PROFESSIONAL INFORMATION

SCHEDULING STATUS: S2

1 NAME OF THE MEDICINE

DEHRIN® SOLUTION

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of DEHRIN SOLUTION contains 2,5 mg desloratadine.

Contains sugar (147,15 mg sorbitol per ml), sweetener (1 mg sucralose per ml) and propylene glycol (102,30 mg per ml oral solution).

Contains sodium (4,4 mg per ml oral solution).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution

DEHRIN SOLUTION is a clear colourless solution, free from foreign matter.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

DEHRIN SOLUTION is used in the symptomatic relief of seasonal allergic rhinitis.

4.2 Posology and method of administration

Children 2 to 5 years old

2,5 ml (1,25 mg) once daily with or without food.

Children 6 to 11 years old

5 ml (2,5 mg) once daily with or without food.

Adults and children 12 years of age and older

10 ml (5 mg) once daily with or without food.

Patients with mild to moderate hepatic impairment or renal impairment should initially receive the recommended dose every other day.

Safety and efficacy have not been established for treatment periods in excess of 4 weeks.

4.3 Contraindications

- Hypersensitivity to desloratadine, loratadine or any of the excipients of DEHRIN SOLUTION (see section 6.1).
- Cross sensitivity to other antihistamines.

4.4 Special warnings and precautions for use

Seizures

DEHRIN SOLUTION should be used with caution in patients with a medical or familial history of seizures, and mainly young children (see section 4.8), being more susceptible to develop new seizures under DEHRIN SOLUTION treatment. Healthcare providers may consider discontinuing DEHRIN SOLUTION in patients who experience a seizure while on treatment.

Efficacy and safety of DEHRIN SOLUTION in children under 2 years of age have not been reported to be established.

Safety and efficacy of DEHRIN SOLUTION have not been reported to be established for treatment periods in excess of 4 weeks for allergic rhinitis.

Hepatic function and/or renal function impairment

Dosage adjustment is recommended for patients with hepatic or renal function impairment.

In the case of severe renal insufficiency, DEHRIN SOLUTION should be used with caution.

Impaired metabolism of desloratadine

Patients that are slow metabolisers of desloratadine may be more susceptible to dose-related adverse events.

Weight gain

Increased appetite and weight gain have been reported (see section 4.8).

Use in the elderly

In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or with concomitant medicines.

Paediatric population

In children under 2 years of age, the diagnosis of allergic rhinitis is particularly difficult to distinguish from other forms of rhinitis. The absence of upper respiratory tract infection or structural abnormalities, as well as patient history, physical examinations, and appropriate laboratory and skin tests should be considered.

Approximately 6 % of adults and children 2 to 11 years of age are reported to be phenotypic poor metabolisers of desloratadine and exhibit a higher exposure. The safety of desloratadine (contained in DEHRIN SOUTION) in children 2 to 11 years of age who are poor metabolisers is reported to be the same as in children who are normal metabolisers. The effects of desloratadine in poor metabolisers < 2 years of age have not been reported.

Increased appetite and weight gain have been reported in children (see section 4.8). Weight should be monitored, and cardiovascular effects assessed from time to time.

Skin tests

DEHRIN SOLUTION should be discontinued prior to skin tests using allergen extracts as it may inhibit the cutaneous histamine response, thus producing false negative results. DEHRIN SOLUTION should be discontinued at least 48 hours before the test.

Excipients

Sucralose

DEHRIN SOLUTION contains 1 mg sucralose per ml solution.

Sorbitol

DEHRIN SOLUTION contains 147,15 mg sorbitol in each ml of solution.

Sorbitol is a source of fructose. Patients with rare hereditary fructose intolerance (HFI) should not take DEHRIN SOLUTION.

The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be considered.

The content of sorbitol in medicines for oral use may affect the bioavailability of other medicines for oral use administered concomitantly.

Propylene glycol

DEHRIN SOLUTION contains 102,3 mg propylene glycol in each ml of oral solution.

Co-administration with any substrate for alcohol dehydrogenase, such as ethanol, may induce adverse effects in children less than 5 years old.

Sodium

DEHRIN SOLUTION contains 4,4 mg sodium per 1 ml oral solution. This is less than 1 mmol sodium per ml oral solution, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicines and other forms of interaction

Laboratory test interactions

DEHRIN SOLUTION may suppress the cutaneous histamine response to allergen extracts and should be stopped several days before skin testing.

Other interactions

Desloratadine taken concomitantly with alcohol reportedly did not potentiate the performance impairing effects of alcohol. However, cases of alcohol intolerance and intoxication have been reported during post-marketing use. Therefore, caution is recommended if alcohol is taken concomitantly.

There was no effect of food or grapefruit juice reported on the disposition of desloratadine.

