Long-Acting, Non-Sedating Antihistamine

Formulation:

Each LORATADINE (CLARITIN®) Reditabs® tablet contains Loratadine.....10 mg.

1 Description Of The Product

Loratadine rapidly disintegrating tablets contain loratadine (SCH 29851; Figure 1.1), a tri-cyclic antihistamine with selective peripheral H_1-receptor antagonistic activity, which is currently used for the relief of symptoms associated with allergic rhinitis, and urticaria and other dermatologic disorders.

1.1 Drug Substance

The structure of loratadine is shown in Figure 1.1. Its chemical names are: 1-Piperidinecarboxylic acid 4-(8-chloro-5,6-dihydro-11H-benzo[5,6]cyclohepta [1,2-b]pyridin-11-ylidene)-ethylester, and ethyl 4-(8-chloro- 5,6-dihydro-11 H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-1-piperidine carboxylate. The empirical formula is $C_{22}H_{23}ClN_2O_2$ and Molecular Weight (MW) is 382.89 (Reference 1).

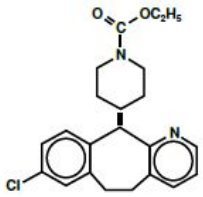

FIGURE: Chemical Structure of Loratadine (SCH 29851)

1.2 Drug Product

1.2.3 LORATADINE (CLARITIN®) Reditabs® Tablet

1.2.3.1 **What is in the Medicine? (Composition)**

LORATADINE (CLARITIN®) Reditabs® tablets contain 10 mg loratadine that can be taken orally without water.

1.2.3.2 List of excipients

Gelatin, mannitol, citric acid, and mint flavor.

1.2.3.3 **How should you keep this Medicine? (Special Precautions for Storage)**

Store at temperatures not exceeding between 30°C, and protect from excessive moisture.

2 Preclinical Information

2.1 Pharmacodynamic Properties

Loratadine, the active ingredient in Loratadine tablets, syrup and Loratadine (Claritin®) Reditabs® tablets, is a tri-cyclic antihistamine with selective peripheral H_1–receptor antagonistic activity.

Whole body autoradiographic studies in rats and monkeys, radiolabeled tissue distribution studies in mice and rats, and in vivo radioligand studies in mice have shown that neither loratadine nor its metabolites readily cross the blood-brain barrier. Radioligand binding studies with guinea pig pulmonary and brain H_1-receptors indicate that there was preferential binding to peripheral versus central nervous system H_1-receptors.

2.2 Preclinical Information

2.2.1 Carcinogenesis, Mutagenesis and Impairment of Fertility

No significant findings were noted.

2.2.2 LORATADINE (CLARITIN®) Reditabs® Mucous Membrane Irritation

No evidence of mucous membrane irritation was observed after daily administration of up to 12 tablets (120 mg) of LORATADINE (CLARITIN®) Reditabs® tablets into the hamster cheek pouch for five days.

3 Clinical Pharmacology

3.1 Pharmacokinetic Properties

After oral administration of loratadine in the conventional tablet formulation, the drug is rapidly and well absorbed and undergoes extensive first pass metabolism. In normal subjects, plasma distribution half-lives of loratadine and its active metabolite are approximately 1 and 2 hours, respectively. The mean elimination half-lives found in normal 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 (descarboethoxyloratadine). In nearly all patients, exposure (AUC) to the metabolite is greater than exposure to parent loratadine.

Pharmacokinetic studies showed that LORATADINE (CLARITIN®) Reditabs® provides plasma concentrations of loratadine and its active metabolite, descarboethoxyloratadine, that are similar to those achieved with loratadine in conventional formulations.

Loratadine is highly bound (97% to 99%) and its active metabolite moderately bound (73% to 76%) to plasma proteins.

Approximately 40% of the dose is excreted in the urine and 42% in the feces over a 10-day period and that mainly in the form of conjugated metabolites.

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

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

In patients with chronic alcoholic liver disease, the AUC and 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 half-lives for loratadine and its metabolite were 24 hours and 37 hours, respectively, and increased with increasing severity of liver disease.

Loratadine and its active metabolite are excreted in the breast milk of lactating women. Forty-eight hours after dosing, only 0.029% of the loratadine dose is detected in the milk as unchanged loratadine and its active metabolite.
The bioavailability parameters of loratadine and of the active metabolite are dose proportional.
The effect of food on the pharmacokinetic profile of loratadine and its metabolite is not regarded as clinically significant. Consumption of food with LORATADINE (CLARITIN®) Reditabs® may delay the time and increase the extent of absorption without influencing clinical effects.
The bioavailability of loratadine or its active metabolite was not compromised when a 10 mg LORATADINE (CLARITIN®) Reditabs® was placed on the tongue and swallowed without water.

