1. NAME OF THE MEDICINE

Orphesic Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Orphenadrine citrate 35 mg and paracetamol 450mg tablets.

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Tablet, uncoated

A White, round, tablets Plain on one side of the tablet and a dividing line on the other side of the tablet.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Tension headache, occipital headaches associated with spasm of skeletal muscles in the region of the head and neck. Acute and traumatic conditions of the limbs and trunk: sprains, strains, whiplash injuries, acute torticollis, prolapsed intervertebral
disc.

4.2 DOSE AND METHOD OF ADMINISTRATION

2 tablets three times daily.

4.3 CONTRAINDICATIONS

- Glaucoma
- Prostatic hypertrophy or obstruction at the bladder neck,
- Myasthenia gravis
- Oesophageal spasm and pyloric or duodenal obstruction.
- Hypersensitivity to paracetamol or orphenadrine citrate.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Identified precautions

Orphenadrine citrate should be used with caution in patients with tachycardia, cardiac decompensation, coronary insufficiency or cardiac arrhythmias.

Paracetamol should be used with caution in patients with hepatic or renal dysfunction.

Concomitant treatment with other medicines that contains Orphenadrine or Paracetamol is not recommended.

Safety of continuous long-term therapy with orphenadrine has not been established. Therefore, if orphenadrine is prescribed for prolonged use, periodic monitoring of blood, urine and liver function is recommended.

Use in the elderly

The elderly should be advised to take a reduced dosage as they may be more

susceptible to anti-cholinergic side effects at regular doses.

Paediatric use

Orphesic Tablet is not recommended for children under 12 years of age.

Effects on laboratory tests

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Interactions have been reported between orphenadrine and phenothiazines and other drugs with anti-muscarinic properties. Concomitant use with alcohol or other CNS depressants should be avoided.

Anticoagulant dosage may require reduction if Paracetamol medication is prolonged. Paracetamol absorption is increased by medicines that increase gastric emptying, e.g. metoclopramide, and decreased by medicines that decrease gastric emptying, e.g. propantheline, antidepressants with anticholinergic properties and narcotic analgesics. Paracetamol may increase chloramphenicol concentrations. The likelihood of Paracetamol toxicity may be increased by the concomitant use of enzyme inducing agents such as alcohol or anticonvulsant medicines.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available

Use in pregnancy – Pregnancy Category B2

Orphesic Tablet is not recommended for use during pregnancy.

Use in lactation.

Orphesic Tablet should not be taken during lactation as Orphenadrine and

Paracetamol are excreted into breast milk.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Orphenadrine may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; ambulatory patients should therefore be cautioned accordingly.

4.8. ADVERSE EFFECTS (UNDESIRABLES EFFECTS)

Adverse effects are mainly due to the anti-cholinergic action of Orphenadrine and are usually associated with higher doses.

Orphenadrine citrate

More common reactions

The known adverse effects include; dryness of the mouth, tachycardia, palpitation, urinary hesitancy or retention, blurred vision, dilation of the pupils, increased ocular tension, weakness, nausea, headache, dizziness, constipation and drowsiness.

These effects can usually be eliminated by reducing the dose.

Less common reactions

Sedation, skin rashes and other allergic reactions are very uncommon adverse effects. Infrequently an elderly patient may experience some degree of mental confusion. Very rare cases of aplastic anaemia associated with the use of orphenadrine have been reported.

Paracetamol

Reports of adverse reactions are rare. Although the following reactions have been reported, a causal relationship to the administration of paracetamol has been neither confirmed nor refuted; dyspepsia, nausea, allergic and haematological

reactions.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.Nafdac.gov.ng.

4.9 OVERDOSE

Paracetamol: Symptoms: Paleness, nausea, vomiting, anorexia, abdominal pain, metabolic acidosis and glucose metabolism disturbances. Liver damage may surface 12-48 hr after overdose. In severe cases, encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, acute renal failure and death. Management: Immediate medical treatment even if there are no symptoms. If presented within 1 hr of poisoning, admin activated charcoal. If needed, admin IV N-acetylcysteine or oral methionine. Orphenadrine: Symptoms: Vomiting, gastric irritation, dilated pupils, pruritus, urinary retention, tachycardia, hyperpyrexia, euphoria, hallucinations, agitation, paranoid reactions, tremor, excitement, confusion, delirium, circulatory and respiratory failure, coma and convulsions. Management:

Treatment is symptomatic and supportive.

Symptoms and Signs

Orphenadrine overdosage: Known symptoms of overdose with Orphenadrine include tachycardia, excitement, confusion and delirium leading to coma.