It is reported that co-administration of desloratadine with ketoconazole increases the maximum desloratadine concentration (C_{max}) by 45 % and the area under the time concentration curve (AUC) by 37 %.

It is reported that co-administration of desloratadine with erythromycin increased the C_{max} of desloratadine by 24 % and the AUC by 14 %.

Co-administration of desloratadine with azithromycin reportedly resulted in an increase of both C_{max} (31 %) and AUC (12 %) of azithromycin.

The increase in C_{max} and AUC of desloratadine when co-administered with either ketoconazole or erythromycin reportedly did not cause any clinically relevant adverse events in the populations studied.

Co-administration of cimetidine with desloratadine reportedly did not significantly affect the pharmacokinetics of desloratadine.

Co-administration of fluoxetine with desloratadine reportedly caused an increase in the C_{max} of desloratadine by 15 % and an increase of 13 % in AUC and 17 % in C_{max} of 3-0H desloratadine respectively.

The C_{max} and AUC of fluoxetine were reportedly reduced by 9 % and 11 % respectively. The corresponding mean parameters of norfluoxetine increased by 23 % and 18 % respectively with co-administration of desloratadine and fluoxetine.

No clinically relevant changes in desloratadine plasma concentrations were reported in multiple-dose ketoconazole, erythromycin, azithromycin, fluoxetine and cimetidine interaction trials.

Paediatric population

Interaction studies have only been reported in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

DEHRIN SOLUTION should not be used during pregnancy. Safety and efficacy in pregnancy have not been established.

Breastfeeding

Desloratadine and its metabolites have been detected in breast milk.

Small amounts of DEHRIN SOLUTION entering the breast milk may cause drowsiness or excitement in infants.

DEHRIN SOLUTION should not be used during lactation.

Safety and efficacy in lactation have not been established.

Fertility

There are no data reported on male and female fertility.

4.7 Effects on ability to drive and use machines

DEHRIN SOLUTION lacks significant sedative effects. Patients should however be warned that a small number of individuals may experience sedation and dizziness. It is therefore advisable to determine individual response before driving or performing complicated tasks.

4.8 Undesirable effects

The following undesirable effects have been observed during treatment with DEHRIN SOLUTION:

Summary of the safety profile

Paediatric population

In reported clinical trials in a paediatric population, the desloratadine as in DEHRIN SOLUTION formulation was administered to children aged 6 months through 11 years. The overall incidence of adverse events in children 2 through 11 years of age was similar for the desloratadine and the placebo groups. In infants and toddlers aged 6 to 23 months, the most frequent adverse reactions reported in excess of placebo were diarrhoea, fever and insomnia. In an additional reported study, no adverse events were seen in persons between 6 and 11 years of age following a single 2,5 mg dose of desloratadine oral solution.

In a reported clinical trial with adolescent patients, 12 through 17 years of age, the most common adverse event was headache; this occurred in 5,9 % of patients treated with desloratadine and 6,9 % of patients receiving placebo.

Adults and adolescents

At the recommended dose, in reported clinical trials involving adults and adolescents in a range of indications including allergic rhinitis, undesirable effects with desloratadine were reported in 3 % of patients in excess of those treated with placebo. The most frequent adverse events reported in excess of placebo were fatigue, dry mouth and headache.

Tabulated summary of adverse reactions

Blood and the lymphatic system disorders

Less frequent: Blood disorders, including agranulocytosis, leucopenia, haemolytic anaemia, thrombocytopenia.

Immune system disorders

Less frequent: Hypersensitivity reactions including bronchospasm, anaphylaxis, angioedema, dyspnoea, pruritus, rash and urticaria.

Metabolism and nutrition disorders

Frequency unknown: Increased appetite (see section 4.4).

Psychiatric disorders

Less frequent: Hallucinations.

Frequency unknown: Depression, abnormal behaviour, aggression.

Nervous system disorders

Frequent: Headache.

Insomnia *(frequent in children less than 2 years)*

Less frequent: Dizziness, somnolence, insomnia, psychomotor hyperactivity, seizures.

Frequency unknown: Paraesthesia, extrapyramidal effects, tremor.

Eye disorders

Less frequent: Blurred vision.

Ear and labyrinth disorders

Frequency unknown: Tinnitus.

Cardiac disorders

Less frequent: Tachycardia, palpitations, dysrhythmia.

Frequency unknown: QT prolongation, bradycardia.

Vascular disorders

Less frequent: Hypotension.

Respiratory, thoracic and mediastinal disorders

Frequent: Pharyngitis.

Frequency unknown: Dyspnoea.

Gastrointestinal disorders

Frequent: Dry mouth, diarrhoea *(frequent in children less than 2 years)*.

Less frequent: Abdominal or stomach pain, dyspepsia, nausea, vomiting, diarrhoea, anorexia.

