Bilastine Tablets IP 20mg

Bepozal® 20

10 x10 Tablets

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

1. Generic name
Bilastine 20mg Tablets

2. Qualitative and quantitative composition
Each film coated tablet contains:
Bilastine IP .....20 mg
Excipients ..... q.s.
Colour: Titanium Dioxide IP

3. Dosage form(s) and strength(s)
Bepozal 20mg tablet for oral use

4. Clinical particulars
4.1 Therapeutic Indications
Symptomatic treatment of allergic rhino-conjunctivitis (seasonal and perennial) and urticaria (itching, hives, and rash) in adults.

4.2 Posology & method of administration
20 mg Bepozal once daily for the relief of symptoms of allergic rhinoconjunctivitis (SAR and PAR) and urticaria.
The tablet should be taken one hour before or two hours after intake of food or fruit juice.
Older people
No dosage adjustments are required in older patients. There is little experience in patients above the age of 65.
Patients with renal impairment
No dosage adjustment is required in patients with renal impairment
Method of administration:
Oral use. The tablet is to be swallowed with water. It is recommended to take the daily dose in one single intake.

4.3 Contraindication
Hypersensitivity to the active substance or to any of the excipients

4.4 Special warnings & precaution for use
Paediatric population
Efficacy and safety of Bilastine in children under 2 years of age have not been established and there is little clinical experience in children aged 2 to 5 years, therefore Bilastine should not be used in these age groups.
In patients with moderate or severe renal impairment co-administration of Bilastine with P-glycoprotein inhibitors, such as e.g., ketoconazole, erythromycin, cyclosporine, ritonavir or diltiazem, may increase plasmatic levels of Bilastine and therefore increase the risk of adverse effects of Bilastine. Therefore, co-administration of Bilastine and P-glycoprotein inhibitors should be avoided in patients with moderate or severe renal impairment.

4.5 Drugs interactions
Interaction studies have only been performed in adults and are summarised below.

Interaction with food: Food significantly reduces the oral bioavailability of Bilastine by 30%.

Interaction with grapefruit juice: concomitant intake of Bilastine 20 mg and grapefruit juice decreased Bilastine bioavailability by 30%. This effect may also apply to other fruit juices. The degree of bioavailability decrease may vary between producers and fruits. The mechanism for this interaction is an inhibition of OATP1A2, an uptake transporter for which Bilastine is a substrate (see section 5.2). Medicinal products that are substrates or inhibitors of OATP1A2, such as ritonavir or rifampicin, may likewise have the potential to decrease plasma concentrations of Bilastine.

Interaction with ketoconazole or erythromycin: Concomitant intake of Bilastine 20 mg o.d. and ketoconazole 400 mg o.d. or erythromycin 500 mg t.i.d. increased Bilastine AUC 2-fold and Cmax 2-3 fold. These changes can be explained by interaction

with intestinal efflux transporters, since Bilastine is substrate for P-gp and not metabolised (see section 5.2). These changes do not appear to affect the safety profile of Bilastine and ketoconazole or erythromycin, respectively. Other medicinal products that are substrates or inhibitors of P-gp, such as cyclosporine, may likewise have the potential to increase plasma concentrations of Bilastine.

Interaction with diltiazem: Concomitant intake of Bilastine 20 mg o.d. and diltiazem 60 mg o.d. increased Cmax of Bilastine by 50%. This effect can be explained by interaction with intestinal efflux transporters, and does not appear to affect the safety profile of Bilastine.

Interaction with alcohol: The psychomotor performance after concomitant intake of alcohol and 20 mg Bilastine o.d. was similar to that observed after intake of alcohol and placebo.

Interaction with lorazepam: Concomitant intake of Bilastine 20 mg o.d. and lorazepam 3 mg o.d. for 8 days did not potentiate the depressant CNS effects of lorazepam.

Paediatric population: Interaction studies have only been performed in adults. As there is no clinical experience regarding the interaction of Bilastine with other medicinal products, food or fruit juices in children, the results obtained in adult interactions studies should be at present taken into consideration when prescribing Bilastine to children. There are no clinical data in children to state whether changes to the AUC or Cmax due to interactions affect the safety profile of Bilastine.

