For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

TORKAST-FX

1. Generic Name

Fexofenadine Hydrochloride & Montelukast Tablets

2. Qualitative and quantitative Composition:

Each film coated tablet contains:

Fexofenadine Hydrochloride I.P…….. 120mg

Montelukast sodium I.P.

equivalent to Montelukast…… 10mg

Colours: Yellow oxide of Iron & Titanium dioxide I.P.

The List of excipients used are Hydroxy Propyl Methyl Cellulose, Polyethylene glycol, Titanium Dioxide, Talcum powder, Iron Oxide, Colloidal Silicon Dioxide, Croscarmellose Sodium, Crospovidone, Hydroxy Propyl Cellulose, Lactose, Microcrystalline Cellulose, Magnesium Stearate, Polysorbate 80, Pregelatinised Starch, Sodium Bicarbonate, Sodium Lauryl Sulphate, Talcum.

3. Dosage form and strength

Dosage form: Film coated tablet

Strength: 120mg+10mg

4. Clinical particulars

4.1. Therapeutic indication

TORKAST-FX is indicated for treatment of allergic rhinitis in adults only.

4.2. Posology and method of administration

Posology

The recommended dose for adults is one tablet once daily.

SPECIFIC POPULATIONS

Renal Impairment: There is no data of this combination in renally impaired patients.

Hepatic Impairment: No dosage adjustment is required in case of mild to moderate hepatic insufficiency.

Geriatric Use: No dosage adjustment in the elderly is required.

Method of Administration:

Torkast-FX should be taken orally with or without food.

4.3. Contraindications

TORKAST-FX is contraindicated in patients with known hypersensitivity to montelukast sodium, Fexofenadine or to any other component of this product.

4.4. Special warnings and precautions for use

Fexofenadine hydrochloride

As with most new medicinal products 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 of tachycardia and palpitations.

Based on 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, fexofenadine has been shown to have no significant effects on the 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.

Montelukast sodium

Eosinophilic Conditions

In rare cases, patients on therapy with Montelukast may present with systemic eosinophilia, sometimes presenting with clinical features of vasculitis consistent with Churg-Strauss syndrome, a condition, which is often treated with systemic corticosteroid therapy. These events usually, but not always, have been associated with the reduction of oral corticosteroid therapy.

4.5. Drugs interactions

Fexofenadine hydrochloride

Fexofenadine does not undergo hepatic biotransformation and, therefore, will not interact with other drugs through hepatic mechanisms. Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole has been found to result in an increase by two to three times in the level of fexofenadine in plasma. The changes were not accompanied by any effects on the QTc 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 the co-administration of erythromycin or ketoconazole, appears to be due to an increase in gastrointestinal absorption and a decrease in either the 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 the bioavailability, most likely due to binding in the gastrointestinal tract. It is advisable to leave a 2-hour gap between the administration of fexofenadine hydrochloride and aluminium- and magnesium hydroxide-containing antacids.

Fruit juices such as grapefruit, orange and apple may reduce the bioavailability and exposure of fexofenadine. Based on the population pharmacokinetics analysis of the combined data from grapefruit and orange juices studies with the data from a bioequivalence study, the bioavailability of fexofenadine was reduced by 36%. Therefore, to maximize the effects of fexofenadine, it is recommended that fexofenadine should be taken with water.

Montelukast sodium

In drug-interaction studies, the recommended clinical dose of montelukast did not have clinically important effects on the pharmacokinetics of the following drugs: theophylline, prednisone, prednisolone, oral contraceptives (norethindrone 1 mg/ethinyl estradiol 35 mcg), terfenadine, digoxin, and warfarin.

Although additional specific interaction studies were not performed, montelukast was used concomitantly with a wide range of commonly prescribed drugs in clinical studies without evidence of clinical adverse interactions. These medications included thyroid hormones, sedative hypnotics, non-steroidal anti-inflammatory agents, benzodiazepines, and decongestants.

Phenobarbital, which induces hepatic metabolism, decreased the AUC of montelukast approximately 40% following a single 10-mg dose of montelukast. No dosage adjustment for montelukast is recommended. It is reasonable to employ appropriate clinical monitoring when potent cytochrome P450 enzyme inducers, such as phenobarbital or rifampin, are co-administered with montelukast.

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are no adequate and well-controlled studies of either montelukast or fexofenadine in pregnant women. Limited animal studies do not indicate the direct or indirect harmful outcomes with respect to the effects on pregnancy, embryonal/foetal development, parturition, or postnatal development. Because animal reproduction studies are not always predictive of human response, TORKAST-FX Tablets should be used during pregnancy only if it is considered to be clearly essential.

Lactation

It is not known if montelukast is excreted in human milk. 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, TORKAST-FX Tablets are not recommended for nursing mothers.

