SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Trihexyphenidyl Hydrochloride 5mg/5ml Syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains 5mg trihexyphenidyl hydrochloride

Excipients with known effect
Sucrose: 2.6g/5ml
Ethanol: 0.817mg/5ml
Propylene Glycol: 19.27mg per 5ml
Sodium Benzoate: 5.9mg per 5ml

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

A blackcurrant scented and flavoured colourless syrup.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Parkinsonism and drug induced extrapyramidal syndrome.

4.2 Posology and method of administration

Posology

Adults and Elderly:
Initial dose 2mg. Subsequent doses up to 20mg as recommended by a physician.

Children:
Not recommended.

Method of administration

For oral administration

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Precautions: Since the use of trihexyphenidyl may, in some cases, continue indefinitely, the patient should be under careful observation over the long term. It should be administered with care to avoid allergic or other untoward reactions.

Except in the case of vital complications, abrupt discontinuation of the drug should be avoided.

Incipient glaucoma may be precipitated by para-sympatholytic drugs such as trihexyphenidyl.

Hypertension, cardiac, liver or kidney disorders are not contraindicated, but such patients should be followed closely. As trihexyphenidyl may provoke or exacerbate tardive dyskinesia, it is not recommended for use in patients with this condition.

Trihexyphenidyl should be used with caution in patients with glaucoma, obstructive disease of the gastro-intestinal or genito-urinary tracts, and in elderly males with possible prostatic hypertrophy.

Since trihexyphenidyl has been associated with clinical worsening of myasthenia gravis, the drug should be avoided or used with great caution in patients with this condition.

Since certain psychiatric manifestations such as confusion, delusions and hallucinations, all of which may occur with any of the atropine-like drugs, have been reported rarely with trihexyphenidyl, it should be used with extreme caution in elderly patients (see section 4.2).

Warnings: Trihexyphenidyl may be the subject of abuse (on the basis of hallucinogenic and euphoriant properties, common to all anti-cholinergic drugs) if given in sufficient amounts.

Excipient Warnings:
This product contains –

- Sucrose – 2.6g per 5ml. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
- Ethanol – this medicine contains 0.817 mg of alcohol (ethanol) in each 5 ml, which is equivalent to 0.1634 mg/ml. The amount in 5ml of this medicine is equivalent to less than 1 ml beer or 1 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.
- Propylene glycol – this medicine contains 19.27mg per 5ml. Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce adverse effects in children less than 5 years old.

While propylene glycol has not been shown to cause reproductive or developmental toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case by case basis.
Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

- Sodium benzoate – this medicine contains 5.9mg sodium benzoate in each 5ml, which is equivalent to 1.18mg/ml.
- Sodium – this medicine contains less than 1mmol sodium (23 mg) per 5ml, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Extra care should be taken when trihexyphenidyl is given concomitantly with phenothiazines, clozapine, antihistamines, disopyramide, nefopam and amantadine because of the possibility of increased antimuscarinic side-effects.

Synergy has been reported between trihexyphenidyl and tricyclic antidepressants, probably because of an additive effect at the receptor site.
This can cause dry mouth, constipation and blurred vision. In the elderly, there is a danger of precipitating urinary retention, acute glaucoma or paralytic ileus.

Monoamine oxidase inhibitors can interact with concurrently administered anticholinergic agents including trihexyphenidyl. This can cause dry mouth, blurred vision, urinary hesitancy, urinary retention and constipation.

In general, anticholinergic agents should be used with caution in patients who are receiving tricyclic antidepressants or monoamine oxidase inhibitors. In patients who are already on antidepressant therapy the dose of trihexyphenidyl should be initially reduced and the patient reviewed regularly.

Trihexyphenidyl may be antagonistic with the actions of metoclopramide and domperidone on gastro-intestinal function.

The absorption of levodopa may possibly be reduced when used in conjunction with trihexyphenidyl.

