

PHENYLEPHRINE HYDROCHLORIDE- phenylephrine hydrochloride solution/ drops
Paragon BioTeck, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PHENYLEPHRINE HYDROCHLORIDE OPHTHALMIC SOLUTION, USP 2.5% and 10 % safely and effectively. See full prescribing information for PHENYLEPHRINE HYDROCHLORIDE OPHTHALMIC SOLUTION, USP 2.5% and 10 %.

PHENYLEPHRINE HYDROCHLORIDE OPHTHALMIC SOLUTION, USP 2.5% and 10 %, for topical ophthalmic use

Initial U.S. Approval: 1939

----- **INDICATIONS AND USAGE** -----

Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% and 10% is an alpha-1 adrenergic receptor agonist indicated to dilate the pupil [1].

----- **DOSAGE AND ADMINISTRATION** -----

- For patients 1 year of age and older, apply one drop of Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% or 10% at 3 to 5 minute intervals up to a maximum of 3 drops per eye [2.1].
- In pediatric patients less than 1 year of age, one drop of Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% should be instilled at 3 to 5 minute intervals up to a maximum of 3 drops per eye [2.2].

----- **DOSAGE FORMS AND STRENGTHS** -----

2.5% and 10% sterile ophthalmic solutions [3].

----- **CONTRAINDICATIONS** -----

- Phenylephrine Hydrochloride Ophthalmic Solution, USP 10% is contraindicated in patients with hypertension, or thyrotoxicosis. Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% should be used in these patients [4.1].
- Phenylephrine Hydrochloride Ophthalmic Solution, USP 10% is contraindicated in pediatric patients less than 1 year of age due to the increased risk of systemic toxicity. Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% should be used in these patients [4.2].

----- **WARNINGS AND PRECAUTIONS** -----

- Not for injection. Topical ophthalmic use only [5.1].
- Reports of serious cardiovascular reactions, some fatal, with phenylephrine hydrochloride 10% solution. Monitor blood pressure in patients with cardiovascular disease [5.2].
- Significant elevations in blood pressure have been reported. Caution in pediatric patients less than 5 years of age, and in patients with elevated blood pressure [5.3].
- Rebound miosis has been reported one day after instillation [5.4].

----- **ADVERSE REACTIONS** -----

- Ocular adverse reactions include eye pain and stinging on instillation, temporary blurred vision and photophobia [6.1].
- Cardiovascular adverse reactions include increase in blood pressure, syncope, myocardial infarction, tachycardia, arrhythmia and subarachnoid hemorrhage [6.2].

To report SUSPECTED ADVERSE REACTIONS, contact Paragon BioTeck, Inc. at 1-888-424-1192 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----- **DRUG INTERACTIONS** -----

- May exaggerate the adrenergic pressor response in patients taking atropine-like drugs [7.1].
- May potentiate the cardiovascular depressant effects of potent inhalation anesthetic agents [7.1].

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 5/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 General Dosing Recommendations
- 2.2 Pediatric Patients Less Than 1 Year of Age

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

- 4.1 Cardiac and Endocrine Disease
- 4.2 Pediatric Patients Less Than 1 Year of Age

5 WARNINGS AND PRECAUTIONS

- 5.1 Topical Ophthalmic Use Only
- 5.2 Cardiovascular Reactions
- 5.3 Elevation in Blood Pressure
- 5.4 Rebound Miosis

6 ADVERSE REACTIONS

- 6.1 Ocular Adverse Reactions
- 6.2 Systemic Adverse Reactions

7 DRUG INTERACTIONS

- 7.1 Agents That May Exaggerate Pressor Responses

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Phenylephrine Hydrochloride Ophthalmic Solution, 2.5% and 10% is indicated to dilate the pupil.

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Recommendations

In patients 1 year of age or greater, apply one drop of either Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% or 10% every 3 to 5 minutes to the conjunctival fornix as required up to a maximum of 3 drops. If necessary, this dose may be repeated.

In order to obtain a greater degree of mydriasis, Phenylephrine Hydrochloride Ophthalmic Solution, USP 10% may be needed.

2.2 Pediatric Patients Less Than 1 Year of Age

In pediatric patients less than 1 year of age, one drop of Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% should be instilled at 3 to 5 minute intervals up to a maximum of 3 drops per eye.