4.6 Use in special populations

Pregnant women

There are no or limited amount of data from the use of Bilastine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity, parturition or postnatal development.

Lactating women

It is unknown whether Bilastine is excreted in human breast milk. The excretion of Bilastine in milk has not been studied in animals. A decision on whether to discontinue/abstain from Bilastine therapy must be made taking into account the benefit of breast-feeding for the child and the benefit of Bilastine therapy for the mother.

Fertility

There are no or limited amount of clinical data. A study in rats did not indicate any negative effect on fertility with Bilastine.

Paediatric patients

The safety and efficacy of Bilastine 20mg tablets in children under 12 years of age have not been established therefore Bilastine should not be used in these age groups.

Geriatric patients

No dosage adjustments are required in elderly patients.

Renal impairment

No dosage adjustment is required in patients with renal impairment.

Hepatic impairment

There are no pharmacokinetic data in subjects with hepatic impairment. Bilastine is not metabolized in human. Since the results of the renal impairment study indicate renal elimination to be a major contributor in the elimination, biliary excretion is expected to be only marginally involved in the elimination of Bilastine. Changes in liver function are not expected to have a clinically relevant influence on Bilastine pharmacokinetics.

4.7 Effects on ability to drive & use machines

A study performed in adults to assess the effects of Bilastine on the ability to drive demonstrated that treatment with 20 mg did not affect the driving performance. However, as the individual response to the medicinal product may vary, patients should be advised not to drive or use machines until they have established their own response to Bilastine.

4.8 Undesirable effects

Summary of safety profile in adults and adolescent patients

The incidence of adverse events in patients suffering from allergic rhinoconjunctivitis or chronic idiopathic urticaria treated with 20 mg Bilastine in clinical trials was comparable with the incidence in patients receiving placebo (12.7% versus 12.8%).

The phase II and III clinical trials performed during the clinical development included 2525 patients treated with different doses of Bilastine, of which 1697 received Bilastine 20 mg. In these trials 1362 patients received placebo. The ADRs most commonly reported by patients receiving 20 mg Bilastine for the indication of allergic rhinoconjunctivitis or chronic idiopathic urticaria were headache, somnolence,

dizziness, and fatigue. These adverse events occurred with a comparable frequency in patients receiving placebo.

Tabulated summary of adverse reactions in adult and adolescent patients
ADRs at least possibly related to Bilastine and reported in more than 0.1% of the patients receiving 20 mg Bilastine during the clinical development (N = 1697) are tabulated below.
Frequencies are assigned as follows:
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)
Rare, very rare and reactions with unknown frequency have not been included in the table.

