Dilating eye drops used for examination

Mydrin®-P Ophthalmic Solution

Mydrin®-P

Tropicamide and Phenylephrine Ophthalmic Solution

DOH Import No. 005728

Contraindications (This product is contraindicated in the following patients.)

1) Patients with glaucoma or those predisposed to ocular hypertension as evidenced by a narrow angle or shallow anterior chamber. [Acute angle-closure glaucoma may occur.]
2) Patients with a history of hypersensitivity to any ingredients of this product

Composition, Characteristics

Product Name	Mydrin®-P Ophthalmic Solution	
Active Ingredients	tropicamide	phenylephrine hydrochloride
Content (per 1 mL)	5mg	5 mg
Additives	e-aminocaproic acid, benzalkonium chloride, chlorobutanol, boric acid, hydrochloric acid, purified water	
pH	4.5~5.8	
Ratio of osmotic pressure	0.9~1.1	
Characteristics	Colorless to light yellow, clear, sterile water-based ophthalmic solution	

Indication

Mydriasis and cycloplegia

Category

This drug must be prescribed by a physician

Administration and Dosage

For pupil dilation, usually 1-2 drops per time, or 1 drop each time at an interval of 3 to 5 minutes and 2 attempts in total. For cycloplegia, usually 1 drop each time at an interval of 3 to 5 minutes and 2 to 3 attempts in total. The dosage may be increased or decreased as appropriate depending on the symptoms.

Precautions

1. Careful administration (This product should be administered with care in the following patients)
   1) Children [See “6. Pediatric Use” section]
   2) Patients with hypertension [Symptoms may be aggravated due to hypertensive effect of phenylephrine]
   3) Patients with atherosclerosis [Symptoms may be aggravated due to the hypertensive effect of phenylephrine]
   4) Patients with heart disease, including coronary artery disease or heart failure [Symptoms may be aggravated due to the β_1 agonistic effect of phenylephrine]
   5) Patients with diabetes [Symptoms may be aggravated due to gluconeogenesis promoting effect of phenylephrine]
   6) Patients with hyperthyroidism [Since hyperthyroidism may be accompanied with the development of sympathomimetic symptoms such as palpitation and tachycardia, administration of this product may aggravate these symptoms.]

2. Important precautions
   1) As bradycardia, apnea, etc. may occur when this product is administered to premature infants for the purpose of funduscopy, this product should be administered with care while closely observing the patient’s condition. [See “6. Pediatric Use” section]
   2) Since this product causes mydriasis and/or cycloplegia, patients should be cautioned against engaging in potentially hazardous activities requiring clear vision, such as operating machinery or driving a car. Instruct the patients to protect their eyes from direct sunlight or other powerful light by wearing sunglasses or by other means.

3. Drug interaction
   [Caution on Concomitant Use] (Precautions on concomitant use)

Name of agent	Clinical symptoms, and treatment	Mechanism and risk factors
MAO inhibiters (during treatment and within 3 weeks after treatment)	A rapid increase in the blood pressure may occur	MAO inhibiters may inhibit metabolic enzymes of this drug, and may increase catecholamine sensitivity.
Tricyclic or tetracyclic anti-depressants: maprotiline hydrochloride, clomipramine hydrochloride, amoxapine	A rapid increase in the blood pressure may occur	These drugs may inhibit norepinephrine reuptake at sympathetic nerve endings, and may increase the concentration of epinephrine at receptor sites.

4. **Adverse reactions**

This product has not been investigated to determine the incidence of adverse drug reactions.
If any systemic symptoms occur, administration should be discontinued.

1) Clinically significant adverse reactions
Shock, anaphylactoid reaction (incidence unknown): Since shock and anaphylactoid reaction may occur, patients should be carefully observed. If any symptoms such as erythema, rash, dyspnea, decreased blood pressure, and eyelid oedema, etc. are observed, administration should be discontinued and appropriate measures should be taken.

2) Other adverse reactions
If an adverse drug reaction is observed, appropriate measures including discontinuing administration should be taken.

Incidence / Type	Incidence unknown
Hypersensitivity	Blepharitis (eyelid redness and eyelid swelling, etc.), eyelid dermatitis, itching, rash, urticaria
Ophthalmic	Conjunctivitis (conjunctival hyperaemia and conjunctival oedema, eye discharge, etc.), corneal epithelial disorder, increased intraocular pressure
Gastrointestinal	Thirst, nausea, vomiting
Others	Facial flushing, tachycardia, blood pressure increased, headache

5. **Use in the Elderly**

Because physiological function is generally reduced in the elderly, caution should be exercised.

6. **Pediatric Use**

Since systemic adverse drug reactions are likely to occur when administered to pediatric patients, this product should be administered with care while observing the patient's condition. Especially, when applied to premature infants, administer cautiously under close observation of the patient's condition, since it has been reported that bradycardia or apnea occurred. In case of any abnormal findings, administration should be discontinued immediately and appropriate measures should be taken. It is advisable that this product should be diluted for use, if necessary.