Paediatric Use:

Fexofenadine hydrochloride

The safety and effectiveness of montelukast and fexofenadine in paediatric patients below the age of 6 months have not been established.

Montelukast sodium

The safety of Montelukast 4- mg chewable tablets in pediatric patients aged 2 to 14 years with allergic rhinitis is supported by data from studies conducted in pediatric patients aged 2 to 14 years with asthma. A safety study in pediatric patients 2 to 14 years of age with seasonal allergic rhinitis demonstrated a similar safety profile. The safety and effectiveness in pediatric patients below the age of 12 months with asthma and 6 months with allergic rhinitis have not been established.

Geriatric Use

Fexofenadine hydrochloride

There is no data on the geriatric use of this combination. However, the following data is available on the individual components

Montelukast sodium

No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Renal Impairment

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

Hepatic Impairment

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

4.7. Effects on ability to drive and use machines

Fexofenadine hydrochloride

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 reported 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 medicinal products, it is advisable to check the individual response before driving or performing complicated tasks.

Montelukast sodium

Montelukast is not expected to affect a patient's ability to drive a car or operate machinery. However, in very rare cases, individuals have reported drowsiness or dizziness.

4.8. Undesirable effects

Fexofenadine hydrochloride

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 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

Skin and subcutaneous tissue disorders rash, urticaria, pruritus

Montelukast Sodium

The observations in reported clinical study for Montelukast as follows:

10 mg film-coated tablets in approximately 4000 adult asthmatic patients 15 years of age and older 10 mg film-coated tablets in approximately 400 adult asthmatic patients with seasonal allergic rhinitis 15 years of age and older. 5 mg chewable tablets in approximately 1750 paediatric asthmatic patients 6 to 14 years of age.

The following drug-related adverse reactions in clinical studies were reported commonly (≥1/100 to <1/10) in asthmatic patients treated with montelukast and at a greater incidence than in patients treated with placebo:

Body System Class	**Adults Patient 15 years and older (two 12-week studies; n=795)**	**Paediatric Patients 6 to 14 years old (one 8-week study; n=201) (two 56-week studies; n=615)**
Nervous system disorders	Headache	Headache
Gastro-intestinal disorders	Abdominal pain	

With prolonged treatment in clinical trials with a limited number of patients for up to 2 years for adults, and up to 12 months for paediatric patients 6 to 14 years of age, the safety profile did not change

Post-marketing Experience

Adverse reactions reported in post-marketing use are listed, by System Organ Class and specific Adverse Experience Term, in the table below. Frequency Categories were estimated based on relevant clinical trials.

System Organ Class	**Adverse Experience Term**	**Frequency Category**
Infections and infestations	Upper respiratory infection	Very common
Blood and lymphatic system disorders	increased bleeding tendency	Rare
Immune system disorder	Hypersensitivity reactions including anaphylaxis	Uncommon
	Hepatic eosiniophilic infiltration	Very Rare

System Organ Class	Adverse Experience Term	Frequency Category
Psychiatric disorders	dream abnormalities including nightmares, insomnia, somnambulism, anxiety, agitation including aggressive behaviour or hostility, depression, psychomotor hyperactivity (including irritability, restlessness, tremor§)	Uncommon
	disturbance in attention, memory impairment	Rare
	hallucinations,disorientation, suicidal thinking and behaviour (suicidality)	Very rare
Nervous system disorder	Dizziness, drowsiness, paraesthesia/hypoesthesia, seizure	Uncommon
Cardiac Disorders	palpitations	Rare
Respiratory, thoracic and mediastinal disorders	Epistaxis	Uncommon
	Churg- Strauss Syndrome (CSS) and pulmonary eosinophilia	Very Rare
Gastrointestinal disorders	Diarrhoea, nausea, vomiting	Common
	dry mouth, dyspepsia	Uncommon
Hepatobiliary disorders	elevated levels of serum transaminases (ALT, AST)	Common
	hepatitis (including cholestatic, hepatocellular, and mixed-pattern liver injury).	Very Rare
Skin and subcutaneous tissue disorders	Rash	Common
	Bruising, urticaria, pruritus	Uncommon
	Angioedema	Rare
	Erythema nodosum, erythema multiforme	Very rare
Musculoskeletal, connective	arthralgia, myalgia including muscle	Uncommon
tissue and bone disorders	cramps	
General disorders and administration site conditions	pyrexia	Common
	Asthenia/fatigue, malaise, oedema	Uncommon

Reporting of 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. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com.

4.9. Overdose

There is no data to prove the overdosage of this combination. However, overdosage has been reported with individual molecules.

