SUMMARY OF PRODUCT CHARACTERISTICS

1.NAME OF THE MEDINICAL PRODUCT

BUTIROL FORT 22.5 mg/5 ml syrup

2.QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Ingredient:

Each 5 ml of syrup contains 22.5 mg of butamirate citrate

Excipient:

Each 5 ml of syrup;

Sorbitol, liquid, non-crystalline (70%) ..... 2500 mg

Fructose ..... 400 mg

Sodium benzoate ..... 5 mg

Azorubin ..... 0.005 mg

See Section 6.1 for excipients.

3. PHARMACEUTICAL FORM

Syrup

Light pink, clear, fruit-flavored solution

4. CLINICAL PROPERTIES

4.1. Therapeutic indications

BUTIROL FORT:

- It is indicated for the symptomatic treatment of cough caused by various causes.

4.2. Posology and method of administration

In children 6-12 years old (including 6 and 12 years old): 5 mL (22.5 mg) 2 times a day

In adolescents over 12 years of age (adolescents): 5 mL (22.5 mg) 3 times a day

Adults: 5 mL (22.5 mg) 4 times a day

The maximum duration of treatment is 7 days, unless prescribed by a doctor (see section 4.4).

The lowest dose required for efficacy should be used for the shortest duration of treatment.

Method of administration:

It is used orally.

The 5 ml measuring spoon should be washed and dried after each use.

Additional information on special populations:

Kidney/Liver failure:

BUTIROL FORT has not been studied in patients with renal or hepatic impairment.

Pediatric population:

The use of BUTIROL FORT in children under 3 years of age is contraindicated. Not recommended for use in children under 6 years of age.

Geriatric population:

BUTIROL FORT has not been studied in elderly patients.

4.3. Contraindications

Butamirate is contraindicated in people with known hypersensitivity to citrate or any of the other ingredients of BUTIROL FORT.

Use under 3 years of age is contraindicated.

4.4. Special warnings and precautions for use

Since the cough reflex is inhibited by butamirate, concomitant use of expectorants may cause mucus to accumulate in the respiratory tract, increasing the risk of bronchospasm and airway infection.. Therefore, simultaneous use of BUTIROL FORT with expectorants should be avoided.

Not recommended for use under 6 years of age.

A doctor or pharmacist should be consulted to evaluate the underlying cause in patients with a worsening cough or lasting longer than 7 days and/or accompanied by fever or persistent headache.

BUTIROL FORT contains sorbitol as an excipient. Patients with rare hereditary problems of fructose intolerance should not take this medicine. Sorbitol may cause gastrointestinal discomfort and mild laxative effect.

BUTIROL FORT also contains sucralose and fructose as sweeteners. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.
This medicinal product contains azorubin as a colorant. May cause allergic reactions.

4.5. Interactions with other medicinal products and other forms of interaction
Concomitant administration of expectorant should be avoided (see section 4.4).

Additional information on special populations
There are no interaction studies in special populations.

Pediatric population:
There are no interaction studies in the pediatric population.

4.6. Pregnancy and Lactation
General advice
Pregnancy category: C

Women of childbearing potential/Contraception
Since the fetal and neonatal effects of butamirate citrate are not fully known, those who have to use the drug should be protected from pregnancy with an appropriate contraceptive method.

Pregnancy period
For butamirate citrate, no clinical data on pregnancies are available..
Animal studies are insufficient for effects on pregnancy/and-or/embryonic/fetal development/and-or/partum/and-or/postnatal development (see section 5.3). The potential risk for humans is unknown.
The use of BUTIROL FORT should be avoided during the first 3 months of pregnancy. After the first 3 months of pregnancy, BUTIROL FORT should be used only if clearly needed by the doctor.

Lactation period

It is not known whether butamirate citrate and/or its metabolites are excreted in human milk. The benefit of breastfeeding for the child and the benefit of BUTIROL FORT treatment for the nursing mother should be taken into account when deciding whether to stop breastfeeding or to stop the treatment with BUTIROL FORT.

Reproductive ability/Fertility

No safety hazards were observed in studies of reproductive toxicity (see section 5.3).

4.7. Effects on the ability to drive and use machines

BUTIROL FORT may cause drowsiness in rare cases. Therefore, it may have a minor effect on the ability to drive and use machines. Caution should be exercised when driving or performing other tasks that require attention (eg operating machinery).

4.8. Undesirable effects

The frequency order of undesirable effects is as follows:

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)

Nervous system disorders

Rare: somnolence

Gastrointestinal disorders

Rare: nausea, diarrhea.

Skin and subcutaneous tissue disorders

Rare: urticaria

4.9. Overdose and its treatment

In case of overdose of BUTIROL FORT, the following symptoms may occur: drowsiness, nausea, vomiting, diarrhoea, drowsiness and hypotension.

Treatment

Additional therapy should be administered as clinically indicated or as recommended by the national poison center whenever possible. There is no known specific antidote. In the event of overdose, supportive therapy should be administered with appropriate monitoring as necessary.

