13-09-2023
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210mm

Bistavo™ Tablet
(Bilastine)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Bistavo™ 20mg Tablet
Each tablet contains:
Bilastine MS.....20mg

PHARMACEUTICAL FORM

Tablet.

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS:

- Symptomatic treatment of allergic rhino-conjunctivitis (seasonal and perennial) and urticaria.
- **Bistavo™** is indicated in adults and adolescents (12 years of age and over).

POSOLOGY AND METHOD OF ADMINISTRATION:
Posology:
Adults and adolescents (12 years of age and over):
Bistavo™ 20mg (1 tablet) once daily for the relief of symptoms of allergic rhino-conjunctivitis (SAR and PAR) and urticaria. The tablet should be taken one hour before or two hours after intake of food or fruit juice.
Duration of treatment:
For allergic rhino-conjunctivitis, treatment should only be given during allergen exposure. Seasonal allergic rhinitis treatment can be stopped when symptoms are gone and restarted when they reappear.
Perennial allergic rhinitis patients may continue treatment during allergen exposure. Duration of treatment for urticaria depends on type, duration, and course of symptoms.
Special populations:
Elderly: No dosage adjustments are required in elderly patients.
Renal impairment: Studies conducted in adults in special risk groups (renally impaired patients) indicate that it is not necessary to adjust the dose of bilastine in adults.
Hepatic impairment: There is no clinical experience in adult patients with hepatic impairment. However, since bilastine is not metabolized and is eliminated as unchanged in urine and faeces, hepatic impairment is not expected to increase systemic exposure above the safety margin in adult patients.Therefore, no dosage adjustment is required in adult patients with hepatic impairment.
Paediatric population:

- ***Children 6 to 11 years of age with a body weight of at least 20kg:*** Bilastine 10mg orodispersible tablets and bilastine 2.5mg/mL oral solution are appropriate for administration to this population.
- ***Children under 6 years of age and under 20kg:*** Bilastine should not be used in this age group.
- The safety and efficacy of bilastine in renally and hepatically impaired children have not been established.

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.

CONTRAINDICATIONS:
Hypersensitivity to the active substance.

SPECIAL WARNINGS AND PRECAUTIONS 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 coadministration 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, coadministration of bilastine and P-glycoprotein inhibitors should be avoided in patients with moderate or severe renal impairment.
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium free'.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:
Interaction with food:
Food significantly reduces the oral bioavailability of bilastine by 30%.
Interaction with grapefruit juice:
Concomitant intake of bilastine 20mg and grapefruit juice decreased bilastine bioavailability by 30%. The mechanism for this interaction is an inhibition of OATP1A2, an uptake transporter for which bilastine is a substrate. 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 20mg o.d. and ketoconazole 400mg o.d. or erythromycin 500mg t.i.d. increased bilastine AUC 2-fold and C_{max} 2-3-fold. These changes can be explained by interaction with intestinal efflux transporters, since bilastine is substrate for P-gp and not metabolized. 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 20mg o.d. and diltiazem 60mg o.d. increased C_{max} 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 20mg bilastine o.d. was similar to that observed after intake of alcohol and placebo.
Interaction with lorazepam:
Concomitant intake of bilastine 20mg o.d. and lorazepam 3mg 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 C_{max} due to interactions affect the safety profile of bilastine.

FERTILITY, PREGNANCY AND LACTATION:
Fertility:
There are no or limited amount of clinical data.
Pregnancy:
There are no or limited amount of data from the use of bilastine in pregnant women. As a precautionary measure, it is preferable to avoid the use of bilastine during pregnancy.
Breast-feeding:
The excretion of bilastine in milk has not been studied in humans. A decision on whether to continue/discontinue breast-feeding or 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.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
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.