System Organ Class		Bilastine 20 mg N = 1697	All Bilastine Doses N = 2525	Placebo N = 1362
Frequency	Adverse reaction			
Infections and infestations				
Uncommon	Oral herpes	2 (0.12%)	2 (0.08%)	0 (0.0%)
Metabolism and nutrition disorders				
Uncommon	Increased appetite	10 (0.59%)	10 (0.59%)	10 (0.59%)
Psychiatric disorders				
Uncommon	Anxiety	6 (0.35%)	8 (0.32%)	0 (0.0%)
	Insomnia	2 (0.12%)	4 (0.16%)	0 (0.0%)
Nervous system disorders				
Common	Somnolence	52 (3.06%)	82 (3.25%)	39 (2.86%)
	Headache	68 (4.01%)	90 (3.56%)	46 (3.38%)
Uncommon	Dizziness	14 (0.83%)	23 (0.91%)	8 (0.59%)
Ear and labyrinth disorders				
Uncommon	Tinnitus	2 (0.12%)	2 (0.08%)	0 (0.0%)
	Vertigo	3 (0.18%)	3 (0.12%)	0 (0.0%)
Cardiac disorders				
Uncommon	Right bundle branch block	4 (0.24%)	5 (0.20%)	3 (0.22%)
	Sinus arrhythmia	5 (0.30%)	5 (0.20%)	1 (0.07%)
	Electrocardiogram QT prolonged	9 (0.53%)	10 (0.40%)	5 (0.37%)
	Other ECG abnormalities	7 (0.41%)	11 (0.44%)	2 (0.15%)
Respiratory, thoracic and mediastinal disorders				
Uncommon	Dyspnoea	2 (0.12%)	2 (0.08%)	0 (0.0%)
	Nasal discomfort	2 (0.12%)	2 (0.08%)	0 (0.0%)
	Nasal dryness	3 (0.18%)	6 (0.24%)	4 (0.29%)
Gastrointestinal disorders				
Uncommon	Upper abdominal pain	11 (0.65%)	14 (0.55%)	6 (0.44%)
	Abdominal pain	5 (0.30%)	5 (0.20%)	4 (0.29%)
	Nausea	7 (0.41%)	10 (0.40%)	14 (1.03%)
	Stomach discomfort	3 (0.18%)	4 (0.16%)	0 (0.0%)
	Diarrhoea	4 (0.24%)	6 (0.24%)	3 (0.22%)
	Dry mouth	2 (0.12%)	6 (0.24%)	5 (0.37%)
	Dyspepsia	2 (0.12%)	4 (0.16%)	4 (0.29%)
	Gastritis	4 (0.24%)	4 (0.16%)	0 (0.0%)
Skin and subcutaneous tissue disorders				
Uncommon	Pruritus	2 (0.12%)	4 (0.16%)	2 (0.15%)
General disorders and administration site conditions				
Uncommon	Fatigue	14 (0.83%)	19 (0.75%)	18 (1.32%)
	Thirst	3 (0.18%)	4 (0.16%)	1 (0.07%)
	Improved pre existing condition	2 (0.12%)	2 (0.08%)	1 (0.07%)
	Pyrexia	2 (0.12%)	3 (0.12%)	1 (0.07%)
	Asthenia	3 (0.18%)	4 (0.16%)	5 (0.37%)
Investigations				
Uncommon	Increased gamma glutamyltransferase	7 (0.41%)	8 (0.32%)	2 (0.15%)
	Alanine aminotransferase increased	5 (0.30%)	5 (0.20%)	3 (0.22%)
	Aspartate aminotransferase increased	3 (0.18%)	3 (0.12%)	3 (0.22%)
	Blood creatinine increased	2 (0.12%)	2 (0.08%)	0 (0.0%)
	Blood triglicerides increased	2 (0.12%)	2 (0.08%)	3 (0.22%)
	Increased weight	8 (0.47%)	12 (0.48%)	2 (0.15%)

Frequency not known (cannot be estimated from the available data): Palpitations, tachycardia, hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, rash, localised oedema/local swelling, and erythema), and vomiting have been observed during the post-marketing period.

Description of selected adverse reactions in adult and adolescent patients:
Somnolence, headache, dizziness and fatigue were observed either in patients treated with Bilastine 20 mg or with placebo. The frequency reported was 3.06 % vs. 2.86% for somnolence; 4.01% vs. 3.38% for headache; 0.83% vs. 0.59% for dizziness, and 0.83% vs. 1.32% for fatigue.

The information collected during the post-marketing surveillance has confirmed the safety profile observed during the clinical development.

4.9 Overdose
Information regarding acute overdose of Bilastine is retrieved from the experience of clinical trials conducted during the development and the post-marketing surveillance. In clinical trials, after administration of Bilastine at doses 10 to 11 times the therapeutic dose (220 mg as single dose; or 200 mg/day for 7 days) to healthy volunteers frequency of treatment emergent adverse events was two times higher than with placebo. The adverse reactions most frequently reported were dizziness, headache and nausea. No serious adverse events and no significant prolongation in the QTc interval were reported. The information collected in the post-marketing surveillance is consistent with that reported in clinical trials.

Critical evaluation of Bilastine's multiple dose (100 mg x4 days) effect on ventricular repolarization by a "thorough QT/QTc cross-over study" involving 30 healthy volunteers did not show significant QTc prolongation.
In the event of overdose symptomatic and supportive treatment is recommended. There is no known specific antidote to Bilastine.

5. Pharmacological properties

5.1 Mechanism of action
Bilastine is a non-sedating, long-acting histamine antagonist with selective peripheral H1 receptor antagonist affinity and no affinity for muscarinic receptors. Bilastine inhibited histamine-induced wheal and flare skin reactions for 24 hours following single doses.

