Public Assessment Report

UKPAR

Propranolol hydrochloride 5mg/5ml Oral Solution
Propranolol hydrochloride 10mg/5ml Oral Solution
Propranolol hydrochloride 40mg/5ml Oral Solution
Propranolol hydrochloride 50mg/5ml Oral Solution

(Propranolol hydrochloride)

UK Licence Numbers: PL 39307/0059-0062

Syri Limited t/a Thame Laboratories
LAY SUMMARY

Propranolol hydrochloride 5mg/5ml Oral Solution
Propranolol hydrochloride 10mg/5ml Oral Solution
Propranolol hydrochloride 40mg/5ml Oral Solution
Propranolol hydrochloride 50mg/5ml Oral Solution

(Propranolol hydrochloride)

This is a summary of the Public Assessment Report (PAR) for Propranolol hydrochloride 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml Oral Solution (PL 39307/0059-0062). It explains how Propranolol hydrochloride 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml Oral Solution were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Propranolol hydrochloride 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml Oral Solution.

These products will be collectively referred to as Propranolol hydrochloride Oral Solution throughout the remainder of this public assessment report (PAR).

For practical information about using Propranolol hydrochloride Oral Solution, patients should read the package leaflet or contact their doctor or pharmacist.

What is Propranolol hydrochloride Oral Solution and what is it used for?
Propranolol hydrochloride 10mg/5ml and 40mg/5ml Oral Solution are ‘generic medicines’. This means that they are similar to ‘reference medicines’ already authorised in the European Union (EU) called Inderal 10 mg and 40 mg film-coated tablets (AstraZeneca UK Limited).

Propranolol hydrochloride 5mg/5ml and 50mg/5ml Oral Solution are ‘hybrid medicines’. This means that they are similar to a reference medicine containing the same active substance, but differ in pharmaceutical form and strength.

The reference medicine for Propranolol hydrochloride 5mg/5ml and 50mg/5ml Oral Solution is Inderal 10 mg tablets (AstraZeneca UK Limited).

Propranolol can be used for many conditions including:
- Hypertension (high blood pressure)
- Angina (chest pain)
- Some arrhythmias (disorders of heart rhythm)
- Protection of the heart after a myocardial infarction (heart attack)
- Prevention of migraine
- Essential tremor, anxiety
- Certain thyroid conditions (such as thyrotoxicosis, which is caused by an overactive thyroid gland)
- Hypertrophic cardiomyopathy (thickened heart muscle)
- Phaeochromocytoma (high blood pressure due to a tumour usually near the kidney)
- Bleeding in the oesophagus caused by high blood pressure in the liver.

How does Propranolol hydrochloride Oral Solution work?
Propranolol hydrochloride Oral Solution contains the active ingredient propranolol, which is one of a group of drugs called betablockers. This medicine works by blocking certain receptors in the heart to lower heartbeat and blood pressure.
How is Propranolol hydrochloride Oral Solution used?
This medicine can be taken by mouth. Patients must use the measuring syringe or cup provided in the pack to deliver the required dose.

The patient should always take this medicine exactly as their doctor or pharmacist has told them. A doctor will decide how much Propranolol patients need to take each day depending on their condition. Patients must follow a doctor’s instructions about when and how to take this medicine. The patient should check with their doctor or pharmacist if they are not sure.

The following table shows the recommended total daily dosages for an adult:

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (high blood pressure)</td>
<td>160 mg to 320 mg</td>
</tr>
<tr>
<td>Angina (chest pains)</td>
<td>120 mg to 240 mg</td>
</tr>
<tr>
<td>Arrhythmias (disorders of heart rhythm)*</td>
<td>30 mg to 160 mg</td>
</tr>
<tr>
<td>Protection of the heart after a heart attack</td>
<td>160 mg</td>
</tr>
<tr>
<td>Prevention of migraine*</td>
<td>80 mg to 160 mg</td>
</tr>
<tr>
<td>Essential tremor</td>
<td>80 mg to 160 mg</td>
</tr>
<tr>
<td>Anxiety</td>
<td>40 mg to 120 mg</td>
</tr>
<tr>
<td>Certain thyroid conditions (such as thyrotoxicosis)*</td>
<td>30 mg to 160 mg</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy (thickened heart muscle)</td>
<td>30 mg to 160 mg</td>
</tr>
<tr>
<td>Phaeochromocytoma*</td>
<td>30 mg to 60 mg</td>
</tr>
<tr>
<td>Bleeding in the oesophagus caused by high blood pressure in the liver</td>
<td>80 mg to 160 mg</td>
</tr>
</tbody>
</table>

Please read section 3 of the package leaflet for detailed dosing recommendations, the route of administration, and the duration of treatment.

