Summary of Product Characteristics

Bistavo® Tablet

Bistavo® Oral Solution

Bistavo®
(Bilastine)

1. NAME OF THE PRODUCT
Bistavo® (Bilastine) 20mg Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Bistavo® 20mg Tablet

Each tablet contains:
Bilastine MS.....20mg

3. PHARMACEUTICAL FORM
Tablet.

Appearance: White color, oval shaped tablet, break line on one side and plain on the other side.

4. CLINICAL PARTICULARS
4.1. 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).

4.2. 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.

4.3. CONTRAINDICATIONS:

Hypersensitivity to the active substance or to any of the excipients.

4.4. 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.

Cases of Electrocardiogram QT prolonged have been reported in patients using bilastine. Medicinal products that cause QT/QTc prolongation are suspected to increase the risk of Torsade de pointes.

Therefore, caution should be exercised when administering bilastine to patients who are at increased risk of experiencing QT/QTc-prolongation. This includes patients with a history of cardiac arrhythmias; patients with hypokalaemia, hypomagnesaemia, hypocalcaemia; patients with known prolongation of the QT

interval or significant bradycardia; patients with concomitant use of other medicinal products associated with QT/QTc-prolongation.
This medicine contains less than 1mmol sodium (23mg) per tablet, that is to say essentially 'sodium free'.

4.5. 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.

4.6. 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.

4.7. 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.

4.8. 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.

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.

4.9. 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.

5. PHARMACOLOGICAL PROPERTIES

5.1. 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 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. 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.

5.3. PRECLINICAL SAFETY DATA:

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 (20mg/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 1000mg/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.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS:

- Microcrystalline cellulose
- Sodium starch glycolate
- Silicon dioxide fumed
- Magnesium stearate

6.2. INCOMPATIBILITIES:

Not applicable.

6.3. SHELF LIFE:

See expiry on the pack.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:

Do not store over 30°C, and protect from heat, light and moisture.
Improper storage may deteriorate the medicine.
Keep out of the reach of children.

6.5. NATURE AND CONTENTS OF CONTAINER:

Alu/Alu Blister, pack size is 10's.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL OF A USED PRODUCT:

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

6.7. DRUG PRODUCT SPECIFICATIONS:

Innovator's Specs.

7. REGISTRATION / MARKETING AUTHORISATION HOLDER

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, Off Hub River Road, S.I.T.E., Karachi-Pakistan
www.samipharma.com
Mfg Lic. No. 000072

8. REGISTRATION / MARKETING AUTHORISATION NUMBER(S)

117980

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

27th September, 2023

10. DATE OF REVISION OF THE TEXT

بِستاوو® ٹیبلٹ
(بِلیسٹین)

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت 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۔

Bistavo®
(Bilastine)

1. NAME OF THE PRODUCT

Bistavo® (Bilastine) Oral Solution 2.5mg/ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Bistavo® Oral Solution 2.5mg/ml

Each ml contains:

Bilastine MS.....2.5mg

3. PHARMACEUTICAL FORM

Oral Solution

Appearance: Clear colorless to slightly colored solution.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS:

Symptomatic treatment of allergic rhino-conjunctivitis (seasonal and perennial) and urticaria. **Bistavo®** is indicated in children aged 2 to 11 years with a body weight of at least 15kg.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION:

Posology:

Paediatric population: Children 2 to 11 years of age with a body weight of at least 15kg 10mg bilastine (4ml of oral solution) once daily for the relief of symptoms of allergic rhino-conjunctivitis (seasonal allergic rhinitis and perennial allergic rhinitis) and urticaria. The oral solution should be taken one hour before or two hours after intake of food or fruit juice.

In adults and adolescents (over 12 years of age) the administration of bilastine 20mg tablets is appropriate.

Duration of treatment: For allergic rhino-conjunctivitis the treatment should be limited to the period of exposure to allergens. For seasonal allergic rhinitis treatment could be discontinued after the symptoms have resolved and reinitiated upon their reappearance. In perennial allergic rhinitis continued treatment may be proposed to the patients during the allergen exposure periods. For urticaria the duration of treatment depends on the type, duration and course of the complaints.

Special populations:

Renal impairment: The safety and efficacy of bilastine in renally impaired children have not been established. 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: The safety and efficacy of bilastine in hepatically impaired children have not been established. 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.

Method of administration:

For oral use.

4.3. CONTRAINDICATIONS:

Hypersensitivity to the active substance or to any of the excipients.

4.4. 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, ciclosporin, 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.

Cases of Electrocardiogram QT prolonged have been reported in patients using bilastine. Medicinal products that cause QT/QTc prolongation are suspected to increase the risk of Torsade de pointes. Therefore, caution should be exercised when administering bilastine to patients who are at increased risk of experiencing QT/QTc-prolongation. This includes patients with a history of cardiac arrhythmias; patients with hypokalemia, hypomagnesaemia, hypocalcemia; patients with known prolongation of the QT interval or significant bradycardia; patients with concomitant use of other medicinal products associated with QT/QTc-prolongation.

Bistavo® contains methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216) which may cause allergic reactions (possibly delayed).

This medicine contains 0.44mg of alcohol (ethanol) in each dose (4mL) which is equivalent to 11mg/100mL (0.011% w/v). The amount in 4mL of this medicine is equivalent to less than 0.02ml beer or 0.005ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

This medicine contains less than 1mmol sodium (23mg) per 4ml, that is to say essentially 'sodium free'.

