1. Name of the drug product:

LORATADINE TABLETS BP 10 MG

2. Qualitative and quantitative composition :

Each Uncoated Tablet Contains:
Loratadine BP.....10mg
Approved Colour Used.
Excipients.....q.s.

Sr. No.	Ingredients	Specifi-cation	Label Claim / Tablet (In mg)	Over-ages added (In %)	Qty. / Tablet (In mg)	Reason for Inclusion
a)	**Dry Mixing**					
1.	Lactose Monohydrate	BP	NA	NA	44.00	Diluent
2.	Microcrystalline Cellulose	BP	NA	NA	40.00	Diluent
3.	Povidone K-30	BP	NA	NA	1.70	Binder
4.	Colloidal Anhydrous Silica	BP	NA	NA	0.30	Glidant
b)	**Binder Preparation**					
5.	Maize Starch	BP	NA	NA	5.00	Binder
6.	Purified Water	BP	NA	NA	----	Vehicle
c)	**Lubrication**					
7.	Loratadine (micronized)	BP	10.00	NA	10.00	Medicament
8.	Magnesium Stearate	BP	NA	NA	1.00	Lubricant
9.	Croscarmellose Sodium	BP	NA	NA	2.40	Disintegrant
10.	Colloidal Anhydrous Silica	BP	NA	NA	0.50	Glidant
11.	Titanium Dioxide	BP	NA	NA	0.10	Colour
	Average Weight of Uncoated Tablet (In mg)				**105.00**	

3. Pharmaceutical form: Uncoated Tablet
Description: White, capsule shaped, biconvex uncoated tablet, breakline on one side and plain on other side.

4. Clinical Particulars
4.1 Therapeutic indications:
LORATADINE TABLETS BP 10MG is indicated for the symptomatic treatment of allergic rhinitis and chronic idiopathic urticaria.

4.2 Posology and method of administration
Route: Oral
Method of Administration
Adults and children over 12 years of age: l0 mg once daily (one tablet once daily). The tablet may be taken without regard to mealtime.
Children 2 to 12 years of age are dosed by weight:
Body weight more than 30kg: l0 mg once daily (one tablet once daily).
Body weight 30 kg or less: The l0 mg strength tablet is not appropriate in children with a body weight less than 30kg.
Efficacy and safety of **LORATADINE TABLETS BP 10 MG** in children under 2 years of age has not been established. The use is therefore not recommended in these patients. Patients with severe liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine. An

initial dose of lOmg every other day is recommended for adults and children weighing more than 30kg and for children weighing 30kg or less, 5mg every other day is recommended. No dosage adjustments are required in older people or in patients with renal insufficiency.

4.3 Contraindications
LORATADINE TABLETS BP 10 MG is contraindicated in patients who are hypersensitive to the active substance or to any of the excipients in these formulations.

4.4 Special warnings and precautions for use
LORATADINE TABLETS BP 10 MG should be administered with caution in patients with severe liver impairment.
This medicinal product contains lactose; thus patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
The administration of **LORATADINE TABLETS BP 10 MG** should be discontinued at least 48 hours before skin tests since antihistamines may prevent or reduce otherwise positive reactions to dermal reactivity index.

4.5 Interaction with other medicinal products and other forms of interaction
Potential interaction may occur with all known inhibitors of CYP3A4 or CYP2D6 resulting in elevated levels of loratadine which may cause an increase in adverse events. When administered concomitantly with alcohol **LORATADINE TABLETS BP 10 MG** has no potentiating effects as measured by psychomotor performance studies

4.6 Pregnancy and Lactation
Pregnancy
A large amount of data on pregnant women (more than 1000 exposed outcomes) indicate no malformative nor feto/ neonatal toxicity of loratadine. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of **LORATADINE TABLETS BP 10 MG** during pregnancy.

Breast-feeding
Loratadine is excreted in breast milk, therefore the use of loratadine is not recommended in breastfeeding women.