This medicine can only be obtained with a prescription.

What benefits of Propranolol hydrochloride Oral Solution have been shown in studies?
Propranolol hydrochloride Oral Solution was designated as a Biopharmaceutics Classification System (BCS) Class I drug based on its properties (highly soluble, highly permeable). With these applications the applicant claimed BCS biowaiver.

What are the possible side effects of Propranolol hydrochloride Oral Solution?
Because Propranolol hydrochloride Oral Solution are either generic or hybrid medicines that have been shown to have comparable quality and bioequivalent to Inderal 10 mg and 40 mg film-coated tablets (AstraZeneca UK Limited), the benefits and possible side effects are taken as being the same as the reference medicines.

For the full list of restrictions, see the package leaflet.

For the full list of all side effects reported with Propranolol hydrochloride Oral Solution, see section 4 of the package leaflet available on the MHRA website.

Why was Propranolol hydrochloride Oral Solution approved?
The MHRA decided that the benefits of Propranolol hydrochloride Oral Solution are greater than its risks and recommended that it be approved for use.
What measures are being taken to ensure the safe and effective use of Propranolol hydrochloride Oral Solution?
A risk management plan (RMP) has been developed to ensure that Propranolol hydrochloride Oral Solution is used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics (SmPCs) and the package leaflet for Propranolol hydrochloride Oral Solution including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore new safety signals reported by patients/healthcare professionals will be monitored/reviewed continuously.

Other information about Propranolol hydrochloride Oral Solution
Marketing authorisations were granted in the UK on 12 January 2017.

The full PAR for Propranolol hydrochloride Oral Solution follows this summary.

This summary was last updated in March 2017.
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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) granted Syri Limited t/a Thame Laboratories, Marketing Authorisations for the medicinal products Propranolol hydrochloride 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml Oral Solution (PL 39307/0059-0062). The products are prescription only medicines (POM) indicated for:

a) the control of hypertension
b) the management of angina pectoris
c) long term management against re-infarction after recovery from acute myocardial infarction
d) the control of most forms of cardiac dysrhythmias
e) the prophylaxis of migraine
f) the management of essential tremor
g) relief of situational anxiety and generalised anxiety symptoms, particularly those of somatic type
h) prophylaxis of upper gastrointestinal bleeding in patients with portal hypertension and oesophageal varices;
i) the adjunctive management of thyrotoxicosis and thyrotoxic crisis
j) management of hypertrophic obstructive cardiomyopathy
k) management of phaeochromocytoma peri-operatively (with an alphablocker).

The applications for Propranolol hydrochloride 10mg/5ml and 40mg/5ml Oral Solution (PL 39307/0060-0061) were submitted under Article 10(1) of Directive 2001/83/EC, as amended, as generic applications. The applications for Propranolol hydrochloride 5mg/5ml and 50mg/5ml Oral Solution (PL 39307/0059 & 62) were submitted under Article 10(3) of Directive 2001/83/EC, as amended, as hybrid applications.

The reference products for the 10mg/5ml and 40mg/5ml strengths are Inderal 10 mg and 40 mg film-coated tablets which were first authorised to Imperial Chemical Industries Limited (PL 00029/5063R-5064R) on 01 September 1993. These reference medicines underwent changes of ownership to Zeneca Limited (PL 12619/0030-0031) on 01 June 1993, and then to the current Marketing Authorisation Holder, AstraZeneca UK Limited (PL 17901/0021-0022), on 11 June 2000.

The reference product for the 5mg/5ml and 50mg/5ml strengths is Inderal 10 mg film-coated tablets.

No bioequivalence study was submitted and these applications are based on Biopharmaceutics Classification System (BCS) class I biowaiver.

This was waived given that:

- the proposed product is a liquid formulation and data submitted confirm that any differences in excipients will not significantly impact gastrointestinal (GI) transit, absorption, or in vivo solubility/stability at the level used in the formulation.

- The formulation is similar to another propranolol hydrochloride oral solution previously shown to be bioequivalent to Inderal tablets.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place at all sites responsible for the manufacture, assembly and batch release of these products.