Trihexyphenidyl may be antagonistic with the actions of parasympathomimetics.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is inadequate information regarding the use of trihexyphenidyl in pregnancy. Animal studies are insufficient with regard to effects on pregnancy, embryonal/foetal development, parturition and postnatal

development. The potential risk for humans is unknown. Trihexyphenidyl should not be used during pregnancy unless clearly necessary.

Breastfeeding

It is unknown whether trihexyphenidyl is excreted in human breast milk. The excretion of trihexyphenidyl in milk has not been studied in animals. Infants may be very sensitive to the effects of antimuscarinic medications. Trihexyphenidyl should not be used during breast feeding.

4.7 Effects on ability to drive and use machines

Trihexyphenidyl hydrochloride may affect the performance of skilled tasks such as driving and operating machinery as it can cause blurring of vision, dizziness and mild nausea. Also mental confusion in some cases.

4.8 Undesirable effects

Modern clinical data required to determine the frequency of undesirable effects are lacking for trihexyphenidyl. Minor side effects such as dryness of mouth, constipation, blurring of vision, dizziness, mild nausea or nervousness will be experienced by 30-50% of all patients. These reactions tend to become less pronounced as treatment continues. Patients should be allowed to develop a tolerance using the smaller initial dose until an effective level is reached.

Immune system disorders: Hypersensitivity.

Psychiatric disorders: Nervousness, restlessness, confusional states, agitation, delusions, hallucinations, insomnia, especially in the elderly and patients with arteriosclerosis. The development of psychiatric disturbances may necessitate discontinuation of treatment.

Euphoria may occur. There have been reports of abuse of trihexyphenidyl due to its euphoric and hallucinogenic properties.

Nervous system disorders: Dizziness.

Impairment of immediate and short-term memory function has been reported. Worsening of myasthenia gravis may occur (see section 4.4).

Eye disorders: Dilatation of the pupils with loss of accommodation and photophobia, raised intraocular pressure (see section 4.4).

Cardiac disorders: Tachycardia.

Respiratory, thoracic and mediastinal disorders: Decreased bronchial secretions.

Gastrointestinal disorders: Dry mouth with difficulty swallowing, constipation, nausea, vomiting.

Skin and subcutaneous tissue disorders: Flushing and dryness of skin, skin rashes.

Renal and urinary disorders: Urinary retention, difficulty in micturition.

General disorders: Thirst, pyrexia.

Reporting of suspected 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. Healthcare professional are asked to report any suspected adverse reactions via Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

Symptoms of overdose with antimuscarinic agents include flushing and dryness of the skin, dilated pupils, dry mouth and tongue, tachycardia, rapid respiration, hyperpyrexia, hypertension, nausea, vomiting. A rash may appear on the face or upper trunk. Symptoms of CNS stimulation include restlessness, confusion, hallucinations, paranoid and psychotic reactions, incoordination, delirium and occasionally convulsions. In severe overdose, CNS depression may occur with coma, circulatory and respiratory failure and death.

Treatment

Treatment should always be supportive. An adequate airway should be maintained. Diazepam may be administered to control excitement and convulsions but the risk of central nervous system depression should be considered. Hypoxia and acidosis should be corrected. Antiarrhythmic drugs are not recommended if dysrhythmias occur.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anti-cholinergic agents
ATC code: NO4A A 01

Trihexyphenidyl is a tertiary amine antimuscarinic. It also has a direct antispasmodic action on smooth muscle.

5.2 Pharmacokinetic properties

Trihexyphenidyl is well absorbed from the gastro-intestinal tract.

5.3 Preclinical safety data

No formal preclinical studies have been undertaken with Trihexyphenidyl Syrup, as its active ingredient is a well established pharmaceutical.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Monohydrate citric acid, sodium benzoate, propylene glycol, glycerol, ethanol, blackcurrant flavour, sucrose and purified water.

6.2 Incompatibilities

None known.

6.3 Shelf life

24 months.

6.2 *Special precautions for storage*

Do not store above 25°C. Do not refrigerate or freeze. Store in the original package.

6.5 Nature and contents of container

200ml pack size in amber glass bottle with child resistant cap.

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL00427/0222

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24/03/2023