SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DIFILIN 300 mg/3 ml I.M. Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:

Each 3 ml ampoule contains 300 mg of dihydroxypropyltheophylline.

Excipient(s):

Methylparaben.....3 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

Clear, colorless, odorless solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DIFILIN ampoules are used in acute bronchial asthma and in reversible bronchospasms associated with chronic bronchitis and emphysema.

4.2. Posology and method of administration

Posology/frequency and duration of administration

According to the doctor's recommendation, DIFILIN is injected into the muscle 1-2 times a day.

Method of administration:

DIFILIN is administered into the muscle.

Additional information on special populations:

Renal impairment:

Difilin is primarily excreted in the urine by the kidneys without being metabolized. Therefore, it should not be used in patients with kidney failure, or the dosage should be adjusted.

Hepatic impairment:

Caution should be exercised when adjusting the dose in patients with hepatic impairment.

Pediatric population:

Excessive use in children may cause toxic effects. As its safety and efficacy in pediatric use have not been established, its use in infants is not recommended.

Geriatric population:

Dosage adjustments should be made taking into account the reduced kidney function in elderly patients.

4.3. Contraindications

DIFILIN is contraindicated in the following situations:

- In the acute phase of myocardial infarction,
- In severe peptic ulcer,
- In individuals who are hypersensitive to dihydroxypropyltheophylline, xanthine compounds, or any of the excipients in DIFILIN.

4.4. Special warnings and precautions for use

It should be used with caution in patients with heart disease; hypothyroidism, hypertension, and congestive heart failure, or those who have had an acute myocardial infarction.

Excessive doses in status asthmaticus and children may cause toxic effects. Its safety and efficacy in pediatric use have not been established, so its use in infants is not recommended.

It should be used with caution in patients with COPD. Theophylline increases serum AST concentrations. This medicinal product contains methylparaben. Methylparaben may cause allergic reactions (possibly delayed) and unusual bronchospasm.

4.5. Interactions with other medicinal products and other forms of interaction

DIFILIN; when used in combination with other xanthine compounds (such as theophylline), ephedrine, and other sympathomimetic bronchodilators, synergism may occur.

Acyclovir, alcohol, allopurinol, calcium channel blockers (such as diltiazem, verapamil), cimetidine, corticosteroids (such as hydrocortisone, prednisone), disulfiram, hormonal contraceptives containing estrogen, fluvoxamine, influenza vaccine virus, interferon, macrolide antibiotics (azithromycin), methotrexate,

mexiletine, non-selective beta blockers (such as propranolol), pentoxifylline, propafenone, quinolone antibiotics (such as ciprofloxacin and norfloxacin), tacrine, thiabendazole, thyroid hormones (such as levothyroxine), ticlopidine, zilotone active substances may lead to an increase in theophylline level.

Aminoglutethimide, barbiturates (e.g., pentobarbital, phenobarbital, primidone, secobarbital), hydantoins (e.g., phenytoin), isoproterenol IV, ketoconazole, morisizin, rifampin, smoking (i.e., marijuana and tobacco), St. John's wort, sulfinpyrazone, sympathomimetics (e.g., albuterol, isoproterenol, terbutaline) use may decrease theophylline levels.

Theophylline may antagonize the sedative effects of benzodiazepines and propofol.

Cardiovascular adverse effects may be increased when theophylline is used with beta-agonists. However, beneficial effects may also be increased when used together.

Carbamazepine, isoniazid, and loop diuretics may decrease or increase theophylline levels.

Ephedrine and tetracyclines may increase the risk of theophylline toxicity.

The use of erythromycin and theophylline increases theophylline levels and the risk of toxicity while decreasing erythromycin levels.

The combined administration of halothane and theophylline may cause catecholamine-induced arrhythmias.

The combined administration of ketamine and theophylline may cause seizures.

Theophylline may decrease lithium levels.

Nondepolarizing muscle relaxants may antagonize neuromuscular blockade when used with theophylline.

The use of dihydroxypropyltheophylline with probenecid, which competes with it for tubular secretion, has been shown to increase its plasma half-life.

4.6. Pregnancy and lactation

General recommendation:

Pregnancy category is C.

Women of childbearing potential/Birth control (Contraception)

Since the safety of dihydroxypropyltheophylline has not been established in women of childbearing potential, DIFILIN should be used with caution in women who are not using contraception.

Women using DIFILIN should administer an appropriate method of birth control.

Pregnancy

Studies conducted on animals are insufficient in terms of effects on pregnancy and-or embryonic/fetal development/and-or birth and-or/postnatal development. The potential risk to humans is unknown.

Difilin should not be used during pregnancy unless necessary.

Therefore, the drug should be used in cases where the benefit to the mother is considered to outweigh the potential risk to the baby.

Breast-feeding

It is not recommended for use in lactating mothers as it passes into breast milk in large quantities.

Reproductive ability / fertility

There are no clinical or non-clinical studies on reproductive ability.

4.7 Effects on ability to drive and use machines

There is no data available indicating that it affects driving or using machinery.