No new or unexpected safety concerns arose during the review of information provided by the Marketing Authorisation Holder and it was, therefore, judged that the benefits of taking Propranolol
hydrochloride 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml Oral Solution outweigh the risks and Marketing Authorisations were granted.
II QUALITY ASPECTS

II.1 Introduction
Each 5 ml of oral solution contains 5 mg, 10 mg, 40 mg and 50 mg of propranolol hydrochloride, as the active ingredients. Other ingredients consist of the pharmaceutical excipients methyl parahydroxybenzoate (E218), citric acid monohydrate (E330), liquid maltitol (E965), orange flavour (containing propylene glycol (E1520)) and purified water.

All excipients used comply with their respective European Pharmacopoeia monographs with the exception of orange flavour which complies with an in house specification.

None of the excipients contain materials of animal or human origin.

The finished products are supplied in amber (Type III) glass bottles containing 150ml of the oral solution with a tamper evident, child resistant plastic cap consisting of a polypropylene, polyethylene and an expanded polyethylene (EPE) liner.

A 5ml oral syringe with 0.1ml graduation and 30ml cup with 5ml graduation with intermediate graduation at 2.5ml and 7.5ml for measuring and administering the dose and a bottle adaptor.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

II.2 Drug Substance
Propranolol hydrochloride
INN: Propranolol hydrochloride
Chemical name: (2RS)-1-[(1-Methylethyl)amino]-3-(naphthalen-1-yloxy)propan-2-ol hydrochloride

Structure:

![Structure of Propranolol Hydrochloride]

Molecular formula: $\text{C}_{16}\text{H}_{22}\text{ClNO}_2$
Molecular weight: 295.8 g/mol
Description: White or almost white powder.
Solubility: Soluble in water and in ethanol.

Propranolol hydrochloride is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance, propranolol hydrochloride, are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 Medicinal Product
Pharmaceutical Development
The objective of the pharmaceutical development programme was to obtain a stable oral solution containing propranolol hydrochloride that could be considered as generic/hybrid products of Inderal 10 mg and 40 mg film-coated tablets (AstraZeneca UK Limited).

Suitable pharmaceutical development data have been provided for these applications.
Manufacture of the products
Satisfactory batch formulae have been provided for the manufacture of the products, along with an appropriate account of the manufacturing process. The manufacturing process has been validated at pilot scale batch size and has shown satisfactory results. The marketing authorisation holder (MAH) has committed to perform additional process validation studies on future commercial-scale batches.

Finished Product Specification
The finished product specifications proposed are acceptable. The test methods have been described that have been adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

Stability of the Products
Finished product stability studies were performed in accordance with current guidelines on batches of the finished product in the packaging proposed for marketing. The data from these studies support a shelf-life of 24 months with no special storage conditions. Once the bottle is opened, the product should be used within 90 days.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
There are no objections to the approval of these applications from a pharmaceutical viewpoint.

III NON-ClinICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of propranolol hydrochloride are well-known, no new non-clinical studies are required and none have been provided. An overview based on the literature review is, thus, appropriate.

The applicant’s non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

III.2 Pharmacology
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.3 Pharmacokinetics
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.4 Toxicology
Not applicable for this product type. Refer to section ‘III.1; Introduction’ detailed above.

III.5 Ecotoxicity/environmental risk assessment (ERA)
Since these products are intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects
No new non-clinical studies were conducted, which is acceptable given that the applications were based on being generic/hybrid medicinal products of originator products that have been licensed for over 10 years.
There are no objections to the approval of these applications from a non-clinical viewpoint.

IV  CLINICAL ASPECTS

IV.1  Introduction

No bioequivalence study was performed as discussed in section I above.

No new clinical data have been submitted and none are required for applications of this type. A clinical overview has been submitted to justify the biowaiver. The applicant’s clinical overview has been written by an appropriately qualified person and is considered acceptable.

IV.2  BCS Biowaiver

The applicant has adequately justified the absence of a bioequivalence study in accordance with the CHMP Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev.1/Corr**).

The applicant claimed a biowaiver for the lower strengths, as:
- Propranolol hydrochloride Oral Solution 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml are manufactured by the same manufacturer using the same manufacturing process.
- The qualitative compositions of all the test strengths are the same.
- The amount of the active substance is less than 5% of total content in all the test products.
- The comparison of in-vitro dissolution of the higher strength and lower strength test formulations shows that they have similar release profiles with >85% release within 15 minutes. This demonstrates that all proposed formulations have a very rapid and comparable release profile

Satisfactory data has been submitted to justify the biowaiver to the lower strengths.