5.2 Pharmacodynamic properties
Pharmacotherapeutic group: Antihistamines for systemic use, other antihistamines for systemic use. ATC code R06AX29.
Bilastine is a non-sedating, long-acting histamine antagonist with selective peripheral H1 receptor antagonist affinity.
In clinical trials performed in adult and adolescent patients with allergic rhinocon junctivitis (seasonal and perennial), Bilastine 20 mg, administered once daily for 14-28 days, was effective in relieving symptoms such as sneezing, nasal discharge, nasal itching, nasal congestion, ocular itching, tearing and ocular redness. Bilastine effectively controlled symptoms for 24 hours.
No clinically relevant prolongation of QTc interval or any other cardiovascular effect has been observed in the clinical trials performed with Bilastine, even at doses of 200 mg daily (10 times the clinical dose) for 7 days in 9 subjects, or even when co-administered with P-gp inhibitors, such as ketoconazole (24 subjects) and erythromycin (24 subjects). Additionally, a thorough QT study including 30 volunteers has been performed.
In controlled clinical trials at the recommended dose of 20 mg once daily, the CNS safety profile of Bilastine was similar to placebo and the incidence of somnolence was not statistically different from placebo. Bilastine at doses of up to 40 mg q.d. did not affect psychomotor performance in clinical trials and did not affect driving performance in a standard driving test.
Elderly patients (≥ 65 years) included in phase II and III studies showed no difference in efficacy or safety with respect to younger patients. A post- authorisation study in 146 elderly patients showed no differences in the safety profile with respect to the adult population.

5.3 Pharmacokinetics properties
Absorption
Bilastine is rapidly absorbed after oral administration with a time to maximum plasma concentration of around 1.3 hours. No accumulation was observed. The mean value of Bilastine oral bioavailability is 61%.

Distribution
In vitro and in vivo studies have shown that Bilastine is a substrate of P-gp (see section 4.5 "Interaction with ketoconazole, erythromycin and diltiazem") and OATP (see section 4.5 "Interaction with grapefruit juice"). Bilastine does not appear to be a substrate of the transporter BCRP or renal transporters OCT2, OAT1 and OAT3. Based on in vitro studies, Bilastine is not expected to inhibit the following transporters in the systemic circulation: P-gp, MRP2, BCRP, BSEP, OATP1B1, OATP1B3, OATP2B1, OAT1, OAT3, OCT1, OCT2, and NTCP, since only mild inhibition was detected for P-gp,

OATP2B1 and OCT1, with an estimated IC50 ≥ 300 µM, much higher than the calculated clinical plasma Cmax and therefore these interactions will not be clinically relevant. However, based on these results inhibition by Bilastine of transporters present in the intestinal mucosa, e.g. P-gp, cannot be excluded.
At therapeutic doses Bilastine is 84-90% bound to plasma proteins.

Metabolism
Bilastine did not induce or inhibit activity of CYP450 isoenzymes in in vitro studies.

Excretion
In a mass balance study performed in healthy adult volunteers, after administration of a single dose of 20 mg 14C-Bilastine, almost 95% of the administered dose was recovered in urine (28.3%) and faeces (66.5%) as unchanged Bilastine, confirming that Bilastine is not significantly metabolized in humans. The mean elimination half-life calculated in healthy volunteers was 14.5 h.

Linearity
Bilastine presents linear pharmacokinetics in the dose range studied (5 to 220 mg), with a low interindividual variability.

Renal impairment
In a study in subjects with renal impairment the mean (SD) AUC0-∞ increased from 737.4 (± 260.8) ng x hr/mL in subjects without impairment (GFR: > 80 mL/min/1.73 m2) to: 967.4 (± 140.2) ng x hr/mL in subjects with mild impairment (GFR: 50-80 mL/min/1.73 m2), 1384.2 (± 263.23) ng x hr/mL in subjects with moderate impairment (GFR: 30 - <50 mL/min/1.73 m2), and 1708.5 (± 699.0) ng x hr/mL in subjects with severe impairment (GFR: < 30 mL/min/1.73 m2). Mean (SD) half-life of Bilastine was 9.3 h (± 2.8) in subjects without impairment, 15.1 h (± 7.7) in subjects with mild impairment, 10.5 h (± 2.3) in subjects with moderate impairment and 18.4 h (± 11.4) in subjects with severe impairment. Urinary excretion of Bilastine was essentially complete after 48 -72 h in all subjects. These pharmacokinetic changes are not expected to have a clinically relevant influence on the safety of Bilastine, since Bilastine plasma levels in patients with renal impairment are still within the safety range of Bilastine.

