1.NAME OF THE MEDICINAL PRODUCT
Norpiflex Tablets 100mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Orphenadrine Citrate BP 100mg Tablets
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Norpiflex 100 mg: White, round-shaped tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
Conditions involving skeletal muscle spasm such as low back pain and torticollis and also those resulting from trauma such as whiplash injury.

4.2 Posology and method of administration

Posology
Adults
Two tablets per day; one in the morning and one in the evening.

Children
Safety and effectiveness in children have not been established. Orphenadrine is not recommended for children under 12 years.

Special Populations
Elderly
The elderly may be more susceptible to anticholinergic side effects and should be given a reduced dosage.

4.3 Contraindication
Contraindicated in patients with glaucoma, pyloric or duodenal obstruction, stenosing peptic ulcers, prostatic hypertrophy or obstruction of the bladder neck, cardio-spasm (megaesophagus) and myasthenia gravis.
Contraindicated in patients who have demonstrated a previous hypersensitivity to the drug.

4.4 Interaction with other medicinal products and other forms of interaction
Concomitant administration of Orphenadrine with phenothiazine, some antihistamines, antipsychotic tricyclic antidepressants, should be avoided. Avoid concomitant use of alcohol or other CNS depressants.

4.5 Pregnancy and Lactation

Pregnancy
Its use in the first three months of pregnancy is not recommended. Animal reproduction studies have not been conducted with orphenadrine citrate. It is also not known whether orphenadrine citrate can cause fetal harm when administered to a pregnant woman or

can affect reproduction capacity. Orphenadrine citrate should be given to a pregnant woman only if clearly needed.

Breast-feeding
It should also be avoided in breastfeeding. Orphenadrine is excreted in breast milk and is not recommended for use while breastfeeding.

4.6 Effects on ability to drive and use machines
Some patients may experience transient episodes of light-headedness, dizziness or syncope. Orphenadrine citrate 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.

4.7 Undesirable effects
Adverse reactions of orphenadrine citrate are mainly due to the mild anti-cholinergic action of orphenadrine citrate and are usually associated with higher dosage. Dryness of the mouth is usually the first adverse effect to appear. When the daily dose is increased, possible adverse effects include tachycardia, palpitation, urinary hesitancy or retention, blurred vision, dilatation of pupils, increased ocular tension, weakness, nausea, vomiting, headache, dizziness, constipation, drowsiness, hypersensitivity reactions, pruritus, hallucinations, agitation, tremor, gastric irritation and rarely urticaria and other dermatoses. Infrequently, an elderly patient may experience some degree of mental confusion. These adverse reactions can usually be eliminated by reduction in dosage. Very rare cases of aplastic anemia associated with the use of orphenadrine tablets have been reported. No causal relationship has been established.

Adverse reactions are listed below according to system organ class and frequency. Frequencies are defined according to the following convention:

Very common (2/10), Common (21/100 to <1/10), uncommon (21/1,000 to <1/100), Rare (210,000 to <1/1,000), very rare (=1/10,000), Not known (cannot be estimated from the available data).

Cardiac disorders
Frequency unknown: Tachycardia, palpitation.

Eye disorders
Frequency unknown: Blurred vision, dilation of pupils, increased ocular tension.

Nervous system disorders
Frequency unknown: Headache, dizziness, drowsiness, tremor, transient episodes of lightheadedness, syncope.

Psychiatric disorders
Frequency unknown: Hallucinations, agitation, mental confusion.

Immune system disorders
Frequency unknown: Hypersensitivity reactions.

Skin and subcutaneous tissue disorders
Frequency unknown: Pruritus, urticarial and other dermatoses

Renal and urinary disorders
Frequency unknown: urinary hesitancy or retention.

Gastrointestinal disorders
Frequency unknown: Nausea, vomiting, constipation, gastric irritation, dryness of mouth.

4.8 Overdose
Orphenadrine citrate is toxic when overdosed and typically induces anticholinergic effects. In a review of orphenadrine toxicity, the minimum lethal dose was found to be 2 to 3 grams for adults; however, the range of toxicity is variable and unpredictable. Treatment for orphenadrine citrate overdose is evacuation of stomach contents (when necessary), charcoal at repeated doses, intensive monitoring and appropriate supportive treatment of any emergent anticholinergic effects. Supportive therapy should be given as required.

5.0 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Ethers, chemically close to antihistamines. ATC code: MO3BC01.

Orphenadrine is an analgesic and a muscle relaxant. Orphenadrine citrate is a centrally acting compound which in animals selectively blocks faciliatory functions of the reticular formation. Orphenadrine does not produce myoneural block, nor does it affect crossed extensor reflexes. Orphenadrine prevents nicotine induced convulsions but not those produced by strychnine. The mode of action of orphenadrine has not been clearly identified but may be
related to its analgesic properties. Orphenadrine citrate also possesses anticholinergic activity.

Clinical efficacy
There have been numerous clinical trials of Orphenadrine. Unfortunately, study design deficiencies have made interpretation of results and comparisons between studies difficult. These deficiencies include ill-defined patient selection criteria, noncomparable musculoskeletal disorders studied, variability of disease severity and duration, and subjective assessment of the patient's response to therapy.5,18-24 Despite these difficulties, certain conclusions are possible. In almost all studies, Orphenadrine were more effective than placebo in the treatment of acute painful musculoskeletal disorders and muscle spasm. Efficacy was less consistent in the treatment of chronic disorders. When used alone, Orphenadrine were not consistently superior to simple analgesics (for example, aspirin, acetaminophen, and nonsteroidal antiinflammatory medications) in pain relief. However, when Orphenadrine were used in combination with an analgesic, pain relief was superior to that of either drug used alone. Comparative studies of SMR efficacy have failed to document superiority of one drug over another.

Paediatric population
Safety and effectiveness in pediatric patients have not been established.

5.2 Pharmacokinetic properties
The Orphenadrine are generally well absorbed after oral ingestion. They have a rapid onset of action, generally within 1 hour. Some Orphenadrine may be administered parenterally, and this route yields a more rapid onset of action. The drugs undergo biotransformation in the liver and are excreted primarily in the urine as metabolites. There is significant variability between individual drugs, plasma half-life, and duration of action.

Absorption.
Orphenadrine is readily absorbed from the gastrointestinal tract.

Metabolism
Almost completely metabolised to at least eight metabolites.

Excretion.
Orphenadrine and its metabolites are excreted from the body in the urine, with a half-life of 14 hours.

5.3 Preclinical safety data
No additional data available.

6.0 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
- Lactose
- Ethyl Cellulose
- Aerosil 200
- Magnesium Stearate

6.2 Shelf life: 3 years

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

6.4 Nature and contents of container <and special equipment for use, administration or implantation>

Blister packs of 2 X 10 Tables and Blister packs of 10 X 10 Tables

6.5 Special precautions for disposal <and other handling>

Any unused product or waste material should be disposed of in accordance with local requirements.

7.0 APPLICANT:
C' D – DEMERIS PHARMACEUTICALS LTD.,
No. 17 Ikosiro Adoregun, Ikeja,
Lagos**.**

8.0 MANUFACTURER:
SAGA LIFE SCIENCES LTD.,
Survey No. 198/2 & 198/3, Chachrawadi Vasna TA:
Sanand Dist. Ahmedabad 382210, India