*Revised: October 2013 (___2nd version, Section of Packaging)
Prepared: June 2013 (1st version)

Therapeutic Agent for Allergic Disease
Japanese Pharmacopoeia
Fexofenadine Hydrochloride Tablets

FEXOFENADINE HYDROCHLORIDE TABLETS 30mg "TOWA" / TABLETS 60mg "TOWA"

Storage:
Store at room temperature.
Expiration date:
Indicated on the package and label.

Standard Commodity Classification No. of Japan 87449		
	Tablets 30mg	Tablets 60mg
Approval No.	22500AMX00256	22500AMX00255
Date of listing in the NHI reimbursement price	June 2013	June 2013
Date of initial marketing in Japan	June 2013	June 2013

CONTRAINDICATIONS (Fexofenadine Hydrochloride Tablets is contraindicated in the following patients.)

1) Patients with a history of hypersensitivity to any of the ingredients of this product

COMPOSITION AND PRODUCT DESCRIPTION

		FEXOFENADINE HYDROCHLORIDE TABELTS 30mg "TOWA"	FEXOFENADINE HYDROCHLORIDE TABELTS 60mg "TOWA"
Active ingredient per tablet		Fexofenadine Hydrochloride (JP)…30mg	Fexofenadine Hydrochloride (JP)…60mg
Inactive ingredient		Lactose Hydrate, Partly Pregelatinized Starch, Microcrystalline Cellulose, Croscarmellose Sodium, Magnesium Stearate, Hypromellose, Hydroxypropylcellulose, Talc, Titanium Oxide, Red Ferric Oxide, Yellow Ferric Oxide	
Product description		Pale orange film-coated tablets	Pale orange film-coated tablets with a score
Identification code	Tablet	Tw343	Tw344
	Package		
Appearance	Top surface		
	Bottom surface		
	Side surface		
Diameter (mm)		6.0	8.1
Thickness (mm)		3.1	3.7
Weight (mg)		94	186

INDICATIONS

Allergic rhinitis, urticaria, pruritus with dermatosis (eczema, dermatitis, pruritus cutaneous, atopic dermatitis)

DOSAGE AND ADMINISTRATION

The recommended adult dosage is 60 mg of fexofenadine hydrochloride administered orally twice daily. The recommended pediatric dosages are as follows: for children aged 7 to < 12 years, 30 mg of fexofenadine hydrochloride administered orally twice daily, and for children aged 12 years or older, 60 mg of fexofenadine hydrochloride administered orally twice daily. The dosage may be adjusted according to the patient's symptom.

PRECAUTIONS

1. Important Precautions

1) For patients with seasonal allergic conditions, it is recommended that, in reference to the season for disease onset, administration of this product be started immediately before the start of the season and be continued until the end of the season.
2) It should be noted that, for patients showing no response to treatment with this product, this drug should not be administered indefinitely over the long term.

2. Interactions

Precautions for coadministration (Fexofenadine Hydrochloride Tablets should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Clinical Symptoms and Treatment	Mechanism and Risk Factors
Antacids Aluminum hydroxide-magnesium hydroxide-containing preparations	Coadministration with these drugs may decrease the effect of this product and thus precautions should be taken not to administer this product and such drugs concurrently.	The temporary absorption of this product by aluminum hydroxide/magnesium hydroxide is presumed to reduce the absorption volume of this product.
Erythromycin	Coadministration with erythromycin has been reported to increase plasma concentrations of fexofenadine hydrochloride.	Increased plasma concentrations of this product are assumed to be attributable to decreased clearance and increased absorption rate of this product due to inhibition of P-glycoprotein.

3. Adverse Reactions

No investigation such as a drug use investigation clearly showing the incidence of adverse reactions has been conducted.

1) Clinically significant adverse reactions (incidence unknown)

(1) **Shock, anaphylaxis**: Shock or anaphylaxis may occur. Patients should be carefully monitored, and if any hypersensitive symptoms such as dyspnea, decreased blood pressure, loss of consciousness,

angioedema, chest pain, erubescence are observed, administration of this product should be discontinued and appropriate measures should be taken.

(2) **Hepatic dysfunction, jaundice:** Hepatic dysfunction or jaundice associated with increased AST (GOT), ALT (GPT), γ-GTP, Al-P or LDH may occur. Patients should be carefully monitored, and if any abnormalities are observed, administration of this product should be discontinued and appropriate measures should be taken.

(3) **Agranulocytosis, leukocytopenia, neutropenia:** Agranulocytosis, leukocytopenia or neutropenia may occur. Patients should be carefully monitored, and if any abnormalities are observed, administration of this product should be discontinued and appropriate measures should be taken.