Fexofenadine hydrochloride

Dizziness, drowsiness, fatigue and dry mouth have been reported with overdosage 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 medicinal product. Symptomatic and supportive treatment is recommended. Haemodialysis does not effectively remove fexofenadine hydrochloride from blood

Montelukast sodium

There have been reports of acute over-dosage in post-marketing experience and clinical studies with montelukast. These include reports in adults and children with a dose as high as 1000 mg. The clinical and laboratory findings observed were consistent with the safety profile in adults and pediatric patients. There were no adverse experiences in the majority of over-dosage reports. The most frequently occurring adverse experiences were consistent with the safety profile of montelukast and included abdominal pain, somnolence, thirst, headache, vomiting and psychomotor hyperactivity.

It is not known whether montelukast is removed by peritoneal dialysis or hemodialysis.

5. Pharmacological properties

5.1. Mechanism of Action

Fexofenadine Hydrochloride

Fexofenadine hydrochloride is a non sedating H1 antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.

Montelukast sodium

The cysteinyl leukotrienes (LTC4, LTD4, LTE4) are products of arachidonic acid metabolism and are released from various cells, including mast cells and eosinophils. These eicosanoids bind to cysteinyl leukotriene (CysLT) receptors. The CysLT type-1 (CysLT1) receptor is found in the human airway (including airway smooth muscle cells and airway macrophages) and on other pro-inflammatory cells (including eosinophils and certain myeloid stem cells). CysLTs have been correlated with the pathophysiology of asthma and allergic rhinitis. In asthma, leukotriene- mediated effects include airway edema, smooth muscle contraction, and altered cellular activity associated with the inflammatory process. In allergic rhinitis, CysLTs are released from the nasal mucosa after allergen exposure during both early- and late-phase reactions and are associated with symptoms of allergic rhinitis.

Montelukast is an orally active compound that binds with high affinity and selectivity to the CysLT1 receptor (in preference to other pharmacologically important airway receptors, such

as the prostanoid, cholinergic, or β-adrenergic receptor). Montelukast inhibits physiologic actions of LTD4 at the CysLT1 receptor without any agonist activity.

5.2. Pharmacodynamic properties

Fexofenadine hydrochloride

Fexofenadine hydrochloride is a non-sedating H1 antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine. In seasonal allergic rhinitis patients who were given fexofenadine hydrochloride up to 240 mg twice daily for 2 weeks, no significant differences in the QTc intervals were observed when compared to placebo. Also, no significant change in the QTc 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.

Montelukast sodium

Montelukast causes inhibition of airway cysteinyl leukotriene receptors as demonstrated by the ability to inhibit bronchoconstriction due to inhaled LTD4 in asthmatics. Doses as low as 5 mg cause substantial blockage of LTD4 -induced bronchoconstriction.

5.3. Pharmacokinetic properties

Fexofenadine hydrochloride

The single- and multiple-dose pharmacokinetics of fexofenadine are linear for oral doses up to 120 mg b.i.d. A dose of 240 mg b.i.d. produced a slightly greater than proportional increase (8.8%) in the steady-state area under the curve (AUC), indicating that fexofenadine pharmacokinetics are practically linear at doses between 40 mg and 240 mg taken daily.

Absorption

Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with the Tmax occurring at approximately 1–3 hours post-dose. The mean Cmax value was approximately 427 ng/ml following the administration of a 120 mg dose once daily.

Distribution

Fexofenadine is 60–70% plasma protein-bound.

Biotransformation

Fexofenadine undergoes negligible metabolism (hepatic or non-hepatic) as it was the only major compound identified in the urine and faeces of animals and humans. 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.

Elimination

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

Montelukast sodium

Absorption

After administration of a 10-mg tablet to fasted adults, the mean peak montelukast plasma concentration (Cmax) is achieved in 3 to 4 hours (Tmax). The mean oral bioavailability is 64%. The oral bioavailability and Cmax are not influenced by a standard meal in the morning.

Distribution

Montelukast is more than 99% bound to plasma proteins. The steady-state volume of distribution of montelukast averages 8 to 11 liters.

Metabolism

Montelukast is extensively metabolized. In studies with therapeutic doses, plasma concentrations of metabolites of montelukast are undetectable at steady state in adults and pediatric patients.

Elimination

The plasma clearance of montelukast averages 45 mL/min in healthy adults. Following an oral dose of radiolabeled montelukast, 86% of the radioactivity was recovered in 5-day fecal collections and <0.2% was recovered in urines. Coupled with estimates of montelukast oral bioavailability, this indicates that montelukast and its metabolites are excreted almost exclusively via the bile.