3 DOSAGE FORMS AND STRENGTHS

Phenylephrine Hydrochloride Ophthalmic Solution, 2.5% is a clear, colorless, sterile topical ophthalmic solution containing phenylephrine hydrochloride 2.5%.

Phenylephrine Hydrochloride Ophthalmic Solution, 10% is a clear, colorless, sterile topical ophthalmic solution containing phenylephrine hydrochloride 10%.

4 CONTRAINDICATIONS

4.1 Cardiac and Endocrine Disease

Phenylephrine Hydrochloride Ophthalmic Solution, USP 10% is contraindicated in patients with hypertension or thyrotoxicosis. Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% should be used in these patients.

4.2 Pediatric Patients Less Than 1 Year of Age

Phenylephrine Hydrochloride Ophthalmic Solution, USP 10% is contraindicated in pediatric patients less than 1 year of age due to the increased risk of systemic toxicity. Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% should be used in these patients [*See Dosage and Administration section*].

5 WARNINGS AND PRECAUTIONS

5.1 Topical Ophthalmic Use Only

Phenylephrine Hydrochloride Ophthalmic Solution, 2.5% and 10% is not indicated for injection.

5.2 Cardiovascular Reactions

There have been reports of serious cardiovascular reactions, including ventricular arrhythmias and myocardial infarctions, in patients using phenylephrine 10%. These episodes, some fatal, have usually occurred in patients with pre-existing cardiovascular diseases. Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% should be used in these patients.

5.3 Elevation in Blood Pressure

A significant elevation in blood pressure is not common but has been reported following conjunctival instillation of recommended doses of phenylephrine 10%. The risk is less with phenylephrine 2.5%. Caution should be exercised with the use of phenylephrine 10% in pediatric patients less than 5 years of age and patients with hyperthyroidism, or cardiovascular disease. The post-treatment blood pressure of patients with cardiac and endocrine diseases and any patients who develop symptoms should be carefully monitored.

5.4 Rebound Miosis

Rebound miosis has been reported one day after receiving phenylephrine hydrochloride ophthalmic solution, and re instillation of the drug produced a lesser mydriatic effect.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below and elsewhere in the labeling: • Cardiac Disease [See Warnings and Precautions (5.2)] • Elevation in Blood Pressure [See Warnings and Precautions (5.3)] The following adverse reactions have been identified following use of phenylephrine hydrochloride ophthalmic solution. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

6.1 Ocular Adverse Reactions

Eye pain and stinging on instillation, temporary blurred vision and photophobia, and conjunctival sensitization may occur.

6.2 Systemic Adverse Reactions

A marked increase in blood pressure has been reported particularly, but not limited to low weight premature neonates, infants and hypertensive patients.

Cardiovascular reactions which have occurred primarily in hypertensive patients following topical ocular use of phenylephrine hydrochloride ophthalmic solution 10% solution include marked increase in blood pressure, syncope, myocardial infarction, tachycardia, arrhythmia and subarachnoid hemorrhage. [See Warnings and Precautions (5.2 and 5.3)]

7 DRUG INTERACTIONS

7.1 Agents That May Exaggerate Pressor Responses

Concomitant use of phenylephrine and atropine may enhance the pressor effects and induce tachycardia in some patients. Phenylephrine may potentiate the cardiovascular depressant effects of some inhalation anesthetic agents.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Animal reproduction studies have not been conducted with topical phenylephrine. It is also not known whether phenylephrine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Phenylephrine hydrochloride should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

It is not known whether this drug is excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when Phenylephrine Hydrochloride Ophthalmic Solution, 2.5% and 10% is administered to a nursing woman.

8.4 Pediatric Use

Phenylephrine Hydrochloride Ophthalmic Solution, 10% is contraindicated in pediatric patients less than 1 year of age infants. Phenylephrine Hydrochloride Ophthalmic Solution, 2.5% should be used in these patients [See 4.2 Contraindications] .

8.5 Geriatric Use

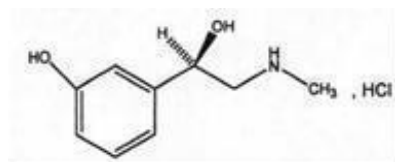
No overall differences in safety and effectiveness have been observed between elderly and younger adult patients.

