

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**217370Orig1s000**

**LABELING**

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TRYPTYR® safely and effectively. See full prescribing information for TRYPTYR.

**TRYPTYR (acotremon ophthalmic solution) 0.003%,  
for topical ophthalmic use  
Initial U.S. Approval: 2025**

### INDICATIONS AND USAGE

TRYPTYR is a TRPM8 thermoreceptor agonist indicated for the treatment of the signs and symptoms of dry eye disease. (1)

### DOSAGE AND ADMINISTRATION

Instill one drop in each eye twice daily (approximately 12 hours apart). (2)

### DOSAGE FORMS AND STRENGTHS

Ophthalmic solution: 0.003% acotremon in a single-dose vial. (3)

### CONTRAINDICATIONS

None. (4)

### WARNINGS AND PRECAUTIONS

To avoid the potential for eye injury and contamination, do not touch the vial tip to the eye or other surfaces. (5.1)

### ADVERSE REACTIONS

The most common adverse reaction was instillation site pain (50%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Alcon Laboratories, Inc. at 1-800-757-9780, or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

See 17 for PATIENT COUNSELING INFORMATION and FDA approved patient labeling.

Revised: 5/2025

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

## **FULL PRESCRIBING INFORMATION**

### **1 INDICATIONS AND USAGE**

TRYPTYR is indicated for the treatment of the signs and symptoms of dry eye disease.

### **2 DOSAGE AND ADMINISTRATION**

#### **2.1 Recommended Dosage**

Instill one drop in each eye twice daily (approximately 12 hours apart).

#### **2.2 Administration Instructions**

Wash hands before use.

The single-dose vials are to be used immediately after opening and can be used to dose both eyes. Discard the single-dose vial, including any remaining contents, immediately after use.

TRYPTYR can be used concomitantly with other topical ophthalmic eye drops. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

Contact lenses should be removed prior to the administration of TRYPTYR and may be reinserted 15 minutes following administration.

If one dose is missed, treatment should continue with the next dose.

### **3 DOSAGE FORMS AND STRENGTHS**

TRYPTYR is a clear to slightly opalescent, colorless ophthalmic solution containing 0.003% acoltremon in a single-dose vial.

### **4 CONTRAINDICATIONS**

None.

### **5 WARNINGS AND PRECAUTIONS**

#### **5.1 Potential for Eye Injury and Contamination**

To avoid the potential for eye injury and contamination, do not touch the vial tip to the eye or other surfaces.

#### **5.2 Use with Contact Lenses**

TRYPTYR should not be administered while wearing contact lenses. If contact lenses are worn, they should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following administration of TRYPTYR.

## 6 ADVERSE REACTIONS

### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In patients with dry eye disease, 766 patients received at least one dose of TRYPTYR in four randomized controlled clinical trials across 71 sites in the United States. The most common ocular adverse reaction observed in controlled clinical studies with TRYPTYR was instillation site pain (50%). Less than 1% of patients discontinued therapy due to burning or stinging sensation in the eyes.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Risk Summary

There are no adequate and well-controlled studies on TRYPTYR in pregnant women. Systemic exposure to acoltremon from ocular administration is negligible [see *Clinical Pharmacology (12.3)*]. Intravenous administration of acoltremon to pregnant rats and rabbits during organogenesis did not produce embryofetal toxicity at 806- and 2151-fold the maximum recommended human ocular dose (MRHOD) of acoltremon on a mg/m<sup>2</sup> basis (see *Data*).

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects is 2 to 4%, and of miscarriage is 15 to 20%, of clinically recognized pregnancies.

#### Data

##### *Animal Data*

In embryofetal developmental studies in pregnant rats and rabbits dosed by intravenous injection daily during organogenesis from gestation days 6-17 and gestation days 7-19, respectively, no maternal or fetal toxicity was observed at 806- and 2151-fold the MRHOD of acoltremon on a mg/m<sup>2</sup> basis.

### 8.2 Lactation

#### Risk Summary

There are no data on the presence of acoltremon in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to acoltremon following topical ocular administration is low. The lack of clinical data during lactation precludes a clear determination of the risk of TRYPTYR to an infant during lactation; however, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TRYPTYR.