In several studies, the mean plasma half- life of montelukast ranged from 2.7 to 5.5 hours in healthy young adults. The pharmacokinetics of montelukast are nearly linear for oral doses up to 50 mg. During once daily dosing with 10-mg montelukast, there is little accumulation of the parent drug in plasma (~14%).

6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

Fexofenadine Hydrochloride

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.

Montelukast sodium

In reported animal toxicity studies, minor serum biochemical alterations in ALT, glucose, phosphorus and triglycerides were observed which were transient in nature The signs of toxicity in animals were increased excretion of saliva, gastrointestinal symptoms, loose stools and ion imbalance. These occurred at dosages which provided >17-fold the systemic exposure seen at the clinical dosage In monkeys, the adverse effects appeared at doses from 150 mg/kg/day (>232- fold the systemic exposure seen at the clinical dose). In reported animal studies, montelukast did not affect fertility or reproductive performance at systemic exposure exceeding the clinical systemic exposure by greater than 24-fold A slight decrease in pup body weight was reported in the female fertility study in rats at 200 mg/kg/day (>69-fold the clinical systemic exposure). In reported studies in rabbits, a higher incidence of incomplete ossification, compared with concurrent control animals, was seen at systemic exposure >24-fold the clinical systemic exposure seen at the clinical dose. No abnormalities were seen in

rats. Montelukast has been shown to cross the placental barrier and is excreted in breast milk of animals.

No deaths occurred following a single oral administration of montelukast sodium at doses up to 5000 mg/kg in mice and rats (15,000 mg/m2 and 30,000 mg/m2 in mice and rats, respectively), the maximum dose tested. This dose is equivalent to 25,000 times the recommended daily adult human dose (based on an adult patient weight of 50 kg).

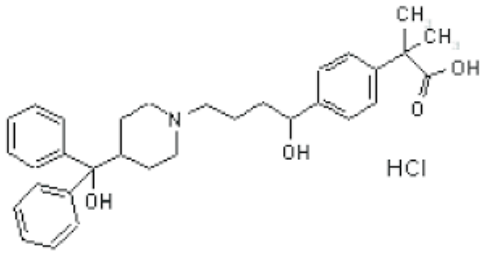
Montelukast was determined not to be phototoxic in mice for UVA, UVB or visible light spectra at doses up to 500 mg/kg/day (approximately >200-fold based on systemic exposure)

Montelukast was neither mutagenic in in vitro and in vivo tests nor tumorigenic in rodent species.

7. Description

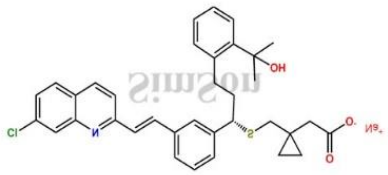
Fexofenadine Hydrochloride

Fexofenadine Hydrochloride is (RS) α,α-dimethyl-4-[1-hydroxy-4[4-(hydroxydi phenylmethyl) -1 piperidinyl]butyl] benzene acetic acid hydrochloride. Having molecular formula $C_{32}H_{39}NO_4HCL$ and molecular weight 538.1. The chemical structure is:



Montelukast Sodium

Montelukast Sodium is sodium [1- [[[(1R)-1-[3-[(E)-2-(7-chloroquinoline -2-yl) ethenyl] phenyl]-3-[2-(1-hydroxy-1 methylethyl)phenyl]propyl]sulfanyl] methyl]cyclopropyl]acetate. Having molecular formula $C_{35}H_{35}ClNNaO_3S$ and molecular weight is 608.2. The chemical structure is:



TORKAST -FX

Torkast-FX is yellow coloured, round, biconvex, both side plain & film coated tablets. The List of excipients used are Hydroxy Propyl Methyl Cellulose, Polyethylene glycol, Titanium Dioxide, Talcum powder, Iron Oxide, Colloidal Silicon Dioxide, Croscarmellose Sodium, Crospovidone, Hydroxy Propyl Cellulose, Lactose, Microcrystalline Cellulose, Magnesium Stearate, Polysorbate 80, Pregelatinised Starch, Sodium Bicarbonate, Sodium Lauryl Sulphate, Talcum.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than the date of expiry.

8.3. Packaging information

TORKAST-FX Tablet is available in a pack of 10 Tablets

8.4. Storage and handing instructions

Store in a dry & dark place, at a temperature not exceeding 30^0C.

Keep out of reach of children

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

Pure and cure Healthcare Pvt. Ltd.

Plot No.: 26A-30, Sector- 8A,IIE, SIDCUL,

Ranipur, Haridwar- 249 403 (Uttarakhand)

11. Details of permission or licence number with date

Mfg. Lic. No. is 31/UA/2013. Issue on 30.06.2014

12. Date of revision

MAR-2026

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/TORKAST-FX 120 and 10 mg/ MAR 2026/03/PI