4.5. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORM OF INTERACTIONS

Interaction studies have only been performed in adults and are summarized below.

Interaction with food: Food significantly reduces the oral bioavailability of bilastine 20mg tablets by 30% and that of bilastine 2.5mg/ml oral solution by 20%.

Interaction with grapefruit juice: concomitant intake of bilastine 20mg 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. 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 a substrate for P-gp and not metabolised. 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 ciclosporin, 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 o.d. bilastine 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: No interaction studies have been performed in children with bilastine oral solution. 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.

4.6. FERTILITY, PREGNANCY AND LACTATION:

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

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.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

A study performed in adults to assess the effects of bilastine on the ability to drive demonstrated that treatment with 20mg bilastine did not affect 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:

Adverse reactions in Paediatric population:

AEs at least possibly related to bilastine and reported in more than 0.1% of children (2-11 years) receiving bilastine during the clinical development are listed 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.

Infections and infestations:

Common: Rhinitis

Nervous system disorders:

Common: Headache

Uncommon: Loss of consciousness, dizziness

Eye disorders:

Common: Allergic conjunctivitis

Uncommon: Eye irritation

Gastrointestinal disorders:

Common: Abdominal pain/ Upper abdominal pain, diarrhoea

Uncommon: Nausea, lip swelling

Skin and subcutaneous tissues disorders:

Uncommon: Eczema, urticaria
General disorders and administration site conditions:
Uncommon: Fatigue

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 20mg bilastine during the clinical development are listed 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.
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 and labyrinth disorders:
Uncommon: Tinnitus, vertigo
Cardiac disorders:
Uncommon: Right bundle branch block, sinus arrhythmia, electrocardiogram QT prolonged*, Other ECG abnormalities
Respiratory, thoracic and mediastinal disorders:
Uncommon: Dyspnoea, nasal discomfort, nasal dryness
Gastrointestinal disorders:
Uncommon: Upper abdominal pain, abdominal pain, nausea, stomach discomfort, diarrhoea, dry mouth, dyspepsia, gastritis.
Skin and subcutaneous tissue disorders:
Uncommon: Pruritus
General disorders and administration site conditions:
Uncommon: Fatigue, thirst, improved pre-existing condition, pyrexia, asthenia
Investigations:
Uncommon: Increased gamma-glutamyltransferase, alanine aminotransferase increased, aspartate aminotransferase increased, blood creatinine increased, blood triglycerides increased, increased weight
*Electrocardiogram QT prolonged have also been reported post marketing.
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.

4.9. OVERDOSE:

There are no data for overdose in children. Information regarding acute overdose of bilastine is retrieved from the experience of clinical trials conducted during the development in adults and the post-marketing surveillance. The adverse reactions most frequently reported were dizziness, headache and nausea. No serious adverse events and no significant prolongation in the QT_c interval were reported. The information collected in the post-marketing surveillance is consistent with that reported in clinical trials. In the event of overdose symptomatic and supportive treatment is recommended. There is no known specific antidote to bilastine.

5. PHARMACOLOGICAL PROPERTIES

5.1. 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.

5.2. 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: 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 adults, 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 was 14.5 h.

5.3. PRECLINICAL SAFETY DATA:

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 (20mg/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 1000mg/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.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS:

- Beta-cyclodextrin
- Methylparaben
- Propylparaben
- Hydroxyethyl cellulose
- Sucralose
- Hydrochloric acid
- Sodium hydroxide pellets
- Blackcurrant flavor
- Purified water

6.2. INCOMPATIBILITIES:

Not applicable

6.3. SHELF LIFE:

Unopened bottle: See expiry on the pack.
Opened bottle: Discard in 6 months after first use.

6.4. SPECIAL PRECAUTIONS FOR STORAGE:

Do not store over 30°C, and protect from heat, light and freezing.
Improper storage may deteriorate the medicine.
Keep out of the reach of children.

6.5. NATURE AND CONTENTS OF CONTAINER:

Amber glass bottle with tamper-proof aluminium cap with P.E. wad, pack size is 60ml.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL OF A USED PRODUCT:

Any unused medicinal product or waste material should be disposed of in accordance with local requirements. Medicine should not be used if container is leaking or it contains undissolved particles(s).

6.7. DRUG PRODUCT SPECIFICATIONS:

Innovator's Specs.

7. REGISTRATION / MARKETING AUTHORISATION HOLDER

Manufactured by:
SAMI Pharmaceuticals (Pvt.) Ltd.
F-95, Off Hub River Road, S.I.T.E., Karachi-Pakistan
www.samipharma.com
Mfg Lic. No. 000072

8. REGISTRATION / MARKETING AUTHORISATION NUMBER(S)

127056

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

22th May, 2025

10. DATE OF REVISION OF THE TEXT

بِستاوو® اورل سلوشن
(بِلیسٹین)

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

بچوں کی پہنچ سے دور رکھیں۔

دوا کو ۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں،

گرمی، روشنی اور منجمد ہونے سے محفوظ رکھیں ورنہ دوا خراب ہو جائیگی۔

دوا کے لیک ہونے یا اس میں کوئی غیر حل پذیر شے

نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