4.7 Effects on ability to drive and use machines
In clinical trials that assessed driving ability, no impairment occurred in patients receiving loratadine. However, patients should be informed that very rarely some people experience drowsiness, which may affect their ability to drive or use machines.

4.8 Undesirable effects
This can consist of
- skin rash or eruptions (including inside the mouth)
- itching
- swelling of the face, tongue, lips, hands, feet
- breathing difficulties

The most commonly reported side effects in adults and children over 12 years of age are:
- drowsiness
- headache
- increased appetite
- difficulty in sleeping

The most commonly reported side effects in children aged 2 to 12 years are:
- headache
- nervousness
- tiredness

The following very rare side effects (may affect up to 1 in 10,000 people) have also been seen during the marketing of loratadine:
- severe allergic reaction (including swelling)
- dizziness

- convulsion
- fast or irregular heartbeat
- nausea (feeling sick)
- dry mouth
- upset stomach
- liver problems
- hair loss
- rash
- tiredness

4.9 Overdose

Overdosage with loratadine increased the occurrence of anticholinergic symptoms. Somnolence, tachycardia, and headache have been reported with overdoses. In the event of overdose, general symptomatic and supportive measures are to be instituted and maintained for as long as necessary. Administration of activated charcoal as a slurry with water may be attempted. Gastric lavage may be considered. Loratadine is not removed by haemodialysis and it is not known if loratadine is removed by peritoneal dialysis. Medical monitoring of the patient is to be continued after emergency treatment.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antihistamines – H1 antagonist, ATC code: R06A X13.

Mechanism of action

Loratadine competes with free histamine and exhibits specific, selective peripheral HI antagonistic activity. This block the action of endogenous histamine, which subsequently leads to temporary relief of the negative symptoms (eg. nasal congestion, watery eyes) brought on by histamine. Loratadine has low affinity for cholinergic receptors and does not exhibit any appreciable alpha-adrenergic blocking activity in-vitro. Loratadine also appears to suppress the release of histamine and leukotrienes from animal mast cells, and the release of leukotrienes from human lung fragments, although the clinical importance of this is unknown.

Pharmacodynamic effects

Loratadine has no clinically significant sedative or anticholinergic properties in the majority of the population and when used at the recommended dosage.

During long-term treatment there were no clinically significant changes in vital signs, laboratory test values, physical examinations or electrocardiograms.

Loratadine has no significant H2-receptor activity. It does not inhibit norepinephrine uptake and has practically no influence on cardiovascular function or on intrinsic cardiac pacemaker activity. Human histamine skin wheal studies following a single 10 mg dose has shown that the antihistamine effects are seen within 1-3 hours reaching a peak at 8-12 hours and lasting in excess of 24 hours. There was no evidence of tolerance to this effect after 28 days of dosing with loratadine.

Clinical efficacy and safety

Over 10,000 subjects (12 years and older) have been treated with loratadine 10 mg tablets in controlled clinical trials.

Loratadine 10 mg tablets once daily was superior to placebo and similar to clemastine in improving the effects on nasal and non-nasal symptoms of AR. In these studies somnolence occurred less frequently with loratadine than with clemastine and about the same frequency as terfenadine and placebo. Among these subjects (12 years and older), 1000 subjects with CIU were enrolled in placebo controlled studies. A once daily 10 mg dose of loratadine was superior to placebo in the management of CIU as demonstrated by the reduction of associated itching, erythema and hives. In these studies the incidence of somnolence with loratadine was similar to placebo.

Paediatric population

Approximately 200 paediatric subjects (6 to 12 years of age) with seasonal allergic rhinitis received doses of loratadine syrup up to 10 mg once daily in controlled clinical trials. In another study, 60 paediatric subjects (2 to 5 years of age) received 5 mg of loratadine syrup once daily. No unexpected adverse events were observed. The paediatric efficacy was similar to the efficacy observed in adults.