7. **Precautions concerning Use**

1) Route of administration: For ophthalmic use only.
2) At the time of administration:
(1) In principle, this product should be applied into the conjunctival sac after eyelid retraction, while the patient is in a supine position. After application, the treated eye should be closed for 1-5 min. while the lacrimal sac is compressed appropriately.
(2) Instruct the patient to be careful not to touch the tip of the bottle to the eye directly in order to avoid the contamination of the drug.

8. **Others**

Do not use this product in case of discoloration or precipitation.

Clinical results

1. Pupillary dilation [1)-2)]

Generally speaking, elderly people have smaller pupils. As such, with only tropicamide, pupil dilation might not be fully reached sometimes. The pupil dilating effect of phenylephrine hydrochloride-based Mydrin®-P is independent of age. When used in patients aged 40 and older, in particular, the pupil dilating effect is obviously reinforced.

2. Cycloplegia [3)]

In 8 healthy subjects without eye disorders except for ametropia, 1 drop of this agent was administered in one of the eyes once every 3 minutes and 3 times in total. The cycloplegic effect reached the highest at 20 to 30 minutes following completion of administration, and the accommodative function returned to normal at 5 to 6 hours later.

Pharmacological effects

1. Pupillary dilation [4)]

(White rabbits)
Solutions of tropicamide and phenylephrine hydrochloride mixed at various ratios accomplished pupil dilation as a result of relaxed pupillae caused by tropicamide and dilatator pupillae contraction caused by phenylephrine hydrochloride. In addition, synergistic effects would result from the combination of the two. The effect was the most significant when tropicamide and phenylephrine were combined at a 1:1 ratio.

2. Cycloplegia [5)]

(Human)
In a refraction test of children with vision disorder and esotropia, the cycloplegic effect of Mydrin®-P administered 1 to 2 times was compared with the effect of 0.5% or 1% atropine 3 times a day for a total of 3 days. Measurement of the refractive state showed that the cycloplegic effect of Mydrin®-P was inferior to that of atropine.

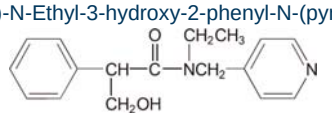
Physical and chemical characteristics of active ingredients

1) tropicamide

Generic name tropicamide

Chemical name (2RS)-N-Ethyl-3-hydroxy-2-phenyl-N-(pyridin-4-ylmethyl) propanamide

Structural formula



Molecular formula $C_{17}H_{20}N_2O_2$

Molecular weight 284.35

Characteristics This product is a white crystalline, odorless, basic-flavor powder.
It dissolves easily in ethanol or chloroform, poorly in water or diethyl ether, and barely in petroleum ether.
The product dissolves in dilute hydrochloric acid.
The pH of 1.0 g of the product dissolved in 500 mL water is 6.5 ~ 8.0.

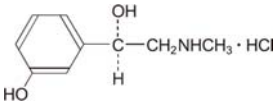
Melting point 96~99°C;

2) phenylephrine hydrochloride

Generic name phenylephrine hydrochloride

Chemical name (R)-1-(3-hydroxyphenyl)-2-(methylamino) ethanol monohydrochloride

Structural formula



Molecular formula $C_9H_{13}NO_2 \cdot HCl$

Molecular weight 203.67

Characteristics: This product appears to be white crystal or crystalline powder that is odorless and bitter tasting.
It is readily soluble in water and easily soluble in ethanol but is barely soluble in diethyl ether.
The pH of 1.0 g of the product dissolved in 100 mL water is 4.5 ~ 5.5.

Melting point 140~145°C;

Precautions for Storage

Storage Store at room temperature (1 – 30°C;)

Expiry date See the external box and label (3 years)

Package

100 ml or smaller plastic bottles

Precautions

After ocular fundus examination with administrationof Mydrin®-P is completed, inform the patient of the following precautions.

1. Since your pupils are dilated, your vision is blurred and your eyes are more easily dazzled than usual for 4-5 hours. These symptoms soon disappear spontaneously.
2. Please avoid potentially hazardous activities requiring clear vision, such as driving a car, for half a day after this ophthalmological examination.
3. Please contact the doctor in charge of the examination or consult with a local ophthalmologist immediately if you suffer following symptoms.
   1) Sudden headache or eye pain after the examination.
   2) In case of persisting the following symptoms until the next day of the examination.
      (1) Larger pupils than usual (or different size of each pupil).
      (2) No signs of improvement for blurred vision.
      (3) More sensitive to lights than usual.
      (4) Headache or eye pain (except known etiology, such as common cold)

   [Note] After the examination, normal vision can be regained more readily if a pilocarpine ophthalmic solution is applied.

Major Literatures

1) 三井幸彦等著 日本眼科學會雜誌66, 174 (1962)

2) 石川哲等著 日本眼科學會雜誌81, 1515 (1977)

3) 所 敬等著 眼科臨床醫報60, 483 (1966)

4) 高瀨小枝子等著 每瞳令-普益的藥理學性研究(1)，社內資料

5) 久保田伸枝等著 眼科臨床醫報64, 18 (1970)

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