10 OVERDOSAGE

Overdosage of phenylephrine may cause a rapid rise in blood pressure. It may also cause headache, anxiety, nausea, and vomiting, and ventricular arrhythmias. Prompt injection of a rapidly acting alpha-adrenergic blocking agent such as phentolamine has been recommended.

11 DESCRIPTION

Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% and 10% is a sterile, clear, colorless, topical mydriatic agent for ophthalmic use. The chemical name is (R)-3-hydroxy- α -[(methylamino)methyl]benzenemethanol hydrochloride. Phenylephrine hydrochloride is represented by the following structural formula:



Phenylephrine hydrochloride has a molecular weight of 203.67 and an empirical formula of $C_9H_{13}NO_2 \cdot HCl$.

Each mL of Phenylephrine Hydrochloride Ophthalmic Solution, 2.5% contains: ACTIVE: phenylephrine hydrochloride 25 mg (2.5%); INACTIVES: sodium phosphate monobasic, sodium phosphate dibasic; boric acid, water for injection. Hydrochloric acid and/or sodium hydroxide may be added to adjust pH (6.0-6.4). The solution has a tonicity of 500 mOsm/kg. PRESERVATIVE: benzalkonium chloride 0.01%.

Each mL of Phenylephrine Hydrochloride Ophthalmic Solution, 10% contains: ACTIVE: phenylephrine hydrochloride 100 mg (10%); INACTIVES: sodium phosphate monobasic, sodium phosphate dibasic; water for injection. Hydrochloric acid and/or sodium hydroxide may be added to adjust pH (6.3-6.7). The solution has a tonicity of 1000 mOsm/kg. PRESERVATIVE: benzalkonium chloride 0.01%.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Phenylephrine is an alpha-1 adrenergic receptor agonist used for dilation of the pupil due to its vasoconstrictor and mydriatic action. Phenylephrine possesses predominantly α -adrenergic effects. In the eye, phenylephrine acts locally as a potent vasoconstrictor and mydriatic, by constricting ophthalmic blood vessels and the radial muscle of the iris.

12.2 Pharmacodynamics

Maximal mydriasis occurs in 20 to 90 minutes with recovery after 3 to 8 hours.

Systemic absorption of sufficient quantities of phenylephrine may lead to systemic α -adrenergic effects, such as rise in blood pressure which may be accompanied by a reflex atropine-sensitive bradycardia.

12.3 Pharmacokinetics

The systemic exposure following topical administration of phenylephrine hydrochloride ophthalmic solution has not been studied. A higher systemic absorption is expected for the 10% solution than the 2.5% solution and when the corneal barrier function is compromised.

14 CLINICAL STUDIES

Pupillary dilation following topical administration of phenylephrine hydrochloride ophthalmic solution has been demonstrated in controlled clinical studies in adults and pediatric patients with different levels of iris pigmentation. Pupil movement is generally seen within 15 minutes, maximal mydriasis between 20 to 90 minutes and recovery after 3 to 8 hours. Darker irides tend to dilate slower than lighter irides

16 HOW SUPPLIED/STORAGE AND HANDLING

Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5% is supplied as a sterile, aqueous, topical ophthalmic solution with a fill volume of 15 mL in a 15 mL opaque, white low density polyethylene (LDPE) bottle with a linear low density polyethylene (LLDPE) dropper tip and red cap. (NDC 42702-102-15)

Phenylephrine Hydrochloride Ophthalmic Solution, USP 10% is supplied as a sterile, aqueous, topical ophthalmic solution with a fill volume of 5 mL in a 10 mL opaque, white LDPE bottle with a LLDPE dropper tip and red cap. (NDC 42702-103-05)

Storage and Handling:

Store in a refrigerator at 2° to 8°C (36°-46°F).

After opening, Phenylephrine Hydrochloride Ophthalmic Solution, USP can be used until the expiration date on the bottle.

