Applicant: Oethmaan Biosims (Pty) Ltd	**SAHPRA approval date:** 16 August 2022
Product: SENSAFEX 180 mg	**Dosage form and strength:** Each film-coated tablet contains: 180 mg Fexofenadine Hydrochloride

APPROVED PROFESSIONAL INFORMATION - CLEAN

SCHEDULING STATUS:

S1

1. NAME OF THE MEDICINE:

SENSAFEX 180 mg, film-coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

SENSAFEX 180 mg, film-coated tablet:

Each film-coated tablet contains 180 mg fexofenadine hydrochloride.

Contains sugar (lactose monohydrate 228.63 mg).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

SENSAFEX 180 mg, film-coated tablet: Peach coloured capsule shaped film-coated tablets debossed as “180” on one side and “FX” on the other side.

Initial:	16/08/2022

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications

SENSAFEX 180 mg is indicated for the relief of symptoms associated with chronic idiopathic urticaria (CIU).

4.2 Posology and method of administration

Posology

Adults and children aged 12 years and over:

SENSAFEX 180 mg: One 180 mg tablet daily.

Paediatric population:

Children under 12 years of age:

The efficacy and safety of SENSAFEX 180 mg has not been studied in children under the age of 12.

Special risk groups:

See sections 4.4 and 5.2.

Method of administration:

SENSAFEX 180 mg should be taken orally. The tablets should be swallowed with liquid and should not be chewed.

SENSAFEX 180 mg should not be broken because the coating is intended to ensure a prolonged release.

4.3 Contraindications

- SENSAFEX 180 mg is contraindicated in patients with known hypersensitivity to fexofenadine hydrochloride or any of the excipients of SENSAFEX 180 mg listed in section 6.1.
- There is no experience with SENSAFEX 180 mg in pregnant women. SENSAFEX 180 mg should not be taken during pregnancy or by mothers breastfeeding their babies.

4.4 Special warnings and precautions for use

There is only limited data for the use of fexofenadine in elderly and renally or hepatically impaired patients. SENSAFEX 180 mg should be administered with care in these special risk groups.

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

Paediatric population

The safety and efficacy of fexofenadine, as in SENSAFEX 180 mg, has not been studied in children under the age of 12 years.

SENSAFEX 180 mg contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take SENSAFEX 180 mg.

4.5 Interaction with other medicines and other forms of interaction

Fexofenadine, as in SENSAFEX 180 mg does not undergo hepatic biotransformation. Co-administration of SENSAFEX 180 mg with erythromycin or ketoconazole has been found to result in 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 medicines given individually.

It was reported that animal studies have shown that the increase in plasma levels of fexofenadine, as in SENSAFEX 180 mg 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.

No interaction between fexofenadine, as in SENSAFEX 180 mg and omeprazole was observed. However, the administration of antacid containing aluminium and magnesium hydroxide gels 15 minutes prior to fexofenadine hydrochloride, as in SENSAFEX 180 mg caused a reduction in bioavailability, most likely due to binding in the gastrointestinal tract. It is advisable to leave 2 hours between administration of SENSAFEX 180 mg and aluminium and magnesium hydroxide containing antacids.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no experience with fexofenadine, as in SENSAFEX 180 mg, in pregnant women.

SENSAFEX 180 mg should not be taken during pregnancy (see section 4.3).

Limited animal studies do not indicate direct or indirect harmful effects with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development.

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. SENSAFEX 180 mg should not be taken by mothers breastfeeding their babies (see section 4.3).

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

Fexofenadine as in SENSAFEX 180 mg lacks significant sedative effects. Patients should, however, be warned that a small number of individuals may experience sedation. It is therefore advisable to determine individual response before driving or performing complicated tasks.

This effect may be compounded by simultaneous intake of alcohol or other central nervous system depressants.

4.8 Undesirable effects

System Organ Class	Adverse reaction	Frequency
Immune system disorders	Hypersensitivity reactions with	Less frequent

	manifestations such as angioedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis	
Psychiatric disorders	Insomnia, nervousness and sleep disorders or nightmares/excessive dreaming (paroniria).	Less frequent
Nervous system disorders	Headache, drowsiness, dizziness	Frequent
Cardiac disorders	Tachycardia, palpitations	Frequency unknown
Gastrointestinal disorders	Nausea	Frequent
	Diarrhoea	Frequency unknown
Skin and subcutaneous tissue disorder	Rash, urticaria, pruritus	Less frequent
General disorders and administrative site conditions	Fatigue	Less frequent

<u>Reporting of suspected adverse reactions</u>

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare

professionals are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Medicine Reaction Reporting Form"**, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose:

Symptoms:

Most reports of fexofenadine hydrochloride overdose contain limited information. However, dizziness, drowsiness and dry mouth have been reported.