### 8.4 Pediatric Use

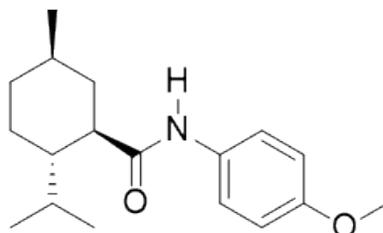
The safety and effectiveness of TRYPTYR have not been established in pediatric patients.

## 8.5 Geriatric Use

No clinically relevant differences in safety have been observed between elderly and younger patients.

## 11 DESCRIPTION

TRYPTYR (acoltremon ophthalmic solution) 0.003% contains an agonist of TRPM8 ion channels. Acoltremon's chemical name is (1*R*,2*S*,5*R*)-2-isopropyl-*N*-(4-methoxyphenyl)-5-methylcyclohexane-1-carboxamide. The molecular formula of acoltremon is C<sub>18</sub>H<sub>27</sub>NO<sub>2</sub> and has a molecular weight of 289.42 g/mol.



Acoltremon is a white to pale yellow crystalline solid, that is insoluble in water.

TRYPTYR is a sterile, clear to slightly opalescent, colorless, isotonic aqueous solution for topical ophthalmic use, with a pH of approximately 7 and an osmolality of 280 to 330 mOsm/kg. Each mL of TRYPTYR contains active: acoltremon 0.003%; and inactives: polyoxyl 35 castor oil, sodium dihydrogen phosphate dihydrate, sodium chloride, hypromellose and purified water. Additionally, sodium hydroxide is used to adjust pH. TRYPTYR does not contain an anti-microbial preservative.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Studies in animals suggest that acoltremon, the active substance in TRYPTYR, is an agonist of transient receptor potential melastatin 8 (TRPM8) thermoreceptors. TRPM8 thermoreceptor stimulation has been shown to activate trigeminal nerve signaling leading to increased basal tear production. The exact mechanism of action for TRYPTYR in dry eye disease is unknown.

### 12.3 Pharmacokinetics

PK was assessed in 25 patients with dry eye disease receiving TRYPTYR administration (1 drop twice daily) on Days 1, 14, and 90. A total of three (3) (12.0%) had plasma concentrations above 20 pg/mL (the lower limit of quantification), with the highest plasma concentration of 213 pg/mL.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

#### Carcinogenicity

Long term studies in animals have not been performed to evaluate the carcinogenic potential of acoltremon.

## Mutagenicity

Acoltremon was not mutagenic or clastogenic in the standard battery of genotoxicity tests including a bacterial reverse mutation assay, an *in vitro* chromosomal aberration assay in human peripheral lymphocytes and micronucleus assay in rats.

## Impairment of Fertility

Studies to evaluate the potential effects of acoltremon on male or female fertility in animals have not been performed.

## 14 CLINICAL STUDIES

The efficacy of TRYPTYR for the treatment of dry eye disease was supported by two randomized, multi-center, double-masked, vehicle-controlled studies (COMET-2 [NCT-05285644] and COMET-3 [NCT-05360966]) enrolling a total of 931 dry eye patients (462 of which received TRYPTYR). Patients were randomized to TRYPTYR or vehicle (placebo) in a 1:1 ratio and dosed twice a day for 90 days. Use of artificial tears was not allowed during the studies. The mean age was 61 years (range, 30-93 years). The majority of patients were female (74.8%). Enrollment criteria included signs (i.e., corneal fluorescein staining score [2-15] and anesthetized Schirmer tear test [2-9 mm]) and symptoms (i.e., SANDE Score [ $\geq 50$ ] and Ocular Discomfort Score [ $\geq 50$ ]) of dry eye disease.

## Efficacy

Tear film production was measured by unanesthetized Schirmer tear test assessed using a Schirmer strip (0 - 35 mm). The average baseline unanesthetized Schirmer scores for TRYPTYR and Vehicle treated patients was 6.2 mm and 5.9 mm in the COMET-2 study, and 6.8 mm and 6.4 mm in the COMET-3 study, respectively. Of the patients treated at Day 14 (primary endpoint) with TRYPTYR, 42.6% achieved  $\geq 10$  mm increase in Schirmer score from baseline in the COMET-2 study and 53.2% achieved  $\geq 10$  mm increase in Schirmer score from baseline at Day 14 in the COMET-3 study, compared to 8.2% and 14.4% of vehicle-treated patients in the COMET-2 study and the COMET-3 study, respectively. A statistically significant improvement in tear production favoring TRYPTYR ( $p < 0.01$ ) was observed in both studies (Table 1).