4.8. Undesirable effects

Although the following side effects have not been observed with the use of DIFILIN ampoules, the pharmacological similarity of xanthine compounds means that these adverse effects may occur with the use of the preparation.

The following terms have been used to determine the frequency of side effects.

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), unknown (cannot be estimated from available data).

Metabolism and nutrition disorders

Unknown: Hyperglycemia

Psychiatric disorders

Unknown: Anxiety, insomnia,

Nervous system disorders

Unknown: Stimulation, headache, irritability, excessive excitability, muscle twitching, generalized clonic and tonic convulsions.

Cardiac disorders

Unknown: Palpitations, tachycardia, extrasystole, hot flashes, circulatory disorders, and ventricular arrhythmia.

Vascular disorders

Unknown: Hypotension (low blood pressure), circulatory disorder

Respiratory, chest disorders, and mediastinal diseases

Unknown: Tachypnea (very rapid breathing), respiratory arrest.

Gastrointestinal diseases

Unknown: Nausea, vomiting, epigastric pain, diarrhea, and hematemesis

Kidney and urinary tract diseases

Unknown: Albuminuria, increased excretion from the renal tubules, hematuria, diuresis

General disorders and administration site diseases:

Unknown: Fever, dehydration, unclear ADH syndrome.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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 in accordance with local requirements.

4.9. Overdose and treatment

Symptoms and Signs:

Anxiety, anorexia, nausea, vomiting, diarrhea, insomnia, irritability, and headache.

Overdose may cause serious toxicity such as agitation, excessive vomiting, dehydration, severe thirst feeling, tinnitus, cardiac arrhythmia, hyperthermia, diaphoresis, and generalized clonic and tonic convulsions.

Treatment:

There is no specific antidote for xanthine derivatives. Symptomatic treatment and fluid and electrolyte replacement should be administered. The stomach should be emptied by gastric lavage or induced vomiting, depending on the patient's condition. Caution should be exercised when performing aspiration in patients who are unresponsive, comatose, or unconscious. The airway must be kept open and should oxygen be administered if necessary. Sympathomimetic agents should be avoided. Short-acting barbiturates may be administered.

Although not recommended under normal circumstances, hemodialysis may be beneficial in very serious, life-threatening cases of intoxication where supportive and symptomatic treatment cannot be provided.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Drugs used in obstructive lung diseases

ATC code: R03DA01

Dihydroxypropyltheophylline is primarily responsible for vasodilation. It also has minimal effects on peripheral vasodilation and other smooth muscle relaxant systems. It exerts its effect by competitively inhibiting the phosphodiesterase enzyme. As a result, cyclic AMP levels increase and relaxation of bronchial smooth muscles is achieved. DIFILIN is better tolerated than aminophylline and other alkali theophylline compounds and reduces the incidence of nausea.

Dihydroxypropyltheophylline is a theophylline derivative that dissolves in water with a neutral reaction. It is a phosphodiesterase inhibitor. It is similar to aminophylline in terms of effect, but it is better absorbed than aminophylline, is better tolerated, and causes nausea and stomach irritation less frequently.

DIFILIN ampoule provides vasodilation in the coronary arteries, ensuring better nourishment of the myocardium. It has a stimulating effect on skeletal muscles and the diaphragm. It also has bronchodilator, diuretic, and myorelaxant effects on the smooth muscles of the pulmonary vessels.

5.2. Pharmacokinetic properties

General properties

Absorption: Dihydroxypropyltheophylline is rapidly absorbed from the gastrointestinal tract and, when administered intramuscularly, from the site of injection.

Distribution: Approximately 40% is transported bound to albumin in plasma. Therapeutic serum levels are 10-20 µg/ml.

Biotransformation: The substance is not metabolized to theophylline.

Elimination: The elimination half-life is approximately 2 hours. It is excreted largely in the urine (unchanged). The plasma half-life is reduced by 30-50% in children and smokers.

Linearity/non-linearity: No data available.

5.3. Preclinical safety data

The active substance contained in the preparation is a substance that has been used clinically for many years. Studies on it have been completed. Any adverse effects that may be seen with its use are listed in the relevant sections (see 4.4. Special warnings and precautions for use, 4.6. Pregnancy and lactation, 4.8. Undesirable effects, 4.9 Overdose and treatment).

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Methylparaben

Water for injection

6.2. Incompatibilities

For information on drug interactions, see 4.5. Interactions with other medicinal products and other forms of interaction.

Dihydroxypropyltheophylline is not incompatible with the excipients used.

6.3. Shelf Life

60 months

6.4. Special precautions for storage

Store in a dry place between 15-30°C.

6.5. Nature and contents of container

3 ml colorless ampoules with a ring, made of Type I glass (high-resistant borosilicate glass).

Each box contains 6 ampoules of 3 ml.

6.6. Special precautions for disposal and other handling

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

7. MARKETING AUTHORIZATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER

57/25

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization: 14.04.1961

Date of last renewal: 28.11.2009

10. DATE OF REVISION OF THE TEXT