Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Telfast 30 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 30 mg of fexofenadine hydrochloride, which is equivalent to 28 mg of fexofenadine.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

Peach round film-coated tablet debossed with "03" on one side and a scripted "e" on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Telfast 30 mg is indicated in children aged 6 to 11 for the relief of symptoms associated with seasonal allergic rhinitis.

4.2 Posology and method of administration

Posology
Paediatric population

- Children 6 to 11 years of age

The recommended dose of fexofenadine hydrochloride in children aged 6 to 11 years is 30 mg twice daily.

- Children under 6 years of age
The efficacy of fexofenadine hydrochloride has not been established in children under 6 years of age.

Special populations
The safety and efficacy of fexofenadine hydrochloride in renally or hepatically impaired children have not been established (see section 4.4 Special Warnings and Precautions for Use). Studies conducted in adults in special risk groups (renally or hepatically impaired patients) indicate that it is not necessary to adjust the dose of fexofenadine hydrochloride in adults.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

The safety and efficacy of fexofenadine hydrochloride in renally or hepatically impaired children have not been established (see section 4.2, Posology and Method of Administration). Fexofenadine hydrochloride should be administered with caution in these patients.

Patients with a history of or ongoing cardiovascular disease should be warned that, antihistamines as a medicine class, have been associated with the adverse reactions, tachycardia and palpitations (see section 4.8 Undesirable Effects).

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

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

Fexofenadine does not undergo hepatic biotransformation and therefore will not interact with other medicinal products through hepatic mechanisms.

Fexofenadine is a P-glycoprotein (P-gp) and organic-anion-transporting polypeptide (OATP) substrate. Concomitant use of fexofenadine with P-gp inhibitors or inducers can affect the exposure to fexofenadine. Co-administration of fexofenadine hydrochloride with P-gp inhibitors erythromycin or ketoconazole has been found to result in a 2-3 times increase in the level of fexofenadine in plasma. The changes were not accompanied by any effects on the QT interval and were not associated with any increase in adverse reactions compared to the medicinal products given singly.

A clinical drug-drug interaction study showed that co-administration of apalutamide (a weak inducer of P-gp) and a single oral dose of 30 mg fexofenadine resulted in a 30 % decrease in AUC of fexofenadine.

No interaction between fexofenadine hydrochloride and omeprazole was observed. However, the administration of an antacid containing aluminium and magnesium hydroxide gels 15 minutes prior to fexofenadine hydrochloride caused a reduction in bioavailability, most likely due to binding in the gastrointestinal tract. It is advisable to leave 2 hours between administration of fexofenadine hydrochloride and aluminium and magnesium hydroxide containing antacids.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of fexofenadine hydrochloride in pregnant women. Limited animal studies do not indicate direct or indirect harmful effects with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3 Preclinical safety data). Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary.

Breastfeeding
There are no data on the content of human milk after administering fexofenadine hydrochloride. However, when terfenadine was administered to nursing mothers fexofenadine was found to cross into human breast milk. Therefore fexofenadine hydrochloride is not recommended for mothers breast-feeding their babies.

Fertility
No human data on the effect of fexofenadine hydrochloride on fertility are available. In mice, there was no effect on fertility with fexofenadine hydrochloride treatment (see section 5.3).

4.7 Effects on ability to drive and use machines

On the basis of the pharmacodynamic profile and reported adverse reactions it is unlikely that fexofenadine hydrochloride tablets will produce an effect on the ability to drive or use machines.
In objective tests, Telfast has been shown to have no significant effects on central nervous system function. This means that patients may drive or perform tasks that require concentration. However, in order to identify sensitive people who have an unusual reaction to medicinal products, it is advisable to check the individual response before driving or performing complicated tasks.

4.8 Undesirable effects

The following frequency rating has been used, when applicable:
very common ≥1/10; common ≥1/100 and <1/10; uncommon ≥1/1,000 and <1/100; rare ≥1/10,000 and <1/1,000; very rare <1/10,000 and not known (frequency cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

In controlled clinical trials in children aged 6 to 11 years, the most commonly reported adverse reaction considered at least possibly related to fexofenadine hydrochloride by the investigator was headache. The incidence of headache in pooled data from clinical trials was 1.0% for patients taking fexofenadine hydrochloride 30 mg (673 children) and for patients taking placebo (700 children). There are no clinical safety data in children treated with fexofenadine hydrochloride for periods longer than two weeks

In controlled clinical trials in 845 children aged 6 months to 5 years with allergic rhinitis, 415 children were administered 15 mg or 30 mg of fexofenadine hydrochloride (capsule content sprinkled onto dosing vehicle) and 430 children were administered placebo. There were no unexpected adverse reactions in the children treated with fexofenadine and the adverse event profile was similar to that of older children and adults (see section 4.2 Posology and Method of Administration).
In adults, the following undesirable effects have been reported in clinical trials, with an incidence similar to that observed with placebo:

Nervous system disorders
Common: headache, drowsiness, dizziness

Gastrointestinal disorders
Common: nausea

General disorders and administration site conditions
Uncommon: fatigue

In adults, the following undesirable effects have been reported in post-marketing surveillance. The frequency with which they occur is not known (cannot be estimated from available data):

Immune system disorders
hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis

Psychiatric disorders
insomnia, nervousness, sleep disorders or nightmares/excessive dreaming (paroniria).