**Table 1: Percent of Patients Achieving  $\geq 10$  mm Improvement from Baseline in Schirmer Score at Day 14 in Patients with Dry Eye Disease**

	Tear Production			
	COMET-2		COMET-3	
	TRYPTYR N = 230	Vehicle N = 235	TRYPTYR N = 232	Vehicle N = 234
$\geq 10$ mm increase in tear production at Day 14	42.6%	8.2%	53.2%	14.4%
Difference (95% CI)	34.4% (26.9, 42.0)		38.8% (30.8, 46.8)	
P-value versus vehicle	< 0.01		< 0.01	

Consistent results were observed at all timepoints through Day 90.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

TRYPTYR (acoltremon ophthalmic solution) 0.003% is supplied as a sterile, clear to slightly opalescent, and colorless solution in a low-density polyethylene (LDPE), single-dose vial with a 0.4

mL fill. One strip of 5 single-dose vials is packaged in a foil pouch with twelve (12) pouches in a carton.

NDC 00658-595-02; Carton of 60 Single-Dose Vials.

## Storage

Store refrigerated at 2°C to 8°C (36°F to 46°F). After opening the carton, TRYPTYR may be stored refrigerated or at room temperature at 2°C to 25°C (36°F to 77°F). If stored at room temperature, TRYPTYR should be used within 30 days, not to exceed the expiration date printed on the carton and foil pouch.

After opening each foil pouch, the single-dose vials should be used within 7 days, not to exceed the expiration date printed on the vial. Store unopened single-dose vials in the original foil pouch until ready to use.

## 17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Instructions for Use).

### Potential for Eye Injury and Contamination

Advise patients not to touch the tip of the single-dose vial to their eye or to any surface in order to avoid eye injury or contamination of the solution [see *Warnings and Precautions (5.1)*].

Advise patients that one single-dose vial can be used to dose both eyes immediately after opening. Discard the single-dose vial, including any remaining contents, after use [see *Dosage and Administration (2)*].

### Use With Contact Lenses

Advise patients that contact lenses should be removed prior to administration of TRYPTYR and can be reinserted 15 minutes after administration [see *Warnings and Precautions (5.2)*].

### Use with Other Ophthalmic Drugs

Advise patients that if more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart [see *Dosage and Administration (2)*].

### Storage Information

Instruct patients to store unopened single-dose vials in the original foil pouch until ready to use [see *How Supplied/Storage and Handling (16)*].

Manufactured for Alcon Laboratories, Inc.

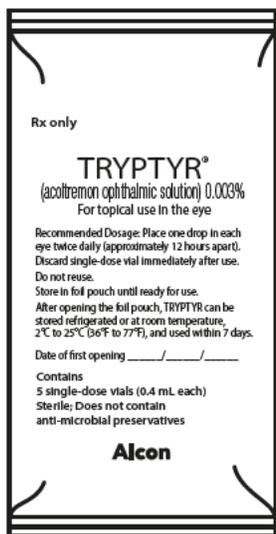
Fort Worth, TX 76134, USA.

U.S. Pat.: [www.alconpatents.com](http://www.alconpatents.com)

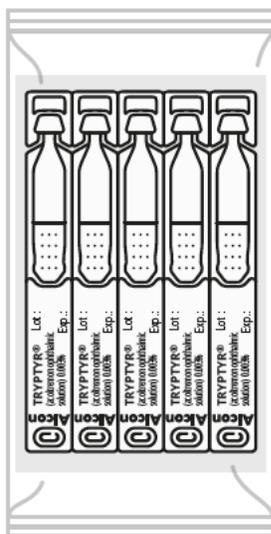
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**INSTRUCTIONS FOR USE**  
**TRYPTYR® [trip'tir]**  
**(acoltremon ophthalmic solution) 0.003%**  
**for topical ophthalmic use**

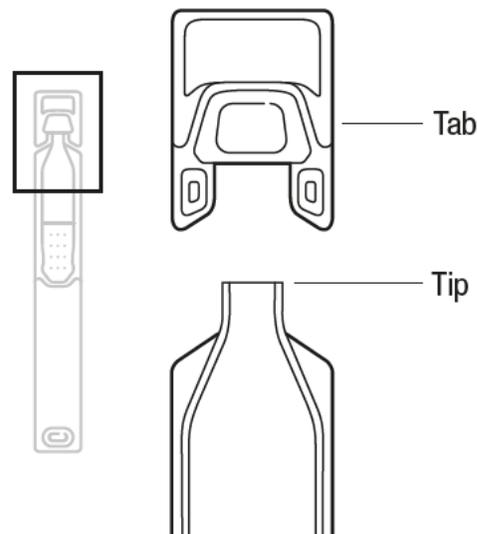
This Instructions for Use contains information on how to use TRYPTYR. Read this Instructions for Use before you start using TRYPTYR and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your healthcare provider about your medical condition or your treatment.



