment of conditions of moderate to intense pain and/or the ones that do not responding to the use peripheral antalgics alone

4.2. Dosage and administration

Administration mode
RESERVED FOR ADULTS.
Orally.
The capsules should be swallowed with a drink as such (eg water, milk, fruit juice).
Dosage
The recommended daily dose of paracetamol is approximately 60 mg / kg / day, divided into 4 or 6 taken, or about 15 mg / kg every 6 hours or 10 mg / kg every four hours.
1 capsule, repeat if necessary after 4 hours or possibly 2 capsules taken in case of severe pain.
Do not exceed 6 capsules per day.
maximum recommended doses : see section 4.4.
Frequency of administration

- Due to the presence of caffeine, avoid taking late in the day,
- Systematic takes can avoid oscillations of pain or fever,
- Takes should be spaced at least 4 hours.

Renal failure
In patients with severe renal impairment (creatinine clearance less than 10 mL / min), the dosing interval is at least 8 hours. The dose of paracetamol should not exceed 3 g per day.

4.3. Cons-indications

Children under 15 years.

Paracetamol related

- Hypersensitivity to paracetamol or other components.

- liver failure.

Codeine related

- Codeine is contra-indicated in respiratory failure regardless of the degree of respiratory failure due to the depressant effect of codeine on the respiratory centers.

- Hypersensitivity to codeine.

- During breastfeeding (see section 4.6).

4.4. Special warnings and precautions

Special warnings

Please note, this drug is not a treatment of migraine or headache.

This medicine contains paracetamol. To avoid the risk of overdose, check for paracetamol in the composition of other drugs. In adults over 50 kg, TOTAL RATE OF Paracetamol SHALL NOT EXCEED 4 GRAMS PER DAY (see section 4.9).
Prolonged high doses of codeine use can lead to dependence.
The neuropathic pain by deafferentation did not respond to acetaminophen-codeine.
The maximum recommended daily dose is 120 mg of codeine.
This medicine contains lactose. Its use is not recommended in patients with lactose intolerance.

Precautions

The excretion of paracetamol and its metabolites is done primarily in the urine. In patients with severe renal insufficiency, takes must be spaced at least 8 hours.
Hepatic old and insufficient Topic : The starting dose will be reduced by half compared to the recommended adult dose, and may possibly be increased according to tolerance and needs.
In case of intracranial pressure, codeine may increase the importance of this pressure.
This drug should not be taken late in the day because of the risk of insomnia related to the presence of caffeine.
This drug is not recommended with mixed agonist-antagonist opioids (buprenorphine, nalbuphine, pentazocine), consumption of alcoholic beverages or alcohol-containing drugs, naltrexone or enoxacin (see section 4.5).

4.5. Interactions with other drugs and other forms of interaction

Paracetamol related

Combinations requiring precautions for use

+ Oral anticoagulants
Risk of increasing the effect of oral anticoagulant and bleeding risk in case of paracetamol at the highest doses (4 g / d) for at least 4 days. Regular monitoring of INR. Possible dose adjustment of the oral anticoagulant during treatment with paracetamol and after his arrest.
Interactions with diagnostic tests
Paracetamol can distort the blood glucose by the method oxidase-peroxidase glucose in case of abnormally high concentrations.
Paracetamol can distort the determination of blood uric acid by the method of phosphotungstic acid.
Codeine related

combinations not recommended

+ Agonist-antagonist opioids (buprenorphine, nalbuphine, pentazocine)
Decreased analgesic effect by competitive blocking of receptors, with a risk of occurrence of withdrawal syndrome.
+ Alcohol
Increase of the sedative effect of opioid analgesics by alcohol
Impaired vigilance may make it dangerous to drive vehicles and use machines.
Avoid the intake of alcoholic beverages or medicines containing alcohol.
Naltrexone +
Risk of reduced analgesic effect. If necessary, increase the doses of the morphine derivative.