2) Other adverse reactions

	Incidence unknown
Psychoneurologic	Headache, sleepiness, fatigue, malaise, dizziness, insomnia, nervousness, nightmare, sleep disorder, numbness
Gastrointestinal	Nausea, vomiting, thirst, abdominal pain, diarrhea, dyspepsia, constipation
Hypersensitivity*1)	Angioedema, pruritus, urticaria, flushing, rash
Hepatic*2)	Increased AST (GOT), increased ALT (GPT)
Renal, urinary organs	Dysuria, pollakiuria
Cardiovascular	Palpitation, elevated blood pressure
Others	Dyspnea, taste disorders, edema, chest pain, menstruation disorder

*1):If such symptoms are observed, administration of this product should be discontinued.

*2):If any abnormalities are observed, appropriate measures should be taken such as reduction of dosage or discontinuation of this product.

4. Use in the Elderly

Elderly patients often have decreased renal function and thus blood concentrations of this product, which is also renally excreted, may increase. If any abnormalities are observed, appropriate measures should be taken.

5. Use during Pregnancy, Delivery or Lactation

1) This product should be used in pregnant women or in women who may possibly be pregnant only if the expected therapeutic benefits outweigh the possible risks associated with treatment. [The safety of this product in pregnant women has not been established.]

2) If this product is administered to lactating mothers, breast feeding should be discontinued during treatment. [It has been reported in animal studies (in rats) that the drug is excreted in breast milk.]

6. Pediatric Use

The safety of this product in low birth weight infants, neonates, nursing infants and infants has not been established (No sufficient data in pediatric patients).

7. Influence on Laboratory Tests

Administration of this product must be discontinued 3 to 5 days before allergen intradermal tests because this drug inhibits allergen intradermal reactions.

8. Overdosage

There have been limited reports on overdosage. In most case reports of overdoses of this product in countries outside Japan, the dose amount taken is unknown. However, in 2 cases in which the highest dose amount (ranging from 1800 to 3600 mg) of this product was taken, no symptoms have been reported in one patient, and dizziness, sleepiness and thirst have been reported in the other patient. In case of overdose, unabsorbed drug remaining in the body should be eliminated by routine drug elimination methods, and subsequently consideration should be given to symptomatic and supportive treatments. This product cannot be eliminated by hemodialysis.

9. Precautions Concerning Use

Precautions regarding dispensing:

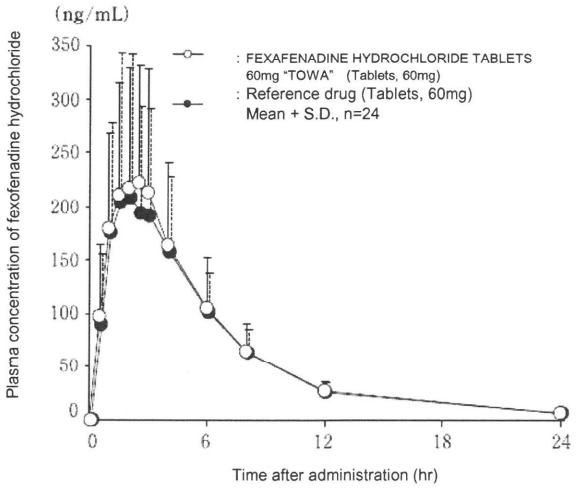
For drugs that are dispensed in a PTP (press-through package) sheet, instruct the patient to remove the drug from the package prior to use [It has been reported that, if the PTP sheet is swallowed, the sharp corners of the sheet may puncture the esophageal mucosa, causing perforation and resulting in severe complications such as mediastinitis.]

PHARMACOKINETICS

1. Bioequivalence test

1) FEXOFENADINE HYDROCHLORIDE TABLETS 60mg "TOWA"

One tablet each of FEXOFENADINE HYDROCHLORIDE TABLETS 60mg "TOWA" and a reference drug (as 60 mg of fexofenadine hydrochloride) were administered orally as a single dose to healthy adult men under fasting conditions (n=24) in a crossover design to measure each unchanged drug concentration in plasma. Obtained pharmacokinetic parameters (AUC and Cmax) were statistically analyzed in a 90% confidence interval design. The analysis results confirmed the bioequivalence of these drugs within the range between log (0.80) and log (1.25) [1].