Front view of foil pouch



5 single-dose vials inside foil pouch



Single-dose vial

**Important Information You Need to Know Before Using TRYPTYR:**

- Use TRYPTYR exactly as your healthcare provider tells you to.
- TRYPTYR is for use in the eye. Each single-dose vial of TRYPTYR will give you enough medicine to treat both of your eyes. There is extra TRYPTYR in each single-dose vial in case you miss getting a drop into your eye.
- Keep the unopened single-dose vials in the original foil package until ready to use.
- **Wash your hands** before each use to make sure you do not infect your eyes.
- If you use TRYPTYR with other eye medicines, wait at least 5 minutes between using TRYPTYR and the other medicines.
- If you wear contact lenses, remove them before using TRYPTYR. Wait 15 minutes after dosing before putting contact lenses back in your eyes.
- If 1 dose is missed, treatment should continue at the next scheduled time.
- Use 1 drop of TRYPTYR in each eye 2 times each day. Use 1 single-dose vial in the morning and another single-dose vial in the evening, approximately 12 hours apart.
- **Do not** let the tip of the single-dose vial touch your eye or any other surface to avoid eye injury or infection.
- **Do not** use the single-dose vial or the medicine inside it if the tip touches your eye or another surface. Throw it away.
- TRYPTYR vial is for 1-time use only. Use right away after opening and **do not** reuse.
- Call your healthcare provider right away if you get an allergic reaction or other eye problems such as eye injury, eye infection, or eye pain. For additional safety information, see the Full Prescribing Information and talk with your healthcare provider.

**Follow steps 1 to 15 each time you use TRYPHYR**

**Step 1**

- Remove the unopened carton from the refrigerator (see Figure A).
- Check the expiration date printed on the carton.
- Write the date the carton is first opened in the space provided on the carton.

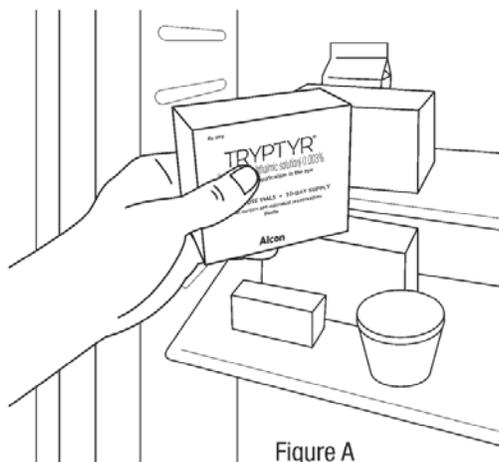


Figure A

**Step 2**

- Open the carton.

**Preparing a single-dose vial**

**Step 3**

- **Wash your hands** before each use to make sure you do not infect your eyes (see Figure B).

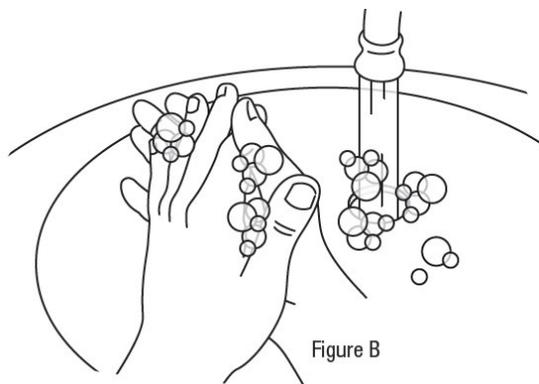


Figure B

#### Step 4

- Take a foil pouch out of the TRYPTYR carton.
- Write the date the foil pouch is first opened in the space provided.
- Tear open the foil pouch (see Figure C).

