Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Xeropam 30 mg Film Coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains, Nefopam Hydrochloride 30 mg.

Excipient with known effect
31.0 mg of lactose/film coated tablets.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film coated Tablets.

7 mm, round, biconvex, white colored film-coated tablets, debossed NP 30 on one side and plain on the other side., blistered in Alu-PVDC blister strip then packed in a carton.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Nefopam Hydrochloride is indicated in adults for the relief of moderate or severe pain such as: muscle pain, post- operative pain, orthopedic pain, pain caused by cancer and dental pain.

Treatment is symptomatic.

4.2 Posology and method of administration

Posology

Adults:

Dosage may range from 1 to 3 tablets three times daily depending on response. The recommended starting dosage is 2 tablets

Elderly:

Older patients may require reduced dosage due to slower metabolism.

It is strongly recommended that the starting dose does not exceed one tablet three times daily as older people appear more

susceptible to, in particular, the CNS side effects and some cases of hallucinations and confusion have been reported in this age group.

Paediatric population:

The safety and efficacy of Azuzote Film-coated Tablets in children under 12 years has not yet been established. No dosage recommendation can be given for patients under 12 years.

Renal insufficiency: In patients with end-stage renal disease, maximum serum concentrations may increase during treatment with nefopam. It is recommended to reduce the daily dosage not only in elderly patients, but also in patients in the terminal phase of renal insufficiency

Method of administration

Oral use.

4.3 Contraindications

Hypersensitivity to nefopam or to any of the excipients listed in section 6.1.

Nefopam Hydrochloride must not be administered to patients with a history of seizures and must not be administered to patients taking monoamine oxidase (MAO) inhibitors.
Nefopam Hydrochloride should not be administered to patients with hepatic or renal insufficiency.

Due to its anticholinergic properties, Nefopam Hydrochloride should be used with caution in patients with glaucoma, prostatic hypertrophy or urinary retention and, if necessary, discontinued.

4.4 Special warnings and precautions for use

Pediatric population:

Nefopam Hydrochloride is not recommended for children.

Nefopam Hydrochloride should be administered with caution to patients with anxiety symptoms, glaucoma, prostatic hypertrophy or urinary retention due to its moderate central adrenergic potentiating and anticholinergic activity.
Particular caution will be exercised in all patients with a history of cardiovascular pathology (symptomatic tachycardia, myocardial infarction, heart failure) due to the tachycardia effect of the product. In any case, before starting treatment with Nefopam Hydrochloride in a cardiac patient, it will be necessary to contact the cardiologist in order to assess the benefits and risks of treatment with Nefopam Hydrochloride.

Hepatic and/or renal insufficiency may interfere with the metabolism and excretion of nefopam.

In elderly patients it may be necessary to reduce the dose due to a slower

metabolism. It is recommended to limit the starting dose to 1 tablet three times a day as elderly patients are more sensitive to the undesirable effects on the central nervous system: some cases of hallucination and confusion have been reported in this patient group.

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interactions

The side effects of Nefopam Hydrochloride may be additive to those of other substances with anticholinergic or sympathomimetic activity.
It will be appreciated that many drugs or substances may add their central nervous system depressant effect to that of Nefopam Hydrochloride and thus accentuate the reduction in vigilance. These are morphine derivatives (analgesics, antitussives and substitution treatments), neuroleptics, barbiturates, benzodiazepines, anxiolytics other than benzodiazepines (e.g. meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserine, mirtazapine, trimipramine), sedative H1 antihistamines, central antihypertensives and baclofen.
Nefopam may interfere with certain tests for benzodiazepines and opioids. These tests can give false positive results in patients taking Nefopam Hydrochloride.
The intensity and incidence of the undesirable effects increases when nefopam is co- administered with codeine, pentazocine or dextropropoxyphene.

Nefopam is intensively metabolised. Since the enzyme responsible for the biotransformation is not known, the potential interactions with the CYP inhibitors/inducers cannot be anticipated. Caution is therefore advised whenever nefopam is co-administered with CYP inhibitors/inducers.
In dogs that had received abnormally high doses of paracetamol, the known hepatotoxicity of paracetamol was enhanced when extremely high doses of nefopam were administered. These studies have shown that repeated oral doses of 236 mg/kg/day of paracetamol together with 24 mg/kg/day nefopam cause a potentiation of the paracetamol hepatotoxicity. These doses are approximately six to eight times higher than average human doses. Lower doses equivalent to three to four times the human dose did not potentiate hepatotoxicity.

4.6 Fertility, pregnancy and lactation Pregnancy

Pregnancy

For Nefopam Hydrochloride no clinical data on exposed pregnancies are

available.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Still, it is better to avoid the use of Nefopam Hydrochloride during pregnancy unless no other safer analgesic is available.

Breast -feeding

Nefopam Hydrochloride is excreted in breast milk. The maximum amount taken by the baby is 0.05 mg/kg/day. Nefopam Hydrochloride should not be used while breastfeeding.