UNDESIRABLE EFFECTS:

- **Infections and infestations:** ***Uncommon:*** Oral herpes.
- **Metabolism and nutrition disorders:** ***Uncommon:*** Increased appetite.
- **Psychiatric disorders:** ***Uncommon:*** Anxiety, insomnia.
- **Nervous System disorders:** ***Common:*** Somnolence, headache. ***Uncommon:*** Dizziness.
- **Ear & Labyrinth disorders:** ***Uncommon:*** Tinnitus, vertigo.
- **Cardiovascular:** ***Uncommon:*** Sinus arrythmia, electrocardiogram QT prolonged, other ECG abnormalities, right bundle branch block.
- **Respiratory, thoracic and mediastinal disorders:** Dyspnoea, nasal discomfort, nasal dryness.
- **Gastrointestinal disorders:** ***Uncommon:*** Upper abdominal pain, abdominal pain, stomach discomfort, dry mouth, dyspepsia, diarrhoea, gastritis, nausea.
- **Skin and subcutaneous tissue disorders:** ***Uncommon:*** Pruritis.
- **General disorders and administration site conditions:** ***Uncommon:*** Fatigue, thirst, improved pre-existing conditions, asthenia, pyrexia.
- **Investigations:** ***Uncommon:*** Increase gamma glutamyltransferase, alanine aminotransferase increased, aspartate aminotransferase increased, blood creatinine & blood triglycerides increased , increased weight.

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Frequency not known:
Palpitations, tachycardia, hypersensitivity reactions (such as anaphylaxis, angioedema, dyspnoea, rash, localized oedema/local swelling, and erythema), and vomiting have been observed during the post-marketing period.
Adverse reactions in paediatric population:
- **Infection & Infestation:** ***Common:*** Rhinitis.
- **Nervous system disorders:** ***Common:*** Headache. ***Uncommon:*** Dizziness and loss of consciousness.
- **Eye Disorders:** ***Common:*** Allergic conjunctivitis. ***Uncommon:*** Eye irritation.
- **Gastrointestinal disorders:** ***Common:*** Abdominal/upper abdominal pain. ***Uncommon:*** Lip swelling, diarrhoea, nausea.
- **Skin and subcutaneous tissue disorders:** ***Uncommon:*** Eczema and urticaria.
- **General disorders and administration site conditions:** ***Uncommon:*** Fatigue.

OVERDOSE:
There are no data for overdose in children. In the event of overdose symptomatic and supportive treatment is recommended. There is no known specific antidote to bilastine.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES:
Pharmacotherapeutic group:
Antihistamines for systemic use, other antihistamines for systemic use. **ATC code:** R06AX29.
Mechanism of action:
Bilastine is a non-sedating, long-acting histamine antagonist with selective peripheral H_1 receptor antagonist affinity and no affinity for muscarinic receptors. Bilastine inhibited histamine-induced wheal and flare skin reactions for 24 hours following single doses.

PHARMACOKINETIC 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 "Interaction with ketoconazole, erythromycin and diltiazem" and OATP "Interaction with grapefruit juice". Bilastine does not appear to be a substrate of the transporter BCRP or renal transporters OCT2, OAT1 and OAT3. At therapeutic doses bilastine is 84-90% bound to plasma proteins.
Biotransformation:
Bilastine did not induce or inhibit activity of CYP450 isoenzymes in in vitro studies.
Elimination:
In a mass balance study performed in healthy adult volunteers, after administration of a single dose of 20mg ^{14}C-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 14.5h.
Linearity:
Bilastine presents linear pharmacokinetics in the dose range studied (5 to 220mg), with a low interindividual variability.
Renal impairment:
The 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 pharmacokinetics of bilastine in elderly aged over 65 years compared to adult population aged between 18 and 35 years.
Paediatric population:
No pharmacokinetic data are available in adolescents (12 years to 17 years) as the extrapolation from adult data was deemed appropriate for this product.

SHELF LIFE

See expiry on the pack.

AVAILABILITY

Bistavo™ 20mg tablet in a pack of 10's.

INSTRUCTIONS

Dosage: As directed by the physician.
To be sold on prescription of a registered medical practitioner only.
Keep out of the reach of children.
Do not store over 30°C, and protect from heat, light and moisture.
Improper storage may deteriorate the medicine.

بِستاوو™ ٹیبلٹ
(بِلیسٹین)

ہدایات:
خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،
گرمی، روشنی اور نمی سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔

Manufactured by:
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