Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Telfast 180mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 180 mg of fexofenadine hydrochloride, which is equivalent to 168 mg of fexofenadine.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Product imported from the UK

Film coated tablets.
Peach capsule-shaped, film-coated tablet debossed with "018" on one side and a scripted "e" on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Relief of symptoms associated with chronic idiopathic urticaria.

4.2 Posology and method of administration

Adults and children aged 12 years and over

The recommended dose of fexofenadine hydrochloride for adults and children aged 12 years and over is 180 mg once daily taken before a meal.

Fexofenadine is a pharmacologically active metabolite of terfenadine.

Children under 12 years of age

The efficacy and safety of fexofenadine hydrochloride has not been studied in children under 12.

Special risk groups

Studies in special risk groups (elderly, renally or hepatically impaired patients) indicate that it is not necessary to adjust the dose of fexofenadine hydrochloride in these patients.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

As with most new drugs there is only limited data in the elderly and renally or hepatically impaired patients. Fexofenadine hydrochloride should be administered with care in these special groups.

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

4.5 Interaction with other medicinal products and other forms of interaction

Fexofenadine does not undergo hepatic biotransformation and therefore will not interact with other drugs through hepatic mechanisms. Coadministration of fexofenadine hydrochloride with 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 events compared to the drugs given singly.

Animal studies have shown that the increase in plasma levels of fexofenadine observed after coadministration of erythromycin or ketoconazole, appears to be due to an increase in gastrointestinal absorption and either a decrease in biliary excretion or gastrointestinal secretion, respectively.

No interaction between fexofenadine 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).* Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary.

Lactation
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.

4.7 Effects on ability to drive and use machines

On the basis of the pharmacodynamic profile and reported adverse events 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 drugs, it is advisable to check the individual response before driving or performing complicated tasks.

4.8 Undesirable effects

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 (≥1/100 to <1/10): headache, drowsiness, dizziness

Gastrointestinal disorders
Common (≥1/100 to <1/10): nausea

General disorders and administration site conditions
Uncommon (≥1/1000 to <1/100): 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

Skin and subcutaneous tissue disorders
rash, urticaria, pruritus

4.9 Overdose

Dizziness, drowsiness, fatigue and dry mouth have been reported with overdose of fexofenadine hydrochloride. 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 subjects without the development of clinically significant adverse events as compared with placebo. The maximum tolerated dose of fexofenadine hydrochloride has not been established.

Standard measures should be considered to remove any unabsorbed drug. 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

Fexofenadine hydrochloride is a non-sedating H_1 antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.
Human histamine wheal and flare studies following single and twice daily doses of fexofenadine hydrochloride demonstrate that the drug exhibits an antihistaminic effect beginning within one hour, achieving maximum at 6 hours and lasting 24 hours. There was no evidence of tolerance to these effects after 28 days of dosing. A positive dose-response relationship between doses of 10 mg to 130 mg taken orally was found to exist. In this model of antihistaminic activity, it was found that doses of at least 130 mg were required to achieve a consistent effect that was maintained over a 24 hour period. Maximum inhibition in skin wheal and flare areas were greater than 80%.

No significant differences in QT_c intervals were observed in seasonal allergic rhinitis patients given fexofenadine hydrochloride up to 240 mg twice daily for 2 weeks when compared to placebo. Also, no significant change in QT_c intervals was observed in healthy 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 to 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.

Fexofenadine hydrochloride (5-10 mg/kg po) inhibited antigen induced bronchospasm in sensitised guinea pigs and inhibited histamine release at supratherapeutic concentrations (10-100 µM) from peritoneal mast cells.

5.2 Pharmacokinetic properties

Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with T_{max} occurring at approximately 1-3 hours post dose. The mean C_{max} value was approximately 494 ng/ml following the administration of a 180 mg dose once daily.

Fexofenadine is 60-70% plasma protein bound. 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 maize starch
Croscarmellose sodium
Magnesium stearate

Film coat:
Hypromellose
Povidone
Titanium dioxide (E171)
Colloidal anhydrous silica
Macrogol 400
Iron oxide (E172)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

The shelf-life expiry date of this product shall be the date shown on the over labelled blister and outer package of the product on the market in the country of origin.

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 over-labelled cardboard boxes.
30 tablets per pack.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 PARALLEL PRODUCT AUTHORISATION HOLDER

McDowell Pharmaceuticals
4 Altona Road
Lisburn
N.Ireland
BT27 5QB

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA 1473/052/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of frst authorisation: 23rd September 2011.

10 DATE OF REVISION OF THE TEXT

September 2013