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POPULAR

# POPULAR PARMACEUTICALS LTD
## QUALITY CONTROL DEPARTMENT
## INDUSTRIAL OPERATIONS
## TONGI

## Certificate of Analysis for Working Standard

| | | |
|---|---|---|
| Material Name | **Tobramycin** | Expiry Date :10.02.2017 |
| Material Code No. | PORA0013 | |
| Batch No. (In House) | WS/16/029 | |

| **Raw material details** | | **Reference Standard details** | |
|---|---|---|---|
| Manufacturer | Iffect Chemphar Co. Ltd, China | Name of the RS | Tobramycin |
| Manufacturer's Batch No. | IF-TO-150416 | RS Batch No. | WS/15/029 |
| GRN No. | PR-1215-0132 | RS Vial No. | '04 |
| Manufacturing date | 16.04.2015 | RS Potency (AS Such) | 902.85 ug/mg |
| Expiry date | 15.04.2018 | Opening Date | 10.11.2015 |
| Analysis date | 05.01.2016 | Valid up to | 10.02.2016 |
| | | Testing Instruction | BP-2015 |
| | | Analyst's log book reference | LB/JEF/07 (Page# 185) |

| *Tests* | *Specifications* | *Results* |
|---|---|---|
| Appearance | White or almost white powder. | Almost white powder. |
| Water | Not more than 8.0% | 7.29% |
| Assay | Not less than 900 µg/mg , calculated on the anhydrous basis. | 975.03 µg/mg |
| Assay (As such) | N/A | 903.95 µg/mg |

Conclusion : *Material complies with in-house specification. Released to use as working standard.*

Authorized person : **Md. Feroz Alam,** Sr. Manager-Quality control. **signature :** 10.02.16.

Certificate issued on 10/02/2016 by

**Popular Pharmaceuticals Limited**

End of report

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| POPULAR | SPECIFICATION | |
|---|---|---|
| POPULAR PHARMACEUTICALS LTD. | | |
| **Product Name : TOBRABAC EYE DROPS** | | |
| **Product Code : 51117** | Document No | SPC/FDF/108/00 |
| **Ref : USP + In - House** | Page | 1 of 1 |
| | Version No | 00 |
| | Effective Date | 21st Nov 2006 |

| Sl. No. | Test | Specification |
|---|---|---|
| 1 | Description | Clear colorless sterile solution free from any foreign particles. |
| 2 | Identification of Tobramycin by TLC | The distances from origin to the pink spots for both the standard and test solution must correspond. |
| 3 | pH | 7.0 to 8.0 |
| 4 | Content / ml<br>Tobramycin 3.00 mg | (2.70 to 3.60) mg<br>(90.0 to 120.0) % of the stated amount. |
| 5 | Sterility | Sterile. |

| Prepared By : | Checked By : | Approved By : |
|---|---|---|
| Sr. Officer, Quality Control | Asst. Manager, Quality Control | Asst. Manager, Quality Compliance |
| Date : 21.11.06 | Date : 21.11.06 | Date : 21.11.06 |

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| POPULAR | | |
|---|---|---|
| **Popular Pharmaceuticals Limited** | **STANDARD TEST PROCEDURE** | |
| **Product Name: TOBRABAC EYE DROPS** | Document No: | STP/FDF/108/00 |
| **Product Code: 51117** | Page | 1 of 4 |
| | Version No | 00 |
| **Ref: USP + In-House** | Effective Date | 21st Nov 2006 |

## 1 General Guiding Principles

| Valid for all the test methods: | |
|---|---|
| Reagents | Analytical grade, if reagents of other quality are only available, their applicability must be examined. Secondary reagents to be prepared as per updated version of QC/SOP/008. |
| Water | Unless stated otherwise, either distilled or demineralised water must be used. |
| Equipment and Apparatus | After examining their suitability, equipment and apparatus would be used. |
| Handling precautions | 1. Solutions should be protected from light and heat during analysis. |

## 2 List of Working Standards

| Name of working standards | Used for |
|---|---|
| Tobramycin | Assay. |

## 3 Test Procedures

### 3.1 Description

| **Procedure** |
|---|
| Check physical appearance of the solution. Take about 10 ml of the test sample in a test tube and observe visually. |
| **Specification** |
| Clear colorless sterile solution free from any foreign particles. |

| **Prepared By:** | **Checked By:** | **Approved By:** |
|---|---|---|
| **Sr. Officer, Quality Control** | **Asst. Manager, Quality Control** | **Asst. Manager, Quality Compliance** |
| **Date:** 21.11.06 | **Date:** 21-11-06 | **Date:** 21.11.06 |

