Summary of Product Characteristics
XITRIENE
(Pranlukast 10% w/w granules for oral suspension)

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1. Name of the medicinal product

XITRIENE (Pranlukast Dry Syrup 10% w/w)

2. Qualitative and quantitative composition

Pranlukast 10% w/w: each gram of granules contains 100 mg of pranlukast (as hydrate). The unit-dose sachets contain 50 mg, 70 mg or 100 mg of pranlukast, corresponding to 0.5 g, 0.7 g and 1.0 g of granules respectively.

Excipients with known effect:

The finished-product excipients were not itemised in the source registration record; any excipient of known effect present (for example a sugar or a colouring agent) must be declared here and warned in section 4.4 (see section 6.1).

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Granules for oral suspension (oral powder in sachet).

White to off-white, free-flowing granules.

4. Clinical particulars

4.1 Therapeutic indications

Pranlukast is a leukotriene receptor antagonist indicated for the prophylaxis and chronic treatment of bronchial asthma, and for the relief of symptoms of allergic rhinitis. It is not indicated for the relief of acute bronchospasm or the treatment of status asthmaticus.

4.2 Posology and method of administration

Posology

Paediatric population: the usual dose is 7 mg/kg body weight per day, given in two divided doses after morning and evening meals, up to a maximum of 10 mg/kg/day and not exceeding the adult dose. The dose should be adjusted according to age, body weight and symptoms, using the appropriate sachet strength, and confirmed against the applicant's approved dosing schedule. Adults: the usual dose is 225 mg twice daily after meals (using the appropriate presentation).

Method of administration

For oral use. The granules are taken after food; they may be dispersed in a small amount of water or soft food immediately before administration and taken at once.

4.3 Contraindications

Hypersensitivity to pranlukast or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Pranlukast should not be used to treat acute attacks of asthma or status asthmaticus, and patients should be advised to have appropriate rescue medication available. It should not be abruptly substituted for inhaled or oral corticosteroids; any reduction in corticosteroid dose should be gradual and under medical supervision.

Eosinophilic conditions

In rare cases, patients on leukotriene receptor antagonists may present with systemic eosinophilia, sometimes with clinical features of vasculitis consistent with Churg-Strauss syndrome, or with eosinophilic or interstitial pneumonia; these events have sometimes been associated with a reduction in corticosteroid therapy. Physicians should be alert to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications and/or neuropathy.

Hepatic effects

Hepatic dysfunction, jaundice and, rarely, fulminant hepatitis and hepatic failure have been reported; periodic monitoring of liver function is advisable, particularly during long-term treatment, and pranlukast should be discontinued if signs of hepatic dysfunction occur. Caution is advised in patients with pre-existing hepatic impairment.

4.5 Interaction with other medicinal products and other forms of interaction

Pranlukast is metabolised by cytochrome P450 (mainly CYP3A4); concomitant use with potent CYP3A4 inhibitors (e.g. azole antifungals, macrolide antibiotics) may increase, and CYP3A4 inducers may decrease, pranlukast exposure. Increases in the plasma concentration of warfarin and, with some CYP3A4 substrates, of the co-administered drug have been reported; monitoring is advised.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data on the use of pranlukast in pregnant women; it should be used during pregnancy only if the expected benefit outweighs the potential risk.

Breast-feeding

Pranlukast is excreted in the milk of lactating animals; breast-feeding is not recommended during treatment unless the benefit outweighs the risk.

4.7 Effects on ability to drive and use machines

Pranlukast has no or negligible influence on the ability to drive and use machines. However, dizziness or somnolence has been reported occasionally; affected patients should exercise caution.

4.8 Undesirable effects

The adverse reactions are listed below by System Organ Class and frequency, defined as: common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100) and not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reaction
Blood and lymphatic system disorders	Not known	Thrombocytopenia, leucopenia, eosinophilia
Immune system disorders	Uncommon	Hypersensitivity reactions
	Not known	Anaphylaxis, angioedema
Hepatobiliary disorders	Uncommon	Increased hepatic enzymes (AST, ALT, alkaline phosphatase)
	Not known	Hepatic dysfunction, jaundice, fulminant hepatitis, hepatic failure
Nervous system disorders	Uncommon	Headache, dizziness, insomnia, somnolence
Respiratory, thoracic and	Not known	Churg-Strauss syndrome, eosinophilic pneumonia,

System Organ Class	Frequency	Adverse reaction
mediastinal disorders		interstitial pneumonia
Gastrointestinal disorders	Common	Diarrhoea, abdominal pain, nausea, vomiting, dyspepsia
	Uncommon	Constipation, gastric discomfort
Skin and subcutaneous tissue disorders	Uncommon	Rash, pruritus, urticaria
	Not known	Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme
Musculoskeletal and connective tissue disorders	Not known	Rhabdomyolysis, myalgia
General disorders and administration site conditions	Uncommon	Malaise, oedema

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the National Regulatory Authority.

4.9 Overdose

There is limited experience of overdose with pranlukast. Treatment should be symptomatic and supportive; the patient should be monitored and appropriate measures instituted as required. There is no specific antidote.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Drugs for obstructive airway diseases, leukotriene receptor antagonists. ATC code: R03DC02.

Pranlukast is an orally active, selective and competitive antagonist of the cysteinyl leukotriene 1 (CysLT1) receptor. The cysteinyl leukotrienes (LTC4, LTD4 and LTE4) are potent mediators of airway inflammation and bronchoconstriction released from mast cells and eosinophils. By blocking their action at the CysLT1 receptor, pranlukast inhibits leukotriene-mediated bronchoconstriction, airway oedema, mucus secretion and inflammatory cell infiltration, thereby improving asthma control and reducing the symptoms of allergic rhinitis. Because a Western (MHRA/EMA) reference SmPC does not exist for pranlukast, the content of this document is based on the approved Asian (PMDA-type) labelling and well-established leukotriene-receptor-antagonist class properties.

5.2 Pharmacokinetic properties

Pranlukast is absorbed after oral administration, with peak plasma concentrations generally reached within a few hours; absorption is enhanced when taken after food, which is the recommended method of administration. It is highly bound to plasma proteins, is metabolised in the liver principally by CYP3A4, and is excreted predominantly in the faeces via the bile, with a terminal elimination half-life of the order of several hours.

5.3 Preclinical safety data

Non-clinical data from repeated-dose toxicity, genotoxicity and reproductive-toxicity studies reveal no special hazard for humans at clinically relevant exposures beyond that reflected in other sections of this Summary of Product Characteristics; hepatic changes were observed in animals at high doses, consistent with the principal route of elimination.

6. Pharmaceutical particulars

6.1 List of excipients

The full quantitative list of excipients was not provided in the source registration record and should be inserted verbatim from the applicant's finished-product formulation (3.2.P.1). Any excipient of known effect present (for example a sugar such as sucrose, or a colouring agent) must additionally be declared in section 2 and warned in section 4.4.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

To be confirmed from the applicant's stability data.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture. Keep out of the reach and sight of children.

6.5 Nature and contents of container

Unit-dose sachets of printed, triple-laminated foil containing 50 mg, 70 mg or 100 mg of pranlukast, presented in a carton together with the package insert.

6.6 Special precautions for disposal and other handling

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

7. Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Cadila Pharmaceutical (E.A.) Ltd.

Manufacturer

Cadila Pharmaceuticals Ltd, 1389, Trasad Road, Dholka 387810, Dist. Ahmedabad, Gujarat, India.

8. Marketing Authorisation Number

H2022/CTD6404/12643

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text