4.7 Effects on ability to drive and use machines

It may be unsafe for patients experiencing central nervous system side effects of Nefopam Hydrochloride to drive or use machines.

4.8 Undesirable effects

Nausea, nervousness, dry mouth and light-headedness, urinary retention, hypotension, syncope, palpitations, gastrointestinal disturbances (including abdominal pain and diarrhoea), dizziness, paraesthesia, convulsions, tremor, confusion, hallucination, angioedema, and allergic reactions may occur.

Less frequently, anaphylactic reactions, coma, vomiting, blurred vision, drowsiness, sweating, insomnia, headache and tachycardia have been reported.

Reporting of suspected adverse reactions

*Although never reported, anticholinergic effects other than those described may theoretically be observed.

Reporting of adverse effects:

Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org.

4.9 Overdose

Symptoms:

These are of anticholinergic origin: tachycardia, **coma,** convulsions and hallucinations.

Adults:

The first signs of toxicity, i.e., tachycardia, occur after taking 30 Nefopam Hydrochloride tablets (15 mg/kg). Hospitalization is required at this dose.

Children:

There are no data on the toxic dose in children, but in case of intoxication hospitalization is recommended from the intake of 10 mg/kg.

Treatment:

General supportive measures will be taken.

If ingestion has taken place less than 1 hour before, the swallowed drug can be removed by gastric lavage or induced emesis with Ipecacuanha syrup.
The oral administration of activated charcoal may be useful to prevent further absorption.

Convulsions and hallucinations should be treated, e.g. with diazepam administered intravenously or rectally. Beta-blockers can help fight cardiovascular complications.

5PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: drugs with analgesic properties only.ATC code: N02BG06

Chemically, Nefopam Hydrochloride is derived from diphenhydramine: nefopam is formed by cyclization of the orphenadrine. Therefore, Nefopam Hydrochloride, like its two precursors, has anti-cholinergic properties. Mechanism of action
We are very poorly informed about its mechanism of action. The pharmacological properties studied do not allow a precise description of its action.
Pharmacodynamic effects:

Nefopam Hydrochloride is an analgesic. Nefopam Hydrochloride stimulates the descending serotoninergic pain modulating pathways.

It inhibits the reabsorption of the synaptosomal noradrenaline, dopamine, 5-hydroxytryptophan and GABA. It stimulates the release of dopamine and GABA in the brain.

It is completely different from the other centrally acting analgesics such as morphine, codeine, pentazocine and propoxyphene. It does not fixate on the receptors of the narcotic analgesics and is not inhibited by naloxone. Unlike narcotic drugs, Nefopam Hydrochloride does not cause respiratory depression. Some cases of habituation have been reported. Nefopam Hydrochloride has no antipyretic or anti-inflammatory properties. It does not inhibit prostaglandin synthesis in vitro.

5.2 Pharmacokinetic properties

Absorption:

After oral administration of 90 mg, peak plasma concentrations of 73 to 154 ng/ml of nefopam were reached after 1-3 hours. Peak plasma levels of 29 to 67 ng/ml were reached approximately2 hours after a 60 mg oral dose. About 73% is bound to plasma proteins.

Biotransformation:

The biotransformation of nefopam is very important: only a small amount of unchanged drug appears in the urine. Seven metabolites could be detected including desmethyl nefopam, its glucuronide and nefopam-N- oxide. However, the enzyme responsible for this biotransformation is not known.

Elimination:

The metabolites and the small unchanged fraction are rapidly eliminated renally.

Most of the administered dose appears in the urine. Less than 5% of the administered dose is excreted unchanged in the urine after an intravenous administration of 20 mg of radio labelled nefopam to 4 volunteers. Within 5 days, 87% of the administered radioactivity appears in the urine and 8% in the faeces. The elimination half-life of nefopam in healthy volunteers is approximately 4 hours (range 3-8 hours).

5.3 Preclinical safety data

Not available.

6PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Lactose Anhydrous (SperTab24AN) Cellulose, Microcrystalline (PH-102) Crospovidone (Type A), Silica Colloidal, Anhydrous Magnesium Stearate.

Film-coat

Opadry OY-S-7335 White

6.2 Incompatibilities

None known

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store in a cool (not above 30°C) & dry place, keep away from light and children.

6.5 Nature and contents of container

Alu – PVDC blister pack containing 14 tablets. 2 blisters packed in a carton.

6.6 Special precautions for disposal and other handling

None

7. MARKETING AUTHORISATION HOLDER

Renata Limited
Rajendrapur Site, Rajendrapur general facility, Noyapara, Bhawal Mirzapur, Rajendrapur, Gazipur-1700
Bangladesh.

8. MARKETING AUTHORISATION NUMBER

H2024/CTD10644/24342

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

23rd February 2024

10. DATE OF REVISION OF THE TEXT

November 2024