5.2 Pharmacokinetic properties

Absorption

Loratadine is rapidly and well-absorbed. Concomitant ingestion of food can delay slightly the absorption of loratadine but without influencing the clinical effect. The bioavailability parameters of loratadine and of the active metabolite are dose proportional.

Distribution

Loratadine is highly bound (97% to 99%) and its active major metabolite desloratadine (DL) moderately bound (73% to 76%) to plasma proteins. In healthy subjects, plasma distribution half-lives of loratadine and its active metabolite are approximately 1 and 2 hours respectively.

Biotransformation

After oral administration, loratadine is rapidly and well absorbed and undergoes an extensive first pass metabolism, mainly by CYP3A4 and CYP2D6. The major metabolite-desloratadine (DL)- is pharmacologically active and responsible for a large part of the clinical effect. Loratadine and DL achieve maximum plasma concentrations (Tmax) between 1–1.5 hours and 1.5–3.7 hours after administration, respectively.

Elimination

Approximately 40% of the dose is excreted in the urine and 42% in the faeces over a 10 day period and mainly in the form of conjugated metabolites. Approximately 27% of the dose is eliminated in the urine during the first 24 hours.

Less than 1% of the active substance is excreted unchanged in the active form, as loratadine or DL.

The mean elimination half-lives in healthy adult subjects were 8.4 hours (range = 3 to 20 hours) for loratadine and 28 hours (range = 8.8 to 92 hours) for the major active metabolite.

Renal impairment

In patients with chronic renal impairment, both the AUC and peak plasma levels (Cmax) increased for loratadine and its active metabolite as compared to the AUCs and peak plasma levels (Cmax) of patients with normal renal function. The mean elimination half-lives of loratadine and its active metabolite were not significantly different from that observed in normal subjects. Haemodialysis does not have an effect on the pharmacokinetics of loratadine or its active metabolite in subjects with chronic renal impairment.

Hepatic impairment

In patients with chronic alcoholic liver disease, the AUC and peak plasma levels (Cmax) of loratadine were double while the pharmacokinetic profile of the active metabolite was not significantly changed from that in patients with normal liver function. The elimination halflives for loratadine and its metabolite were 24 hours and 37 hours, respectively, and increased with increasing severity of liver disease.

Elderly

The pharmacokinetic profile of loratadine and its active metabolite is comparable in healthy adult volunteers and in healthy geriatric volunteers.

5.3 Preclinical safety Data:

Non-Clinical data reveal no special hazard for humans based on conventional studies of safety, pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. In reproductive toxicity studies, no teratogenic effects were observed. However, prolonged parturition and reduced viability of offspring were observed in rats at plasma levels (AUC) 10 times higher than those achieved with clinical doses.

6. Pharmaceutical particulars

6.1 List of excipients

Lactose monohydrate, Microcrystalline Cellulose, Povidone K-30, Colloidal Anhydrous Silica, Maize starch, Magnesium Stearate, Croscarmellose Sodium, Colloidal Anhydrous silica, Titanium dioxide.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C in a dry & dark place.

Keep all medicines out of reach of children.

6.5 Nature and contents of container
Primary packing: 10 Tablets in an ALU-PVC blister.
Secondary packing: 10 Blisters are packed in a carton along with leaflet.
Tertiary packing: 10 Cartons are packed in a shrink. Such 30 shrinks are packed in a 5 ply corrugated box sealed with BOPP tape & strap with strapping roll.

6.5 Special precautions for disposal and other handling
None.

7. Applicant / Manufacturer
Applicant

Applicant name and address	**M/s. PRIYA PHARMACEUTICAL NIG. LTD.,** No. C-1, Airport Road, 2F, Kano State, Nigeria.
Contact person's phone number	
Contact person's email	

Manufacturer

Manufacturer name and address	**M/s. IMPULSE PHARMA PVT. LTD.** J-201, J-202/1 , MIDC Tarapur, Boisar, Dist. Palghar - 401506, Maharashtra State, India.
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