Hepatobiliary disorders

Less frequent: Elevations in liver enzymes, increased bilirubin, hepatitis.

Frequency unknown: Jaundice.

Skin and subcutaneous tissue disorders

Less frequent: Urticaria, pruritus, rash, alopecia.

Frequency unknown: Photosensitivity.

Musculoskeletal, connective tissue and bone disorders

Less frequent: Myalgia.

Reproductive system and breast disorders

Less frequent: Dysmenorrhoea.

General disorders and administrative site conditions

Frequent: Fatigue, fever *(frequent in children less than 2 years).*

Frequency unknown: Oedema, sweating, asthenia.

Investigations

Frequency unknown: Increased weight.

Paediatric population

Other undesirable effects reported during the post-marketing period in paediatric patients with an unknown frequency included QT prolongation, dysrhythmia, bradycardia, abnormal behaviour, and aggression.

A reported retrospective observational safety study indicated an increased incidence of new-onset seizure in patients 0 to 19 years of age when receiving desloratadine as in DEHRIN SOLUTION compared with periods not receiving desloratadine. Among children 0 to 4 years old, the adjusted absolute increase was 37,5 (95 % Confidence Interval (CI) 10,5 - 64,5) per 100 000 person years (PY) with a background rate of new-onset seizure of 80,3 per 100 000 PY. Among patients 5 to 19 years of age, the adjusted absolute increase was 11,3 (95 % CI 2,3 - 20,2) per 100 000 PY with a background rate of 3,4 per 100 000 PY.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and e-Reporting platform (who-umc.org) found on the SAHPRA website.

4.9 Overdose

Symptoms

Increase in mean heart rate, tachycardia, somnolence. In children, extrapyramidal manifestations and palpitations have been reported.

Treatment

Desloratadine and 3-hydroxydesloratadine are not eliminated by haemodialysis. It is not known if desloratadine is eliminated by peritoneal dialysis.

Supportive care

Treatment should be symptomatic and supportive. Patients in whom intentional overdose is confirmed or suspected should be referred for psychiatric consultation.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A.5.7.1 Antihistaminics

Pharmacotherapeutic group: antihistamines – H1 antagonist, ATC code: R06AX27

Desloratadine is a non-sedating long-acting tricyclic second generation histamine antagonist with selective H_1-receptor histamine antagonist activity. Desloratadine has been shown to have antihistaminic, anti-allergic and anti-inflammatory activity.

Desloratadine exerts its action by competing with histamine for H_1-receptor sites on effector cells. It prevents but does not reverse responses mediated by histamine. Desloratadine inhibited histamine release from human mast cells *in vitro.*

Desloratadine does not readily cross the blood-brain barrier.

5.2 Pharmacokinetic properties

Absorption

After oral administration, desloratadine is well absorbed from the gastrointestinal tract and can be detected within 30 minutes of administration. Peak plasma concentrations are reached within approximately 3 hours. Neither food nor grapefruit juice had an effect on the bioavailability of desloratadine. The bioavailability of desloratadine is dose proportional over the range of 5 mg to 20 mg.

Distribution

At therapeutic concentrations, about 82 to 87 % of desloratadine is protein bound.

Metabolism

Desloratadine is extensively metabolised to 3-hydroxydesloratadine, an active metabolite, which is subsequently glucuronidated.

Elimination

The mean elimination half-life of desloratadine is approximately 27 hours. Desloratadine is mainly excreted in the urine.

Desloratadine and 3-hydroxydesloratadine were not removed by haemodialysis. The duration of action is up to 24 hours as determined in histamine skin wheal studies.

Hepatic impairment

Desloratadine is eliminated more slowly during severe liver disease. Dosage adjustment for patients with hepatic impairment is recommended.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate, disodium edetate, hypromellose 2910, propylene glycol (10,23 %), purified water, sodium citrate, sorbitol, sucralose and Tutti Frutti flavouring.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in the original packaging at or below 25 °C.

Keep bottle in carton until required for use. Keep the bottle tightly closed.

Use within 4 months from first opening.

6.5 Nature and contents of container

DEHRIN SOLUTION is supplied in amber glass bottles closed with a white round plastic child resistant (C/R) screw closure consisting of an outer and an inner layer of polypropylene and polyethylene respectively in six different volume sizes, i.e. 50, 60, 100, 120, 150 and 300 ml. The bottles are subsequently packed into cardboard boxes. All packages are supplied with an oral measuring syringe with a final volume of 5 ml marked on every 0,5 ml. Not all pack sizes may necessarily be marketed at any one time.

6.6 Special precautions for disposal and other handling

No special requirements.

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

7 HOLDER OF CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER

46/5.7.1/0004

9 DATE OF FIRST AUTHORISATION

11 June 2015

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12 March 2025