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### 3.2 Identification By TLC

| Procedure |
|---|
| Prepare a Standard solution of USP Tobramycin RS containing 3 mg per mL. Separately apply 6 µL of the Ophthalmic solution, 6 µL of the Standard solution, and 6 µL of a mixture of equal volumes of the two solutions to a thin-layer chromatographic plate coated with a 0.25-mm layer of chromatographic silica gel mixture. Place the plate in a suitable chromatographic chamber, and develop the chromatogram in a solvent system consisting of a mixture of methanol, ammonium hydroxide, and chloroform (60:30:25) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, allow the solvent to evaporate, and heat the plate at 110° for 15 minutes. Immediately locate the spots on the plate by spraying with a 1 in 100 solution in Ninhydrin in a mixture of butyl alcohol and pyridine (100:1). |
| **Specification** |
| The distance from origin to the pink spot for both the standard and the test solutions must correspond. |

### 3.3 pH

| Procedure |
|---|
| As per USP |
| **Specification** |
| 7.0 to 8.0 |

### 3.4 Weight/ml (g/ml)

| Procedure |
|---|
| Weigh a dry calibrated pycnometer and then fill it with the optacarpine solution, remove any excess of the sample and weigh. |
| **Calculation** |
| Weight per ml (g /ml)<br>$= \frac{W_f - W_p}{V_v}$ g/ml<br>Where:<br>$W_p$ = Weight of Empty Pycnometer, g<br>$W_f$ = Weight of Filled Pycnometer, g<br>$V_v$ = Volume of Pycnometer, ml |

| Prepared By: | Checked By: | Approved By: |
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| Sr. Officer, Quality Control | Asst. Manager, Quality Control | Asst. Manager, Quality Compliance |
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| **Popular Pharmaceuticals Limited** | **STANDARD TEST PROCEDURE** | |
| **Product Name: TOBRABAC EYE DROPS** | Document No: | STP/FDF/108/00 |
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### 3.5 Biological Assay Of Tobramycin

**Requirements**

1. Media : Antibiotic Media 1
2. Organism : Staphylococcus aureus (ATCC 29737)
3. Diluting fluid : Purified Water

**Standard Preparation**

Standard to be taken-30 mg

If potency is x %, standard is to be taken (30 X 100/x) mg

Standard high solution (Std/H): Weigh (30 X 100/x) mg of standard in 50 ml volumetric flask and volume up to the mark with purified water. Shake to dissolve. (600µg/ml)

Standard low solution (Std/L): Transfer 2 ml of Std/H solution in test tube containing 6 ml purified water (1: 4 dilution). Mix the solution by vortex. (150µg/ml)

**Sample Preparation**

Sample to be taken-10 ml

Sample high solution (T/H): Transfer 10 ml of sample in 50 ml volumetric flask and volume up to the mark with purified water. Shake to dissolve. (600µg/ml)

Sample low solution (T/L): Transfer 2 ml of T/H solution in test tube containing 6 ml purified water (1: 4 dilution). Mix the solution by vortex. (150µg/ml)

| Prepared By: | Checked By: | Approved By: |
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| **Product Name: TOBRABAC EYE DROPS** | Document No: | STP/FDF/108/00 |
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**Procedure**

a) Fill the petridish or rectangular tray to a depth of 3-4 mm with Antibiotic Media 1.
b) Allow the plate to dry for 30 minute before use.
c) Swab the surface of the media with Staphylococcus aureus (ATCC 29737).
d) Make holes of 8 mm diameter in the inoculated media with a sterile stainless steel borer.
e) By means of a constant delivery dropping pipette fill 140 µL of each dose of sample and standard in to the holes of plates
f) Allow the plate for some time to diffuse the solutions into the media.
g) Then incubate the plate at 35°C overnight.
h) After incubation measure the zone of inhibition.

**Calculation:**

$E = ½ \{(T_H - T_L) + (Std_H - Std_L)\}$

$F = ½ \{(T_H + T_L) - (Std_H + Std_L)\}$

$b = E/I$, where $I = \text{Log } 4$

$M = F/b$

Potency of Product = (Anti log of M) X (Claim)

Where,

$T_H$ = Diameter of Inhibition zone of Sample high dose, mm.
$T_L$ = Diameter of Inhibition zone of Sample low dose, mm.
$S_H$ = Diameter of Inhibition zone of Standard high dose, mm
$S_L$ = Diameter of Inhibition zone of Standard low dose, mm.

**Specification**

(2.70 to 3.60) mg
(90.0 to 120.0) % of the stated amount.

## 3.6 Sterility

**Procedure**

As per BP

**Specification**

Sterile

| Prepared By: | Checked By: | Approved By: |
|---|---|---|
| Sr. Officer, Quality Control | Asst. Manager, Quality Control | Asst. Manager, Quality Compliance |
| Date: 21.11.06 | Date: 21.11.06 | Date: 21.11.06 |