3.2 Pharmacodynamic Properties

In comparative clinical studies, the sedation profile of loratadine 10 mg once daily is comparable to that of placebo. In studies with loratadine tablets at doses 2 to 4 times higher than the recommended dose of 10 mg, a dose-related increase in the incidence of somnolence was observed.
In a study in which loratadine tablets were administered at 4 times the clinical dose for 90 days, no clinically significant increase in the QT_c was seen on ECGs.

4 Indications And Usage

4.1 **What is this Medicine Used for? (Therapeutic Indications)**

LORATADINE (CLARITIN®) Reditabs® Tablet is indicated for the relief of symptoms associated with allergic rhinitis, such as sneezing, nasal discharge (rhinorrhea) and itching, as well as ocular itching and burning. Nasal and ocular signs and symptoms are relieved rapidly after oral administration.
LORATADINE (CLARITIN®) Reditabs® Tablet is also indicated for the relief of symptoms and signs of chronic urticaria and other allergic dermatologic disorders.

5 Company Core Safety Information

5.1 **When should you not take this Medicine? (Contraindications)**

LORATADINE (CLARITIN®) Reditabs® tablets are contraindicated in patients who are hypersensitive to this medication or to any of its ingredients.

5.2 **Care that should be taken when taking this Medicine? (Warnings/Precautions)**

Patients with liver impairment should be administered a lower initial dose because they may have reduced clearance of loratadine. Therefore, the following dosing is recommended: One half the recommended dose every day or the full recommended dose every other day.

5.3 **Undesirable Effects/Adverse Reactions**

Loratadine has no clinically significant sedative properties at the recommended dosage.
The most frequently reported adverse effects were headache, somnolence, fatigue and dry mouth and gastrointestinal disorders such as nausea, gastritis, and also allergic symptoms like rash.
In addition, the following spontaneous adverse events have been reported very rarely during the marketing of loratadine: abnormal hepatic function, alopecia, anaphylaxis, tachycardia, palpitations, and dizziness.

5.4 Drug Abuse And Dependence

There is no information to indicate that abuse or dependency occurs with loratadine.

5.5 **Overdosage (Signs & Symptoms, What to do when you have taken more than the recommended dosage?)**

Somnolence, tachycardia, and headache have been reported with overdoses. In the event of overdosage, general symptomatic and supportive measures should be instituted and maintained for as long as necessary.
Loratadine is not eliminated by hemodialysis. It is not known if loratadine is eliminated by peritoneal dialysis.

5.6 **What other medicine/food should be avoided while taking this Medicine? (Drug Interactions)**

Increase in plasma concentrations of this drug has been reported with concomitant use with ketoconazole, erythromycin or cimetidine in controlled clinical trials, but without clinically significant changes (including electrocardiographic).
Other drugs known to inhibit hepatic metabolism should be coadministered with caution until definitive interaction studies can be completed.

5.7 Interference With Laboratory Tests

5.8 Other Relevant Safety Information

5.8.1 Pregnancy And Lactation

No teratogenic effect was observed in animals. The safe use of Loratadine tablets, syrup and LORATADINE (CLARITIN®) Reditabs® tablets during pregnancy and lactation has not been established. Loratadine should only be used if the potential benefit justifies the potential risk to fetus or newborn.
Loratadine is excreted in breastmilk. Therefore, in lactating females a decision should be made whether to discontinue nursing or discontinue the drug.

6 How much and how often should you use this Medicine? (Dosage and Administration)

6.1 LORATADINE (CLARITIN®) REDITABS® TABLETS

Adults and children 12 years of age and over: One LORATADINE (CLARITIN®) Reditabs® tablet placed in the mouth once daily. Tablet disintegration occurs rapidly and water or other liquid is not required.

Availability:

LORATADINE (CLARITIN®) Reditabs® 10 mg orally disintegrating Tablet: PVC/Polyethylene/Alu blister pack x 10 tablets, box x 10's.

Manufacturer: CATALENT UK SWINDON ZYDIS LIMITED

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Repacker: **PT. Bayer Indonesia**

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If you want to report a product complaint or side effect, please contact your health care professional or the Philippine FDA at adr@fda.gov.ph.
Inquiries can also be directed to: Bayer Philippines, Inc. Taguig City, Philippines, E-mail: medinfoph@bayer.com drugsafety.philippines@bayer.com

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