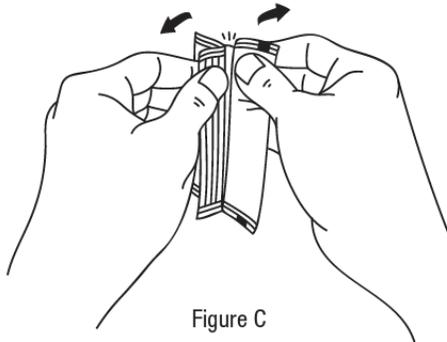


Figure C

#### Step 5

- Remove the strip of 5 single-dose vials from the foil pouch (see Figure D).

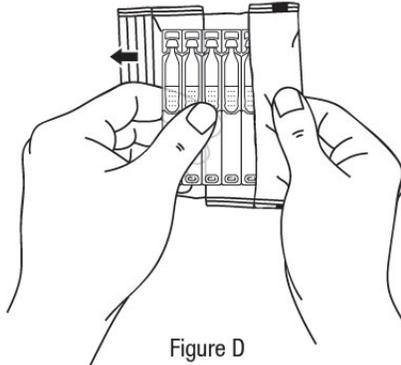


Figure D

#### Step 6

- Pull off one single-dose vial from the strip (see Figure E).
- Place remaining vials back in the carton. Store carton at room temperature or place the carton back in the refrigerator.

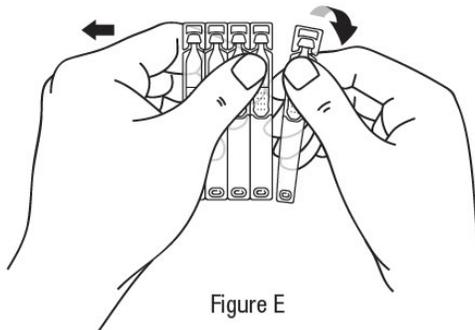
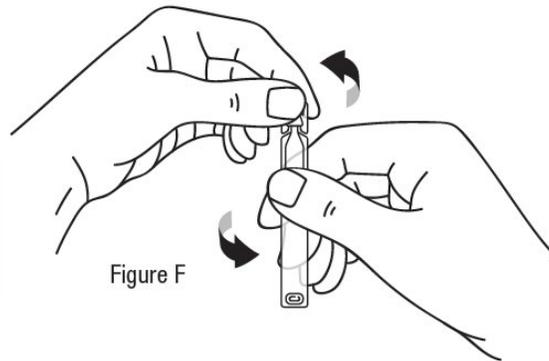


Figure E

### Step 7

- Open the TRYPTYR single-dose vial by twisting off the tab at the top while holding the vial upright (see Figure F). **Do not** touch the tip of the single-dose vial or allow it to touch any surface to avoid possible eye infection.



### Applying a dose of TRYPTYR to your eyes

#### Step 8

- Tilt your head backwards.
- If you are not able to tilt your head, lie down.

#### Step 9

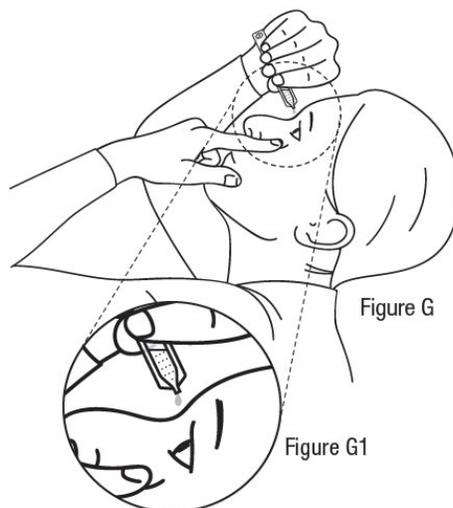
- Gently pull your lower eyelid downwards and look up.

#### Step 10

- Place the tip of the TRYPTYR single-dose vial close to your eye.
- **Do not** allow the tip of the vial to touch your eye to avoid eye injury or infection.

#### Step 11

- Gently squeeze the single-dose vial and let 1 full drop of TRYPTYR coat your eye (see Figure G and G1 below).
- If a drop misses your eye, try again.
- After the drop is in your eye, gently close (do not squeeze) your eye for a few seconds.