5.PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamics properties

Pharmacotherapeutic group: Other cough suppressants

ATC code: R05DB13

Mechanism of action

The active ingredient of BUTIROL FORT, butamirate citrate, is a non-opioid cough suppressant. It is thought that the active substance has a central effect. However, the mechanism of action is not fully known. Butamirate citrate has non-specific anticholinergic and bronchospasmodic effects that facilitate respiratory functions.

Intake, the syrup can help coat and soothe an irritated throat with the moisturizing properties of glycerol.

5.2. Pharmacokinetic properties

General properties

Absorbation:

Based on available data, butamirate is well and rapidly absorbed following oral administration and is hydrolyzed to phenyl-2-butyric acid and diethylaminoethoxyethanol. The effect of food intake has not been studied. Exposure to 2-phenylbutyric acid and diethylaminoethoxyethanol is fully proportional over the dose range of 22.5 mg–90 mg.

Butamirate is detected in the blood at measurable concentrations within 5-10 minutes of administration of 22.5 mg, 45 mg, 67.5 mg and 90 mg doses. Maximum plasma concentrations for all doses are reached within 1 hour, with a mean value of 16.1 nanograms/mL for 90 mg.

Following administration of 90 mg (3052 nanograms/mL) of phenyl-2-butyric acid, the main metabolite, the mean maximum plasma concentration is reached approximately 1.5 hours later.

Following administration of 90 mg (160 nanograms/mL-), diethyl-aminoethoxyethanol has been observed to reach its mean plasma concentration within 0.67 hours.

Distribution:

Butamirate citrate is highly protein bound and has a large volume of distribution of 81–112 L (relative to body weight in kg). 2-phenylbutyric acid is highly (89.3–91.6%) bound to plasma proteins at all doses (22.5–90 mg). Diethylamino Ethoxyethanol shows some degree of protein binding (28.8–45.7%). It is not known whether butamirate crosses the placenta or is excreted in milk.

Biotransformation:

Hydrolysis of butamirate citrate, mainly phenyl-2-butyric acid and diethylamino ethoxyethanol, occurs rapidly, reaching measurable concentrations within 5 minutes. Based on studies on various species, both major metabolites are hypothesized to have cough-relieving effects. There are no human data on Diethylamino Ethoxy Ethanol. Phenyl-2-butyric acid also undergoes partial biotransformation via hydroxylation at the para position.

Elimination:

After 24 hours, the main metabolites (77%) are 2-phenylbutyric acid and parahydroxy 2-phenylbutyric acid. Excretion of 2-phenylbutyric acid, diethylamino ethoxyethanol and parahydroxy 2-phenylbutyric acid occurs mainly through the kidneys. Urinary 2-phenylbutyric acid conjugate levels are much higher than in plasma. Butamirate citrate can be detected in urea for up to 48 hours, and the amount of butamirate excreted in urea over the 96 hour sampling period was 0.02%, 0.02%, 0.03%, and 0.03% at the 22.5 mg, 45 mg, 67.5 mg, and 90 mg doses, respectively. A significant percentage of butamirate citrate compared to butamirate or unconjugated 2-phenylbutyric acid is excreted in urea as diethyl aminoethoxyethanol. he elimination half-lives measured for 2-phenylbutyric acid, butamirate, and diethylamino ethoxyethanol are 23.26–24.42, 1.48–1.93 and 2.72–2.90 hours, respectively.

Characteristics in patients

The effect of hepatic or renal dysfunction on the pharmacokinetic parameters of butamirate is unknown.

5.3. Preclinical safety data

Non-clinical safety data for butamirate at recommended doses and use did not reveal appropriate findings.

Carcinogenesis and mutagenesis

For butamirate, carcinogenicity data are not available, but in-vitro and in-vivo genotoxicity data do not indicate genotoxic potential.

Reproductive toxicity

Although studies in rats and rabbits showed no evidence of reproductive or developmental toxicity, treatment-related maternal deaths in rabbits receiving oral doses approximately 2.3-, 4.6-, or 18.5-fold greater (based on human equivalent dose) at the maximum clinical dose from days 6 to 18 gestation observed.

6.PHARMACEUTICAL PROPERTIES

6.1. List of Excipients

Sorbitol, liquid, non-crystalline (70%)
Sodium benzoate
Raspberry Flavor (FM00192)
Glycerol
Sucralose
Fructose
Citric Acid Monohydrate
Sodium Citrate Dihydrate
Tutti Frutti Flavor (FM04706)
Azorubin(Carmoisine) (E122)
Purified water

6.2. Incompatibilities

It does not have any known incompatibilities.

6.3. Shelf life

36 months

6.4. Special precautions for storage

Store at room temperature below 25°C.

6.5. The nature and content of the packaging

In the box, in a 100 ml Type II amber glass bottle with a PE vistop cap, with a 5 ml measuring spoon.

7. MARKETING AUTHORISATION HOLDER

Drogsan İlaçları San. ve Tic. A.Ş.
Oğuzlar Mah. 1370. sok. No:7/3
06520 Balgat-ANKARA

8. MARKETING AUTHORISATION NUMBER(S)

2015/151

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16.02.2015
Date of latest renewal:

10. DATE OF REVISION OF SPC

08.04.2023