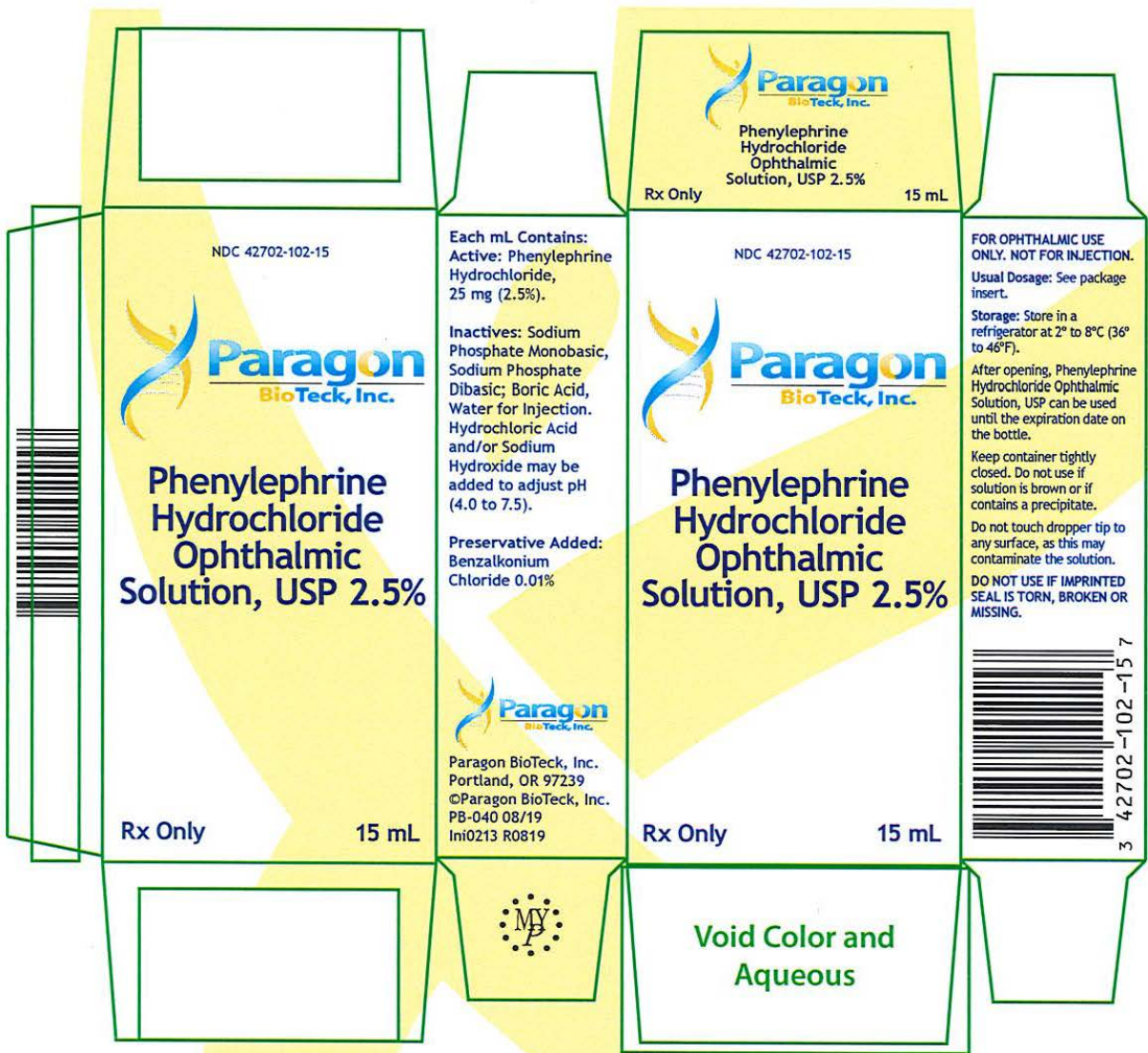
17 PATIENT COUNSELING INFORMATION

Advise patients not to touch the dropper tip to any surface as this may contaminate the solution. Inform patients they may experience sensitivity to light and should protect their eyes in bright illumination while their pupils are dilated.

Paragon BioTeck, Inc.

Portland, OR 97239

©Paragon BioTeck, Inc.



NDC 42702-102-15



Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5%

Rx Only

15 mL

Each mL Contains:
Active: Phenylephrine Hydrochloride, 25 mg (2.5%).

Inactives: Sodium Phosphate Monobasic, Sodium Phosphate Dibasic; Boric Acid, Water for Injection. Hydrochloric Acid and/or Sodium Hydroxide may be added to adjust pH (4.0 to 7.5).

Preservative Added: Benzalkonium Chloride 0.01%



Paragon BioTeck, Inc.
Portland, OR 97239
©Paragon BioTeck, Inc.
PB-040 08/19
Ini0213 R0819



Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5%

Rx Only

15 mL

NDC 42702-102-15



Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5%

Rx Only

15 mL

FOR OPHTHALMIC USE ONLY. NOT FOR INJECTION. Usual Dosage: See package insert.

