SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Fexofenadine 180 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 180 mg of fexofenadine hydrochloride equivalent to 168 mg of fexofenadine.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet

Yellow coloured, oblong, bi-convex film coated tablet; plain on one side with a central breakline on the other. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic relief of chronic idiopathic urticaria.

4.2 Posology and method of administration

Posology

Adults and children 12 years and older:

The recommended dose of fexofenadine hydrochloride to adults and children 12 years and older is 180 mg once daily.

Children under 12 years:

The efficacy and safety of fexofenadine hydrochloride 180 mg has not been studied in children under 12.

Special populations at risk:

Only limited data is available regarding the administration in elderly and in patients with renal or hepatic impairment. It is not necessary to adjust the dose of fexofenadine hydrochloride in these patient groups, however, it should be used with caution in these patient groups.

Method of administration
The tablet should be swallowed with a sufficient amount of water

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

Only limited data is available regarding the administration in elderly and in patients with renal or hepatic impairment. Fexofenadine hydrochloride should be administered with care in these patient 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).

Excipient(s)
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

Fexofenadine does not undergo hepatic biotransformation, and therefore will not interact with other medicinal products through hepatic mechanisms. Fexofenadine is a P-gp and OATP substrate.

Co-administration of fexofenadine with erythromycin or ketoconazole has been found to result in 2-3 fold 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 medicinal products given singly.
Animal studies have shown that the increase in plasma levels of fexofenadine observed after co administration 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.

Also single dose of lopinavir and ritonavir combination (400 mg/100 mg) has been found to increase the AUC of fexofenadine 4.0-fold, while the steady–state lopinavir/ritonavir increased the fexofenadine AUC by 2.9-fold. Thus the adverse effects of fexofenadine may increase. No pharmacodynamic interaction is known.

No interactions between fexofenadine and omeprazole was observed. However administration of an antacid containing aluminium and magnesium hydroxide gels15 min. prior to fexofenadine caused a reduction in the bioavailability of fexofenadine, most likely due to binding in the gastrointestinal tract. It is advisable to leave 2 hours

between administration of fexofenadine and aluminium and magnesium hydroxide containing antacids.

Allergy tests: Use of fexofenadine hydrochloride must be discontinued three days before allergy tests (s.c. pricktest).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of fexofenadine 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 should not be used during pregnancy unless clearly necessary.

Breast-feeding
There are no data on the content in human milk after administration of fexofenadine. However, when terfenadine was administered to nursing mothers, fexofenadine was found to cross into human breast milk. Therefore, it is not recommended to administer fexofenadine to breast-feeding mothers.

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 tablets will produce an effect on the ability to drive or use machines.

In objective tests, fexofenadine 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

The adverse effects are classified below by system organ class according to the following convention:

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)

Immune system disorders

Rare: Hypersensitivity reactions with manifestations such as angio-oedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis

Psychiatric disorders

Uncommon: Insomnia, sleep disorders or nightmares/excessive dreaming (paroniria), nervousness

Nervous system disorders

Common: Headache (7.3%), drowsiness (2.3%), dizziness (1.5%)

Gastrointestinal disorders

Common: Nausea (1.5%), dry mouth (3-5%)

Not known: Diarrhoea

Skin and subcutaneous tissue disorders

Rare: Rash, urticaria, pruritus

Cardiovascular disorders
Uncommon: Tachycardia, palpitations

General disorders and administration site conditions
Uncommon: Fatigue

In controlled clinical trials, the incidence of the common adverse events was similar to that observed with placebo.

Events that have been reported with incidences less than 1% and similar to placebo in controlled trials have also been reported rarely during post marketing surveillance.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms: Dizziness, drowsiness, fatigue and dry mouth have been reported with an overdose of fexofenadine. 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 a month, or 240 mg once daily for 1 year, were administered to healthy adult subjects without the development of clinically significant adverse events as compared with placebo. The maximum tolerated dose of fexofenadine has not been established.

Treatment: In the event of overdose, consider standard measures to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended. Haemodialysis does not effectively eliminate fexofenadine from blood.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antihistamines for systemic use,

ATC-code: R 06 AX 26

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

No changes in the QT_c interval were observed in patients with seasonal allergic rhinitis, who were treated with fexofenadine hydrochloride 240 mg twice daily for two weeks, compared with placebo. Also, no significant changes in the QT_c interval compared to placebo were observed in healthy volunteers, who received up to 60 mg fexofenadine hydrochloride twice daily for 6 months, 400 mg twice daily for 6.5 days and 240 mg once daily for a year.

Fexofenadine concentrations 32 times higher than the therapeutical level in humans did not affect the delayed-rectifier K^+-channel cloned from a human heart.

5.2 Pharmacokinetic properties

Absorption and distribution
Fexofenadine hydrochloride is rapidly absorbed following oral administration. T_{max} is reached approx. 1-3 hours post-dose. Mean value for C_{max} was approx. 494 ng/ml after administration of 180 mg once daily.

Fexofenadine is 60% to 70% bound to plasma proteins.

Biotransformation

Fexofenadine is only metabolised to a limited degree (hepatic or non-hepatic) and was the only major compound found in urine and faeces in animals and humans. The profile for the plasma concentration of fexofenadine follows a bi-exponential decline with a terminal half-life of 11-15 hours after multiple dosing.

Linearity/non-linearity
Single or multiple dose pharmacokinetics for fexofenadine are linear for oral doses of up to 120 mg twice daily. At a dose of 240 mg given twice daily a slightly larger increase was observed (8.8 %) than the proportional increase for the steady state area under the curve, which could indicate that the pharmacokinetics for fexofenadine is linear at doses of 40-240 mg daily.

Elimination
The major route of elimination is presumed to be through biliary excretion, while up to 10% of the administered dose is excreted unchanged through the urine.

5.3 Preclinical safety data

Dogs tolerated doses of 450 mg/kg given twice daily for 6 months and did not exhibit signs of toxicity except for occasional vomiting. No evident treatment related findings in dogs and rodents 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 revealed no evidence of mutagenicity in various *in vitro* and *in vivo* tests.

The carcinogenic potential of fexofenadine was assessed in terfenadine trials by the use of pharmacokinetic tests, which determined the fexofenadine exposure (based on plasma AUC-values). No evidence of carcinogenicity in rats and mice treated with terfenadine (up to 150 mg/kg/day) were observed.

In a reproduction toxicity trial with mice fexofenadine did not impair fertility, was not teratogenic and did not impair the pre- or postnatal development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Microcrystalline cellulose

Croscarmellose sodium

Maize starch

Povidone

Magnesium stearate

Coating:

Hypromellose (E464)

Titanium dioxide (E 171)

Macrogol 400

Macrogol 4000

Iron oxide, yellow (E 172)

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

Blister package. PVC/PVDC/Al blister packed in carton. 2, 7, 10, 15, 20, 30, 50, 100 or 200 (10 x 20) tablets per package.

Not all package sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

TEVA UK Limited

Brampton Road, Hampden Park, Eastbourne,

BN22 9AG, United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00289/1031

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19/03/2010

10 DATE OF REVISION OF THE TEXT

26/05/2020