Hepatic impairment
There are no pharmacokinetic data in subjects with hepatic impairment. Bilastine is not metabolized in human. Since the results of the renal impairment study indicate renal elimination to be a major contributor in the elimination, biliary excretion is expected to be only marginally involved in the elimination of Bilastine. Changes in liver function are not expected to have a clinically relevant influence on Bilastine pharmacokinetics.

Elderly
Only limited pharmacokinetic data are available in subjects older than 65 years. No statistically significant differences have been observed with regard to PK of Bilastine in elderly aged over 65 years compared to adult population aged between 18 and 35 years.

6. Non-clinical properties

6.1 Animal toxicology or pharmacology
Non-clinical data with Bilastine reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

In reproduction toxicity studies effects of Bilastine on the foetus (pre-and post-implantation loss in rats and incomplete ossification of cranial bones, sternebrae and limbs in rabbits) were only observed at maternal toxic doses. The exposure levels at the NOAELs are sufficiently in excess (> 30 fold) to the human exposure at the recommended therapeutic dose.

In a lactation study, Bilastine was identified in the milk of nursing rats administered a single oral dose (20 mg/kg). Concentrations of Bilastine in milk were about half of those in maternal plasma. The relevance of those results for humans is unknown.

In a fertility study in rats, Bilastine administered orally up to 1000 mg/kg/day did not induce any effect on female and male reproductive organs. Mating, fertility and pregnancy indices were not affected.

As seen in a distribution study in rats with determination of drug concentrations by autoradiography, Bilastine does not accumulate in the CNS.

7. Description
Bilastine is a second generation H1-antihistamine, indicated for the treatment of allergic rhinitis. Bilastine is known chemically as 2-[4-(2-{4-[1-(2-ethoxyethyl)-1h-benzimidazol-2-yl] piperidin-1-yl} ethyl) phenyl]-2-methylpropanoic acid; 2-[4-[2-[4-[1-(2-ethoxyethyl) benzimidazol-2-yl] piperidin-1-yl] ethyl] phenyl]-2-methylpropanoic acid. Its empirical formula is C28H37N3O3 and the molecular weight

is 463.61168 g/mol.

8. Pharmaceutical particulars

8.1 Incompatibilities
Not applicable

8.2 Shelf life
Refer pack

8.3 Packaging information
Each box contains 10x10 tablets in Alu-Alu blister pack.

8.4 Storage & handling instruction
Store protected from light and moisture at a temperature not exceeding 30°C

9. Patient counselling information

• If you have allergy to drug Bilastine or any of the other ingredients of this medicine.
• Please discuss with your doctor if you are taking any of the following medicines before starting Bilastine Tablet:

- Ketoconazole (an antifungal medicine)
- Erythromycin (an antibiotic)
- Diltiazem (to treat angina)
- Cyclosporine (to reduce the activity of your immune system, thus avoiding transplant rejection or reducing disease activity in autoimmune and allergic disorders, such as psoriasis, atopic dermatitis or rheumatoid arthritis)
- Ritonavir (to treat AIDS)
- Rifampicin (an antibiotic)

10. Details of manufacturers

Synokem Pharmaceuticals Ltd.,
Plot No. 56-57, Sector-6A, I.I.E. (SIDCUL), Ranipur,
(BHEL), Haridwar–249 403 (Uttarakhand)

11. Details of permission or licence number with date

27/UA/2018

12. Marketed by:

Tricos Dermatologics Pvt. Ltd.,
4, Ground Floor, Print World Industrial,
Complex, Mankoli Village Road, Vehele,
Bhiwandi, Thane-421302.

13. Revision Date

November 2025