To be taken into account

+ Other analgesic opioid agonists (alfentanil, dextromoramide, dextropropoxyphene, dihydrocodeine, fentanyl, hydromorphone, morphine, oxycodone, pethidine, phenoperidine, remifentanil, sufentanil, tramadol), antitussive morphine-like (dextromethorphan, noscapine, pholcodine), antitussive morphine true (codeine , ethylmorphine), benzodiazepines, barbiturates, methadone
Increased risk of respiratory depression which can be fatal in overdose.
+ Other sedative drugs: morphine derivatives (analgesics, antitussives and substitution treatment), neuroleptics, barbiturates, benzodiazepines, anxiolytics other than benzodiazepines (meprobamate), hypnotics, sedatives, antidepressants (amitriptyline, doxepin, mianserin, mirtazapine, trimipramine), sedative H1 antihistamines , central antihypertensives, baclofen, and thalidomide.
Enhancement of the central depression. Impaired vigilance may make it dangerous to drive vehicles and use machines.
Caffeine related

combinations not recommended

+ Enoxacin
Increased plasma concentrations of caffeine can cause excitement and hallucinations by decreasing its hepatic metabolism.

To be taken into account

+ Stiripentol
Possible increase in plasma concentrations of caffeine, with a risk of overdose by inhibition of its hepatic metabolism.

4.6. Pregnancy and breast feeding

Pregnancy

The occasional use of the drug may be considered during pregnancy if necessary, whatever the term is, but its chronic use should be avoided.
When administered in late pregnancy, consider the properties of morphine of the drug (theoretical risk of respiratory depression in the neonate after high doses before delivery, risk of withdrawal syndrome in chronic administration late pregnancy).
Data regarding paracetamol
Clinical, epidemiological studies have not revealed any teratogenic or fetotoxic effect if using the usual doses of paracetamol.
Data of codeine
Clinically, although some case-control studies show an increased risk of developing heart defects, most epidemiological studies deviate malformation risk.
Studies in animals have shown teratogenic effects.
Data on caffeine

Epidemiological studies show no increased risk of malformation due to caffeine. At the end of pregnancy high doses, caffeine can cause fetal or neonatal cardiac arrhythmia.
Accordingly, the use of caffeine should be considered during pregnancy if necessary.

Breastfeeding

Paracetamol, codeine and caffeine pass into breast milk.
Some cases of hypotonia and respiratory breaks were described in infants after the mother ingested supra-therapeutic doses of codeine.
Consequently, apart from a point taken, the drug is contra-indicated during lactation (see section 4.3).

4.7. Effects on ability to drive and use machines

The attention of users of machinery and vehicle drivers is drawn to the risk of drowsiness associated with the use of this drug.

4.8. Side effects

Related to paracetamol

- Rare cases of hypersensitivity reactions such as anaphylaxis, angioedema, rash, hives, skin rash have been reported. In case of occurrence, the drug should be definitively discontinued.

- Very exceptional cases of thrombocytopenia, leukopenia and neutropenia were reported.

Related to codeine
At therapeutic doses, Adverse effects of codeine are comparable to those of other opiates, but they are rarer and more moderate.
Possibility of:

- sedation, euphoria, dysphoria,

- miosis, urinary retention,

- hypersensitivity reactions (itching, hives and rash)

- constipation, nausea, vomiting,

- drowsy, dizzy states,

- bronchospasm, respiratory depression (see section 4.3)

- acute abdominal pain syndrome of biliary or pancreatic type reminiscent of a spasm of the sphincter of Oddi, especially occurring in cholecystectomy patients.

At supratherapeutic doses: There is a risk of dependence and withdrawal syndrome on abrupt, which can be seen in the user and the newborn mother addicted to codeine.
Related to caffeine
Possible excitation, insomnia, palpitations.

4.9. Overdose

SYMPTOMS OF OVERDOSE IN Paracetamol
Intoxication is feared in the elderly and especially in young children (therapeutic overdose or frequent accidental poisoning) in whom it can be fatal.

SYMPTOMS
Nausea, vomiting, anorexia, pallor, abdominal pain usually occur within the first 24 hours.
Overdose, from 10 g paracetamol as a single dose in adults and 150 mg / kg body weight in a single dose in children, causes hepatic cytolysis likely to lead to a complete and irreversible necrosis, resulting in hepatocellular insufficiency, acidosis metabolic encephalopathy can lead to coma and death.
Simultaneously, an increase in hepatic transaminases were observed in lactic dehydrogenase, bilirubin and decreased prothrombin levels that may appear 12 to 48 hours after ingestion.
Emergency Driving

- immediate transfer to hospital.