Convulsions, dilated pupils and urinary retention may occur.

Paracetamol overdosage: Toxic symptoms following an overdose with Paracetamol include vomiting, abdominal pain, hypotension, sweating, central stimulation with exhilaration and convulsions in children, drowsiness, respiratory depression, cyanosis and coma.

In adults, hepatotoxicity may occur after ingestion of a single dose of Paracetamol 10 to 15g; a dose of 25g or more is potentially fatal.

Symptoms during the first two days of Acute poisoning by Paracetamol do not reflect the potential seriousness of the intoxication. Major manifestation of the liver failure such as jaundice, hypoglycaemia, and metabolic acidosis may take at least three days to develop.

Treatment

Prompt treatment is essential even when there are no obvious symptoms.

In cases of overdosage, methods of reducing absorption of ingested medicine are important. Prompt administration of activated charcoal 50 g in 150 mL of water and 150 mL sorbitol 50% solution by mouth may reduce absorption. It is recommended that intravenous fluids such as normal saline be given concurrently. Gastric lavage is indicated if the patient is unwilling or unable to drink an activated charcoal/sorbitol mixture.

If the history suggests that Paracetamol 150mg/kg body weight or 15 g total or more has been ingested, administer the following antidote:

Intravenous acetylcysteine 20%: Administer acetylcysteine immediately without waiting for positive urine test or plasma level results if 8 hours or less since overdose ingestion. Initial dose 150 mg/kg over 15 minutes, followed by continuous infusion of 50 mg/kg in glucose 5% 500 mL over four hours and 100 mg/kg in glucose 5% 1 L over 16 hours. If more than eight hours have elapsed since the overdose was taken, the antidote may be less effective.

Convulsions and delirium respond to relatively large doses of diazepam, preferably by mouth. Adequate hydration of the patient is important.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Orphenadrine is a skeletal muscle relaxant. Paracetamol is an analgesic and antipyretic.

Description: Paracetamol, a para-aminophenol derivative, is a peripherally acting analgesic with antipyretic and weak anti-inflammatory activity. Orphenadrine, an analog of diphenhydramine, is a skeletal muscle relaxant and is postulated to act on cerebral motor center or on the medulla through an atropine-like central action. It has anticholinergic, local anaesthetic effects and some antihistaminic effects. Orphenadrine is used either as the hydrochloride or the citrate and doses are expressed in terms of the relevant salt.

5.2 PHARMACOKINETIC PROPERTIES

Absorption:

Paracetamol: Absorbed readily from GI tract; time to peak plasma concentrations: 10-60 minutes. Orphenadrine: Absorbed readily from GI tract and after IM inj.

Distribution:

Paracetamol: Distributed into most body tissues including breast milk, crosses the placenta; plasma-protein binding: negligible (but dose dependent). Orphenadrine: May cross placenta.

Metabolism:

Paracetamol: Undergoes hepatic metabolism; a minor metabolite, produced in minute amounts by cytochrome P450 isoenzymes in the liver and kidney, is usually removed by conjugation with glutathione, but may accumulate and cause tissue damage in paracetamol overdosage. Orphenadrine: Metabolised to ≥8 metabolites.

Excretion:

Paracetamol: Excreted in the urine mainly as the glucuronide and sulfate conjugates with <5% excreted unchanged; elimination half-life: 1-3 hr. Orphenadrine: Excreted mainly in urine and unchanged drug (small amounts); half-life: 14 hr**5.3**

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Magnesium stearate, Lactose, Maize Starch, Ethyl Cellulose, HPMC, Isopropyl Alcohol, Methyl Paraben, Propyl Paraben, PVPK30, Talcum and colloidal anhydrous silica

6.2 **INCOMPATIBILITIES**

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 **SHELF LIFE**

3 years

6.4 **SPECIAL PRECAUTIONS FOR STORAGE** Store below 30°C.

6.5 **NATURE AND CONTENTS OF CONTAINER**

2 Alu-PVC blisters of 14 Tablets each, packed in a primary carton along with the Pack Insert.

6.6 **SPECIAL PRECAUTIONS FOR DISPOSAL**

No special requirements.

6.7 **PHYSICOCHEMICAL PROPERTIES**

Orphenadrine citrate is white or almost white, crystalline powder. It is sparingly soluble in water, and slightly soluble in alcohol. Paracetamol is a white or almost white, crystalline powder that is sparingly soluble in water and freely soluble in alcohol.

7. **Manufactured by:**

SAGAR VITACEUTICALS LTD.
Commercial District B Block, Plot 6,
New Makun City, Along Lagos/Ibadan
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