Cardiac disorders
tachycardia, palpitations

Gastrointestinal disorders
diarrhoea

Skinandsubcutaneoustissuedisorders
rash, urticaria, pruritus

Eye disorders
Not known: Vision blurred

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 via HPRA Pharmacovigilance. Website: www.hpra.ie

4.9 Overdose

Dizziness, drowsiness, fatigue and dry mouth have been reported with overdose of fexofenadine hydrochloride. Doses up to 60 mg twice daily for two weeks have been administered to children, and single doses up to 800 mg and doses up to 690 mg twice daily for 1 month or 240 mg once daily for 1 year have been administered to healthy adult subjects without the development of clinically significant adverse reactions as compared with placebo. The maximum tolerated dose of fexofenadine hydrochloride has not been established.

Standard measures should be considered to remove any unabsorbed medicinal product. Symptomatic and supportive treatment is recommended. Haemodialysis does not effectively remove fexofenadine hydrochloride from blood.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use, ATC code: R06A X26

Mechanism of action
Fexofenadine hydrochloride is a non-sedating H_1 antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.

Clinical efficacy and safety
In children aged 6 to 11 years, the suppressive effects of fexofenadine hydrochloride on histamine – induced wheal and flare were comparable to that in adults at similar exposure. Inhibition of histamine-induced wheal and flare was observed at one hour post dose following single doses of 30 and 60 mg fexofenadine hydrochloride. Peak inhibitory effects of fexofenadine generally occurred at 3-6 hours post dose.

In a pooled analysis of three placebo-controlled double-blind phase III studies, involving 1369 children with seasonal allergic rhinitis aged 6 to 11 years, fexofenadine hydrochloride at 30 mg twice daily was significantly better than placebo in reducing total symptom score (p=0.0001). All individual component symptoms including rhinorrhea (p=0.0058), sneezing (p=0.0001), itchy/ watery/red eyes (p=0.0001), itchy nose/palate and throat (p=0.0001), and nasal congestion (p=0.0334) were significantly improved by fexofenadine hydrochloride.

In children aged 6 to 11 years, no significant differences in QT_c were observed following up to 60 mg fexofenadine hydrochloride twice daily for two weeks compared with placebo.No significant differences in QT_c intervals were observed in adult and adolescent patients with seasonal allergic rhinitis, when given fexofenadine hydrochloride up to 240 mg twice daily for 2 weeks when compared with placebo. Also, no significant change in QT_c intervals was observed in healthy adult subjects given fexofenadine hydrochloride up to 60 mg twice daily for 6 months, 400 mg twice daily for 6.5 days and 240 mg once daily for 1 year, when compared with placebo. Fexofenadine at concentrations 32 times greater than the therapeutic concentration in man had no effect on the delayed rectifier K+ channel cloned from human heart.

5.2 Pharmacokinetic properties

Absorption
Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with Tmax occurring at approximately 1-3 hours post dose. In children, the mean Cmax value was approximately 128 ng/ml following a single dose oral administration of 30 mg Fexofenadine hydrochloride.
A dose of 30 mg BID was determined to provide plasma levels (AUC) in paediatric patients which are comparable to those achieved in adults with the approved adult regimen of 120 mg once daily.

Distribution
After oral administration in adults, Fexofenadine is 60-70% plasma protein bound.

Biotransformation and elimination
Fexofenadine undergoes negligible metabolism (hepatic or non-hepatic), as it was the only major compound identified in urine and faeces of animals and man. The plasma concentration profiles of Fexofenadine follow a bi-exponential decline with a terminal elimination half-life ranging from 11 to 15 hours after multiple dosing. The single and multiple dose pharmacokinetics of Fexofenadine are linear for oral doses up to 120 mg BID. A dose of 240 mg BID produced slightly greater than proportional increase (8.8%) in steady state area under the curve, indicating that Fexofenadine pharmacokinetics are practically linear at these doses between 40 mg and 240 mg taken daily. The major route of elimination is believed to be via biliary excretion while up to 10% of ingested dose is excreted unchanged through the urine.

5.3 Preclinical safety data

Dogs tolerated 450 mg/kg administered twice daily for 6 months and showed no toxicity other than occasional emesis. Also, in single dose dog and rodent studies, no treatment-related gross findings were observed following necropsy.
Radiolabelled Fexofenadine hydrochloride in tissue distribution studies of the rat indicated that Fexofenadine did not cross the blood brain barrier.
Fexofenadine hydrochloride was found to be non-mutagenic in various *in vitro* and *in vivo* mutagenicity tests.
The carcinogenic potential of Fexofenadine hydrochloride was assessed using terfenadine studies with supporting pharmacokinetic studies showing Fexofenadine hydrochloride exposure (via plasma AUC values). No evidence of carcinogenicity was observed in rats and mice given terfenadine (up to 150 mg/kg/day).
In a reproductive toxicity study in mice, Fexofenadine hydrochloride did not impair fertility, was not teratogenic and did not impair pre- or postnatal development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core :
Microcrystalline Cellulose
Pregelatinised Starch
Croscarmellose Sodium
Magnesium Stearate

Film coat:
Hypromellose
Povidone
Titanium Dioxide (E171)
Colloidal Anhydrous Silica
Macrogol
Pink Iron oxide (E172) blend
Yellow Iron oxide (E172) blend.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PE/PVDC/Al blisters, packaged into cardboard boxes. 1, 2, 4, 8, 10 or 15 (sample only); 20, 30, 40, 50, 60 and 100 tablets per package.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Opella Healthcare France SAS
157 avenue Charles de Gaulle
92200 Neuilly-sur-Seine
France

8 MARKETING AUTHORISATION NUMBER

PA23180/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 February 2004
Date of last renewal: 08 December 2014

10 DATE OF REVISION OF THE TEXT