Storage: Store in a refrigerator at 2° to 8°C (36° to 46°F).

After opening, Phenylephrine Hydrochloride Ophthalmic Solution, USP can be used until the expiration date on the bottle.

Keep container tightly closed. Do not use if solution is brown or if contains a precipitate.

Do not touch dropper tip to any surface, as this may contaminate the solution.

DO NOT USE IF IMPRINTED SEAL IS TORN, BROKEN OR MISSING.



3 42702-102-15 7

Void Color and Aqueous

Each mL Contains:

Active: Phenylephrine Hydrochloride, 25 mg (2.5%).

Preservative: Benzalkonium Chloride 0.01%

Inactives: Sodium Phosphate Monobasic, Sodium Phosphate Dibasic; Boric Acid, Water for Injection. Hydrochloric Acid and/or Sodium Hydroxide may be added to adjust pH (4.0 to 7.5).

PB-039 08/19 Ini0213 R0819

NDC 42702-102-15



Phenylephrine Hydrochloride Ophthalmic Solution, USP 2.5%

Rx Only

15 mL

FOR OPHTHALMIC USE ONLY.
NOT FOR INJECTION.

Usual Dosage: See package insert.

Storage: Store in a refrigerator at 2° to 8°C (36° to 46°F).

Keep container tightly closed. Do not use if solution is brown or if contains a precipitate.

DO NOT USE IF IMPRINTED SEAL ON CAP IS TORN, BROKEN OR MISSING.

After opening Phenylephrine Hydrochloride Ophthalmic Solution, USP can be used until the expiration date on the bottle.

Paragon BioTeck, Inc.
Portland, OR 97239
©Paragon BioTeck, Inc.





NDC 42702-103-05



Phenylephrine Hydrochloride Ophthalmic Solution, USP 10%

Rx Only 5 mL

Each mL Contains:
Active: Phenylephrine Hydrochloride, 100 mg (10%).

Inactives: Sodium Phosphate Monobasic, Sodium Phosphate Dibasic; Water for Injection. Hydrochloric Acid and/or Sodium Hydroxide may be added to adjust pH (4.0 to 7.5).

Preservative Added: Benzalkonium Chloride 0.01%



Paragon BioTeck, Inc.
Portland, OR 97239
©Paragon BioTeck, Inc.
PB-042 08/19
Int0213 R0819



Phenylephrine Hydrochloride Ophthalmic Solution, USP 10%

Rx Only 5 mL

NDC 42702-103-05



Phenylephrine Hydrochloride Ophthalmic Solution, USP 10%

Rx Only 5 mL

FOR OPHTHALMIC USE ONLY. NOT FOR INJECTION. Usual Dosage: See package insert.

Storage: Store in a refrigerator at 2° to 8°C (36° to 46°F).

After opening, Phenylephrine Hydrochloride Ophthalmic Solution, USP can be used until the expiration date on the bottle.

Keep container tightly closed. Do not use if solution is brown or if contains a precipitate.

Do not touch dropper tip to any surface, as this may contaminate the solution.

DO NOT USE IF IMPRINTED SEAL IS TORN, BROKEN OR MISSING.



3 42702-103-05 5

Void Color and Aqueous


Each mL Contains:
Active: Phenylephrine Hydrochloride, 100 mg (10%).
Preservative: Benzalkonium Chloride 0.01%.
Inactives: Sodium Phosphate Monobasic, Sodium Phosphate Dibasic; Water for Injection, Hydrochloric Acid and/or Sodium Hydroxide may be added to adjust pH (4.0 to 7.5).
 PB-041 08/19 Ini0213 R0819

NDC 42702-103-05

Phenylephrine Hydrochloride Ophthalmic Solution, USP 10%
 Rx Only

5 mL

FOR OPHTHALMIC USE ONLY.
 NOT FOR INJECTION.
Usual Dosage: See package insert.
Storage: Store in a refrigerator at 2° to 8°C (36° to 46°F).
 Keep container tightly closed. Do not use if solution is brown or if contains a precipitate.
DO NOT USE IF IMPRINTED SEAL ON CAP IS TORN, BROKEN OR MISSING.
 After opening, Phenylephrine Hydrochloride Ophthalmic Solution, USP can be used until the expiration date on the bottle.
 Paragon BioTeck, Inc.
 Portland, OR 97239
 ©Paragon BioTeck, Inc.