	Determined parameter		Reference parameter	
	AUC_{24} (ng·hr/mL)	Cmax (ng/mL)	Tmax (hr)	$T_{1/2}$ (hr)
FEXOFENADINE HYDROCHLORIDE TABLETS 60mg "TOWA" (Tablets, 60mg)	1527±624	251.25±125.16	2.02±0.76	5.183±0.590
Reference drug (Tablets, 60mg)	1454±606	238.91±126.87	1.94±1.11	5.219±0.777

(Mean ± S.D., n=24)

Plasma concentration and parameters such as AUC and Cmax may differ according to study conditions such as selection of subjects and frequency/time of body fluid sample collection.

2) FEXOFENADINE HYDROCHLORIDE TABLETS 30mg "TOWA"

A bioequivalence study of FEXOFENADINE HYDROCHLORIDE TABLETS 30mg "TOWA" was conducted using FEXOFENADINE HYDROCHLORIDE TABLETS 60mg "TOWA" as the standard formulation in accordance with the "Guideline for Bioequivalence Studies for Different Strengths of Oral Solid Dosage Forms" (PFSB/ELD Notification No. 1124004 dated November 24, 2006), showing equal dissolution behavior and bioequivalence between these 2 formulations [2].

2. Dissolution profile

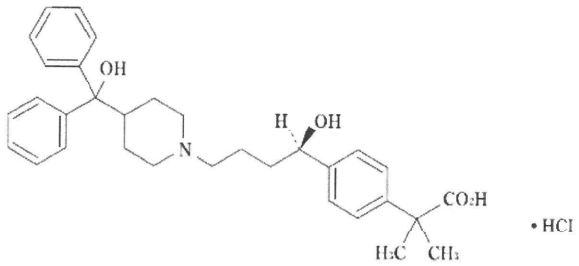
FEXOFENADINE HYDROCHLORIDE TABLETS 30mg "TOWA" and FEXOFENADINE HYDROCHLORIDE TABELTS 60mg "TOWA" have been confirmed to conform to the dissolution standard of Fexofenadine Hydrochloride Tablets defined in the official monographs of the Japanese Pharmacopoeia [3)4)].

PHARMACOLOGY

This product alleviates allergic symptoms by inhibiting the release of chemical mediators such as histamine from mast cells induced by antigen-antibody reactions and antagonizing H_1 action of histamine [5].

PHYSICOCHEMICAL PROPERTIES

Structural formula:



and enantiomer

Nonproprietary name:
Fexofenadine Hydrochloride

Chemical name:
2-(4-{(1*RS*)-1-Hydroxy-4-[4-(hydroxydiphenylmethyl) piperidin-1-yl] butyl} phenyl)-2-methylpropanoic acid monohydrochloride

Molecular formula:
$C_{32}H_{39}NO_4 \cdot HCl$

Molecular weight:
538.12

Description:
Fexofenadine Hydrochloride occurs as a white crystalline powder. It is very soluble in methanol, soluble in ethanol (99.5), and slightly soluble in water.
A solution of Fexofenadine Hydrochloride in methanol (3 in 100) shows no optical rotation.
Fexofenadine Hydrochloride shows crystal polymorphism.

PRECAUTIONS FOR HANDLING

1. Precautions

The color may fade if exposed to light.

2. Stability test

In an accelerated test using final packaged products (at 40°C and 75% relative humidity for 6 months), FEXOFENADINE HYDROCHLORIDE TABLETS 30mg "TOWA" and FEXOFENADINE HYDROCHLORIDE TABLETS 60mg "TOWA" were estimated to be stable for 3 years under normal distribution conditions. [6)7)].

PACKAGING

FEXOFENADINE HYDROCHLORIDE TABLETS 30mg "TOWA"
Boxes of 100 tablets (PTP)

FEXOFENADINE HYDROCHLORIDE TABLETS 60mg "TOWA"
Boxes of 100 tablets, 500 tablets (PTP)
Boxes of 140 tablets (14 tablets x 10: PTP)
Boxes of 700 tablets (14 tablets x 50: PTP)
Polyethylene containers of 300 tablets

REFERENCES

1) Internal data of Towa Pharmaceutical Co., Ltd.: Bioequivalence test (tablets 60mg)
2) Internal data of Towa Pharmaceutical Co., Ltd.: Bioequivalence test (tablets 30mg)
3) Internal data of Towa Pharmaceutical Co., Ltd.: Dissolution test (tablets 30mg)
4) Internal data of Towa Pharmaceutical Co., Ltd.: Dissolution test (tablets 60mg)
5) The 16th revision Japanese Pharmacopoeia explanatory, C-3867, 2011
6) Internal data of Towa Pharmaceutical Co., Ltd.: Stability test (tablets 30mg)
7) Internal data of Towa Pharmaceutical Co., Ltd.: Stability test (tablets 60mg)

Manufacturer and Distributor
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