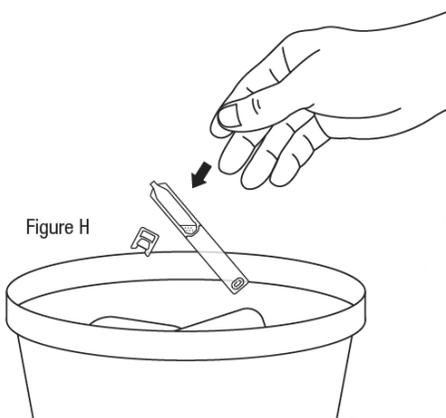
#### Step 12

- **Repeat Steps 8 through 11** for your other eye.
- There is enough TRYPTYR in 1 single-dose vial for both eyes.

## After dosing and disposal instructions

### Step 13

- After you have applied a drop to both eyes, throw away the opened single-dose vial with any remaining solution right away (see Figure H).
- **Do not reuse vial.**



### Step 14

- Wait at least 5 minutes between using TRYPTYR and other eye drops (see Figure I).



Figure I

### Step 15

- If you use contact lenses, wait at least 15 minutes before placing them back in your eyes (see Figure J).

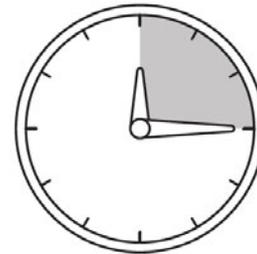


Figure J

## How should I store TRYPTYR?

- Store TRYPTYR in the unopened carton.
- After opening the carton, TRYPTYR may be kept refrigerated or at room temperature at 36°F to 77°F (2°C to 25°C).
- If stored at room temperature, use TRYPTYR within 30 days.
- Always check the expiration date on the vial before use. **Do not** store after the expiration date.
- Throw away (dispose of) unused single-dose vials 7 days after opening the foil pouch.
- Throw away (dispose of) unused TRYPTYR after 30 days if stored at room temperature.
- Throw away (dispose of) TRYPTYR after the expiration date on the carton and pouch.
- **Do not** leave TRYPTYR in a car, outdoors, in the sunlight, or in any other place where temperatures can go above room temperature [**greater than 77°F (25°C)**].
- Keep TRYPTYR and all medicines out of reach of children.

Manufactured for: Alcon Laboratories, Inc. Fort Worth, TX 76134, U.S.A.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Approved: 5/2025

# Carton Labeling – Trade



# Carton Labeling – Sample



# Pouch Label – Trade

NDC 00658-595-02 441120

**Rx only**

**TRYPTYR<sup>®</sup>**  
(acoltremon ophthalmic solution) 0.003%  
For topical use in the eye

Recommended Dosage: Place one drop in each eye twice daily (approximately 12 hours apart). Discard single-dose vial immediately after use. Do not reuse. Store in foil pouch until ready for use. After opening the foil pouch, TRYPTYR can be stored refrigerated or at room temperature, 2°C to 25°C (36°F to 77°F), and used within 7 days.

Date of first opening \_\_\_\_/\_\_\_\_/\_\_\_\_

**Contains**  
5 single-dose vials (0.4 mL each)  
Sterile; Does not contain anti-microbial preservatives

**Alcon**

LOT: #####A  
EXP.: YYYY-MM

Manufactured for:  
Alcon Laboratories, Inc.  
Fort Worth, TX 76134 USA

3129

00658-595-02 7

**Pouch Label – Sample**

3130



NDC 00658-595-01 441130

Rx only Sample

TRYPTYR®

(acoltremon ophthalmic solution) 0.003%

For topical use in the eye

Recommended Dosage: Place one drop in each eye twice daily (approximately 12 hours apart).  
Discard single-dose vial immediately after use.  
Do not reuse.  
Store in foil pouch until ready for use.  
After opening the foil pouch, TRYPTYR can be stored refrigerated or at room temperature, 2°C to 25°C (36°F to 77°F), and used within 7 days.

Date of first opening \_\_\_\_/\_\_\_\_/\_\_\_\_

Contains  
5 single-dose vials (0.4 mL each)  
Sterile; Does not contain  
anti-microbial preservatives

Alcon

LOT : #####

EXP.: YYYY-MM

Manufactured for:  
Alcon Laboratories, Inc.  
Fort Worth, TX 76134 USA

**Container Label**

3390

Alcon

TRYPTYR®

(acoltremon ophthalmic solution) 0.003%

Lot :

Exp.:

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/s/  
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/s/  
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