Treatment:

Standard measures should be considered to remove any unabsorbed medicine. Haemodialysis does not effectively remove fexofenadine hydrochloride from blood.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 5.7.1 Antihistaminics

Pharmacotherapeutic group: Antihistamines for systemic use

ATC Code: R06AX26

Fexofenadine hydrochloride is a pharmacologically active metabolite of terfenadine and is a non-sedating, selective histamine H1-receptor antagonist.

Fexofenadine exhibits an antihistaminic effect beginning within one hour, achieving maximum effect at 6 hours and lasting 24 hours. There was no evidence of tolerance to these effects after 28 days of dosing.

5.2 Pharmacokinetic properties

Absorption:

Fexofenadine is 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 427 ng/mL following the administration of a 180 mg dose once daily.

Distribution:

Fexofenadine is 60-70 % plasma protein bound.

Biotransformation:

Fexofenadine undergoes negligible metabolism, as it was the only major compound identified in urine and faeces of animals and man.

Elimination:

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 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 the ingested dose is excreted unchanged through the urine.

Special populations

Effect of age

It was reported that in older subjects (>65 years old), peak plasma levels of fexofenadine were 99 % greater than those observed in normal volunteers (<65 years old). Mean elimination half-lives were similar to those observed in normal volunteers.

Renally impaired

It was reported that in patients with mild (creatinine clearance 41-80 mL/min) to severe (creatinine clearance 11-40 mL/min) renal impairment, peak plasma levels of fexofenadine were 87 % and 111 % greater, respectively and mean elimination half-lives were 59 % and 72 % longer, respectively, than observed in normal volunteers. Peak plasma levels in patients on dialysis (creatinine clearance <10 mL/min) were 82 % greater and half-life was 31 % longer than observed in normal volunteers.

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

Lactose monohydrate, hydroxypropylcellulose, pregelatinised starch, colloidal anhydrous silica, microcrystalline cellulose, croscarmellose sodium, magnesium stearate. Film-coating containing hypromellose, polyvinylpyrrolidone, titanium dioxide, iron oxide red, iron oxide yellow, colloidal anhydrous silica and polyethylene glycol.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

SENSAFEX 180 mg, film-coated tablets:

3 years

6.4 Special precautions for storage

Store at or below 25 °C.

Protect from light and moisture. Store in the original package/container. Keep the HDPE container closed.

Keep the blister in the carton until required for use.

6.5 Nature and contents of container

SENSAFEX 180 mg

1. Alu/PVC/PVDC Blister Pack:

Alu/PVC/PVDC blister pack comprising of hard tempered aluminium foil and thick, white-opaque, well thermoformable PVC film coated with PVDC on outer side. This blister will be further packed in preprinted cartons along with package leaflet.

Pack sizes: 10 and 30 tablets.

2. Alu/PVC/PE/ACLAR Blister Pack:

Alu/PVC/PE/ACLAR blister pack comprising of hard tempered aluminium foil and clear, transparent PVC film coated with ACLAR on other side, sandwiched with PE layer (Triplex film). This blister will be further packed in preprinted cartons along with package leaflet.

Pack sizes: 10 and 30 tablets.

3. High Density Polyethylene (HDPE) Bottle Pack:

White opaque high density polyethylene (HDPE) bottle packs with white opaque polypropylene continuous threaded closure with wad having induction sealing liner.

Pack sizes: 500 and 1000 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Oethmaan Biosims (Pty) Ltd

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Greenacres Office Park

c/o Victory and Rustenburg Roads

Victory Park

Johannesburg

2195

8 REGISTRATION NUMBER(S):

SENSAFEX 180 mg, film-coated tablet: 47/5.7.1/0978

9 DATE OF FIRST AUTHORISATION

Date of registration: 16 August 2022

10 DATE OF REVISION OF THE TEXT

Not applicable