PHENYLEPHRINE HYDROCHLORIDE

phenylephrine hydrochloride solution/ drops

Product Information

| | | | |
|--------------------------------|-------------------------|---------------------------|---------------|
| Product Type | HUMAN PRESCRIPTION DRUG | Item Code (Source) | NDC:42702-102 |
| Route of Administration | OPHTHALMIC | | |

Active Ingredient/Active Moiety

| Ingredient Name | Basis of Strength | Strength |
|---|-----------------------------|----------------|
| PHENYLEPHRINE HYDROCHLORIDE (UNII: 04JA59TNSJ) (PHENYLEPHRINE - UNII:1WS297W6MV) | PHENYLEPHRINE HYDROCHLORIDE | 2.5 mg in 1 mL |

Inactive Ingredients

| Ingredient Name | Strength |
|---|----------|
| HYDROCHLORIC ACID (UNII: QTT17582CB) | |
| SODIUM HYDROXIDE (UNII: 55X04QC32I) | |
| BORIC ACID (UNII: R57ZHV85D4) | |
| SODIUM PHOSPHATE, MONOBASIC (UNII: 3980JIH2SW) | |
| SODIUM PHOSPHATE, DIBASIC (UNII: GR686LBA74) | |
| WATER (UNII: 059QF0KO0R) | |

Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|---|------------------|---|----------------------|--------------------|
| 1 | NDC:42702-102-15 | 1 in 1 CARTON | 04/15/2013 | |
| 1 | | 15 mL in 1 BOTTLE, DROPPER; Type 0: Not a Combination Product | | |
| 2 | NDC:42702-102-10 | 1 in 1 CARTON | 04/15/2020 | |
| 2 | | 10 mL in 1 BOTTLE, DROPPER; Type 0: Not a Combination Product | | |

Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|--------------------|--|----------------------|--------------------|
|--------------------|--|----------------------|--------------------|

| | | | |
|-----|-----------|------------|--|
| NDA | NDA203510 | 04/15/2013 | |
|-----|-----------|------------|--|

PHENYLEPHRINE HYDROCHLORIDE

phenylephrine hydrochloride solution/ drops

Product Information

| | | | |
|--------------------------------|-------------------------|---------------------------|---------------|
| Product Type | HUMAN PRESCRIPTION DRUG | Item Code (Source) | NDC:42702-103 |
| Route of Administration | OPHTHALMIC | | |

Active Ingredient/Active Moiety

| Ingredient Name | Basis of Strength | Strength |
|--|-----------------------------|----------------|
| PHENYLEPHRINE HYDROCHLORIDE (UNII: 04JA59TNSJ) (PHENYLEPHRINE - UNII:1WS297W6MV) | PHENYLEPHRINE HYDROCHLORIDE | 100 mg in 1 mL |

Inactive Ingredients

| Ingredient Name | Strength |
|---|----------|
| HYDROCHLORIC ACID (UNII: QTT17582CB) | |
| SODIUM HYDROXIDE (UNII: 55X04QC32I) | |
| BORIC ACID (UNII: R57ZHV85D4) | |
| SODIUM PHOSPHATE, MONOBASIC (UNII: 3980JH2SW) | |
| SODIUM PHOSPHATE, DIBASIC (UNII: GR686LBA74) | |
| WATER (UNII: 059QF0K00R) | |

Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|---|------------------|--|----------------------|--------------------|
| 1 | NDC:42702-103-05 | 1 in 1 CARTON | 04/15/2013 | |
| 1 | | 5 mL in 1 BOTTLE, DROPPER; Type 0: Not a Combination Product | | |

Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|--------------------|--|----------------------|--------------------|
| NDA | NDA203510 | 04/15/2013 | |

Labeler - Paragon BioTeck, Inc. (078279037)

Registrant - Paragon BioTeck, Inc. (078279037)

Establishment

| Name | Address | ID/FEI | Business Operations |
|-----------------------|---------|-----------|-----------------------------------|
| Paragon BioTeck, Inc. | | 078279037 | manufacture(42702-102, 42702-103) |

Revised: 5/2020

Paragon BioTeck, Inc.