IV.3  Pharmacokinetics

No new data have been submitted and none are required for applications of this type.

IV.4  Pharmacodynamics

No new data have been submitted and none are required for applications of this type.

IV.5  Clinical efficacy

No new data on efficacy have been submitted and none are required for this type of applications.

IV.6  Clinical safety

No new safety data were submitted and none are required.

IV.6  Risk Management Plan (RMP) and Pharmacovigilance System

The marketing authorisation holder (MAH) has submitted a risk management plan (RMP), in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Propranolol hydrochloride 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml Oral Solution.

A summary of safety concerns and planned risk minimisation activities, as approved in the RMP, is listed below:
<table>
<thead>
<tr>
<th>Safety concern</th>
<th>Routine risk minimisation measures</th>
<th>Additional risk minimisation measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important identified risks</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Bradycardia and increased cardiac conduction time</td>
<td>The risks of bradycardia and increased cardiac conduction time (i) associated with use of the drug product (ii) associated with concomitant use with other medicinal products are described in the SPC Sections 4.3, 4.4, 4.5, 4.8 and PIL Sections 2, 4 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Hypotension</td>
<td>The risk of hypotension (i) associated with use of the drug product and (ii) associated with concomitant use of other medicinal products is described in the SPC Sections 4.3, 4.4, 4.5, 4.8 and PIL Sections 2, 4 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Safety concern</td>
<td>Routine risk minimisation measures</td>
<td>Additional risk minimisation measures</td>
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<tr>
<td></td>
<td>the prescriber to minimise this risk.</td>
<td></td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>The risk of bronchospasm associated with use of the drug product is described in the SPC Sections 4.3, 4.8 and PIL Sections 2, 4 and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
</tr>
<tr>
<td>Cardiac failure, worsening cardiac failure or cardiogenic shock</td>
<td>The risk of cardiac failure, worsening cardiac failure or cardiogenic shock associated with (i) use of the drug product (ii) use of the drug product in patients with cardiovascular conditions/cardiac conduction abnormalities (iii) concomitant use of the drug product with other medicinal products is described in the SPC Sections 4.3 4.4, 4.5, 4.8 and PIL Sections 2, 4, and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
</tr>
<tr>
<td>Use in patients with Prinzmetal's angina</td>
<td>The risks associated with use of the drug product in patients with Prinzmetal's angina is described in the SPC Section 4.3 and PIL Section 2 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Use in patients with metabolic acidosis</td>
<td>The risks associated with use of the drug product in patients with metabolic acidosis are described in the SPC Section 4.3 and PIL Section 2 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Use in patients with untreated phaeochromocytoma</td>
<td>The risks associated with use of the drug product in patients with untreated phaeochromocytoma are described in the SPC Sections 4.2, 4.3, 4.4 and PIL Section 2 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Safety concern</td>
<td>Routine risk minimisation measures</td>
<td>Additional risk minimisation measures</td>
</tr>
<tr>
<td>---------------------------------------------------------</td>
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</tr>
<tr>
<td>Masking of symptoms of hypoglycaemia or thyrotoxicosis</td>
<td>The risk of masking of symptoms of hypoglycaemia or thyrotoxicosis associated with (i) use of the drug product (ii) use of the drug product in patients at risk (iii) concomitant use of the drug product with hypoglycaemic therapy is described in the SPC Sections 4.3, 4.4, 4.5, 4.8 and PIL Sections 2, 4 and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
</tr>
<tr>
<td>Foetal and neonatal toxicity when exposed during pregnancy</td>
<td>The risk of foetal and neonatal toxicity associated with use of the drug product during pregnancy is described in the SPC Sections 4.4, 4.6, 4.8 and PIL Sections 2, 4 and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
</tr>
<tr>
<td>Abrupt discontinuation of treatment</td>
<td>The risks associated with abrupt discontinuation of the drug product is described in the SPC Section 4.4 and PIL Section 2 and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
</tr>
<tr>
<td>Use in the elderly</td>
<td>The risks associated with use of the drug product in the elderly are described in the SPC Sections 4.2, 4.4, 4.8 and PIL Sections 2, 3, 4 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Use in patients with significant hepatic or renal impairment</td>
<td>The risks associated with use of the drug product in patients with significant hepatic or renal impairment are described in the SPC Section 4.4 and PIL Section 2 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Safety concern</td>
<td>Routine risk minimisation measures</td>
<td>Additional risk minimisation measures</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Increased exposure of rizatriptan and lidocaine on concomitant use</td>
<td>The risks associated with increased exposure of rizatriptan and lidocaine on concomitant use of the drug product are described in the SPC Section 4.5 and PIL Section 2 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Increased exposure of propranolol on concomitant use with cimetidine, hydralazine and alcohol</td>
<td>The risks associated with increased exposure of propranolol on concomitant use with cimetidine, hydralazine and alcohol are described in the SPC Section 4.5 and PIL Section 2 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Interference with laboratory tests: estimation of serum bilirubin and catecholamines</td>
<td>The risk of interference with laboratory tests: estimation of serum bilirubin and catecholamines associated with use of the drug product is described in the SPC Section 4.4, and appropriate advice is provided to the prescriber to minimise this risk.</td>
<td>None</td>
</tr>
<tr>
<td>Important potential risks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased sensitivity to allergens, severity of allergic reactions &amp; decreased response to adrenaline used to treat allergic reactions</td>
<td>The risks of increased sensitivity to allergens, severity of allergic reactions &amp; decreased response to adrenaline used to treat allergic reactions associated with use of the drug product is described in the SPC Section 4.4 and PIL Section 2 and appropriate advice is provided to the prescriber to minimise these risks.</td>
<td>None</td>
</tr>
<tr>
<td>Use during breastfeeding</td>
<td>The risks associated with use of the drug product during breastfeeding are described in the SPC Section 4.6 and PIL Section 2 and appropriate advice</td>
<td>None</td>
</tr>
</tbody>
</table>
Routine pharmacovigilance and routine risk minimisation are proposed for all safety concerns.