- Take a tube of blood plasma to the initial dosage of paracetamol.

- Rapid evacuation of the product ingested, gastric lavage,

- Treatment of overdose conventionally comprises the administration as early as possible to the N-acetylcysteine : antidote intravenously or orally if possible before the tenth hour.

- Symptomatic treatment.

SYMPTOMS OF OVERDOSE IN CODEINE
Symptoms in adults
acute depression of the respiratory centers (cyanosis, bradypnea), drowsiness, rash, vomiting, itching, ataxia, pulmonary edema (rare).
Symptoms in children (toxic threshold: 2 mg / kg single dose)
Bradypnea, breathing breaks, miosis, convulsions, histamine release signs flush and facial edema, urticaria eruption, collapse, urine retention.
To behave
Stimulation-assisted ventilation before cardiopulmonary resuscitation in a specialized service.
Specific treatment by naloxone: establishment of a channel first with supervision during the time required for the disappearance of symptoms.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

ANTALGIC CENTRAL AND PERIPHERAL
(N: Central Nervous System)
This drug is a combination of 3 active ingredients:

- Paracetamol peripheral analgesic, antipyretic,

- Codeine phosphate hemi hydrated: central analgesic,

- Caffeine: central stimulant.

5.2. pharmacokinetic properties

Paracetamol, codeine and caffeine absorption and stackable kinetics that are not modified when they are associated.
PARACETAMOL
Absorption
The absorption of paracetamol by oral route is rapid and complete. Maximum plasma concentrations are reached 30 to 60 minutes after ingestion.
Distribution

Paracetamol is rapidly distributed in all tissues. Concentrations are comparable in blood, saliva and plasma. The plasma protein binding is low.
Metabolism
Paracetamol is metabolized primarily in the liver. The two major metabolic pathways are glucuronide conjugation and sulphate conjugation. The latter route is rapidly saturable at doses above the therapeutic doses. A minor pathway catalysed by the cytochrome P 450, is the formation of a reactive intermediate (N-acetyl benzoquinone imine) which, under normal conditions of use, is rapidly detoxified by reduced glutathione and excreted in the urine after conjugation with cysteine and mercapturic acid. However, when mass poisoning, the amount of this toxic metabolite is increased.
Elimination
Elimination is essentially urinary. 90% of the ingested dose is excreted via the kidneys within 24 hours, primarily as glucuronide (60 to 80%) and conjugated with sulphate (20-30%).
Less than 5% is excreted unchanged.
The half-life of plasma elimination is 4 to 5 hours.
Pathophysiological changes:
Renal impairment in patients with severe renal impairment (creatinine clearance less than 10 mL / min), removal of acetaminophen and its metabolites is delayed.
Elderly conjugation capacity is not changed.
CODEINE
It is fairly rapidly absorbed in the intestine: maximum plasma concentration is reached in 60 minutes. The plasma half-life is about 3 hours. Codeine is metabolised in the liver and excreted in urine in inactive form consisting essentially of glucuronide derivatives. It crosses the placenta. Its passage into milk is low in single dose, little known in repeated doses.
CAFFEINE
It is rapidly and completely absorbed; its maximum plasma concentrations are generally achieved within one hour after ingestion. It is mainly metabolized by the liver, its elimination is done largely through urine.

5.3. Preclinical safety data

Unspecified.

6. PHARMACEUTICAL DATA

6.1. List of excipients

Corn starch, anhydrous collodiale silica (Aerosil 200 Pharma), Magnesium stearate, talc.
Composition of the capsule shell Gelatin, titanium dioxide (E 171).

6.2. incompatibility
Not applicable.

6.3. The duration of the conversation

2 years.

6.4. Special precautions for storage

Store at a temperature below 30 ° C and away from moisture.

6.5. Nature and contents of container

15 capsules in blister packs (PVC / aluminum).

6.6. Special precautions for disposal and handling

No special storage conditions.

7. HOLDER OF MARKETING AUTHORIZATION

Laboratoires FRILAB SA
17, rue des Pierres du Niton
1207 Genève
Suisse

Manufacturer
Alifarm, POL.IND "ELS XOPS" N°. 9, Lliça de Vall, 08185 Barcelona, Spain

8. DOSIMETRY

Not applicable.

9. INSTRUCTIONSTHE PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.