

## **Module 2.4: Non-Clinical Overview**

### **Travoprost-Timolol/Pharmathen (40 micro grams/ml and 5 mg/ml)** **preservative free eye drops, solution in multi-dose container**

Formulation of Pharmathen S.A.

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## **2.4 Non-Clinical Overview**

### **2.4.1 Overview of the Non-clinical Testing Strategy**

## **2.4.2 Pharmacology**

### **Travoprost**

### **Timolol**



### **2.4.2.1 Primary Pharmacodynamics**

#### **Travoprost**

























## Timolol



## Travoprost-Timolol Combination Activity

### **2.4.2.3 Pharmacodynamic Interactions**

## **2.4.3 Pharmacokinetics**

### **2.4.3.1. Analytical Methodology**

#### *Travoprost*

#### *Timolol*

### **2.4.3.2 Pharmacokinetics Overview**

#### *Travoprost*

### 2.4.3.3. Absorption

#### *Travoprost*

#### *Timolol*







*Travoprost/Timolol combination*

#### **2.4.3.4 Distribution**

##### *Travoprost*

##### *Timolol*

### *Travoprost – Timolol Combination*

#### **2.4.3.5 Metabolism**

##### *Travoprost*

*Timolol*

*Travoprost-Timolol Combination*

#### **2.4.3.6. Excretion**

##### *Travoprost*

##### *Timolol*

##### *Travoprost-Timolol Combination*

## **2.4.4 Safety/Toxicology**

### **2.4.4.1. Animal toxicology**

#### *Travoprost*

*Timolol*

#### 2.4.4.2 Clinical Safety



#### 2.4.4.3 Carcinogenicity

##### *Travoprost*

##### *Timolol*

#### **2.4.4.4 Genotoxicity**

##### *Travoprost*

##### *Timolol*

#### **2.4.4.5 Reproductive toxicity and Lactation**

##### *Travoprost*

##### *Timolol*

#### **2.4.4.6 Special studies**

##### *Travoprost*

T

##### *Timolol Local toxicity studies*



### *Timolol Effects on lens*

#### **2.4.4.8 Travoprost/Timolol Combination Preclinical Toxicity**

#### **2.4.4.9 Impurities and Excipients**

##### *Travoprost/Timolol combination*

#### **2.4.4.10 Environmental risk assessment**

## *Travoprost*

### 2.4.4.9 Preservative Toxicity



## **2.4.5: Integrated Overview and Conclusions**



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