**IV.7 Discussion on the clinical aspects**
The grant of Marketing Authorisations is recommended for these applications.

**V  User consultation**
The package leaflet has been evaluated via a user consultation study, in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the package leaflet was English.

The results show that the package leaflet meets the criteria for readability, as set out in the *Guideline on the readability of the label and package leaflet of medicinal products for human use*.

**VI  Overall conclusion, benefit/risk assessment and recommendation**
The quality of the product is acceptable, and no new non-clinical or clinical concerns have been identified. Extensive clinical experience with propranolol hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets (PIL) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for Propranolol hydrochloride Oral Solution is presented below:
Propranolol hydrochloride 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml Oral Solution

Pl 39307/0059

KEEP OUT OF THE SIGHT AND REACH OF CHILDREN

PL39307/0060

Administration:
For oral use. Use as directed by your doctor. Read the package leaflet before use.

Storage:
Discard 90 days after first opening.

Marketing Authorisation Holder:
Thame Laboratories
Unit 4, Bradfield Road, Ruslip, Middlesex, HA4 0NJ, UK.

DO NOT TAKE PROPRANOLOL HYDROCHLORIDE IF YOU HAVE A HISTORY OF ASTHMA OR WHEEZING.
PAR Propranolol hydrochloride 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml Oral Solution

Propranolol hydrochloride 40mg/5ml Oral Solution

Propranolol hydrochloride 50mg/5ml Oral Solution

Propranolol hydrochloride 50mg/5ml Oral Solution

Propranolol hydrochloride 50mg/5ml Oral Solution

KEEP OUT OF THE SIGHT AND REACH OF CHILDREN

PL 39307/0059

Administration: For oral use. Use as directed by your doctor. Read the package leaflet before use. Storage: Discard 90 days after first opening.

Marketing Authorisation Holder: Thame Laboratories Unit 4, Bradfield Road, Ruslip, Middlesex, HA4 0NU, UK.
PAR Propranolol hydrochloride 5mg/5ml, 10mg/5ml, 40mg/5ml and 50mg/5ml Oral Solution

Each 5ml of oral solution contains 50mg propranolol hydrochloride.
This product also contains methyl parahydroxybenzoate (E219), propylene glycol (E1520) and liquid maltitol (E965). Read the package leaflet for further information. KEE|O|UT THE SIGHT AND RE|ACH OF CHILDREN PL39307/0062 [PON]

Administration:
For oral use.
Use as directed by your doctor.
Read the package leaflet before use.
Storing:
Discard 90 days after first opening.

DO NOT TAKE PROPRANO|OL HYDRO|CHLORIDE IF YOU HAVE A HISTORY OF ASTHMA OR WHISTLING.
Annex 1

Table of content of the PAR update

Steps taken after the initial procedure with an influence on the Public Assessment Report (Type II variations, PSURs, commitments)

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