Public Assessment Report

UKPAR

Phenergan Night Time 25 mg Film-coated Tablets

(Promethazine hydrochloride)

UK Licence No: PL 04425/0700

Aventis Pharma Limited (trading as Sanofi).
LAY SUMMARY

Phenergan Night Time 25 mg Film-coated Tablets
(Promethazine hydrochloride, film-coated tablet, 25 mg)

This is a summary of the Public Assessment Report (PAR) for Phenergan Night Time 25 mg Film-coated Tablets (PL 04425/0700). It explains how Phenergan Night Time 25 mg Film-coated Tablets 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 Phenergan Night Time 25 mg Film-coated Tablets.

The product will be referred to as Phenergan Night Time throughout the remainder of this public assessment report.

For practical information about using Phenergan Night Time patients should read the package leaflet or contact their doctor or pharmacist.

What is Phenergan Night Time and what is it used for?

Phenergan Night Time is used to treat the following conditions:

- For short term use: to treat adults with difficulty sleeping (insomnia).
- For short term use: as a sedative for children aged 16 years and above.

This medicine is the same as Phenergan 25 mg Tablets (PL 04425/0281) which is already authorised.

The company (Aventis Pharma Limited) that makes Phenergan 25 mg Tablets (PL 04425/0281) has agreed that its scientific data can be used as a basis for the grant of an identical licence for Phenergan Night Time (informed consent).

How does Phenergan Night Time work?

Phenergan Night Time contains the active ingredient called promethazine hydrochloride which belongs to the group of medicines called phenothiazines. It works by blocking a natural substance (histamine) that the body makes during an allergic reaction. It also works directly on the brain to help the patient feel more relaxed.

How is Phenergan Night Time used?

The pharmaceutical form of this medicine is a film-coated tablet and the route of administration is oral (by mouth).

The patient should always take this medicine exactly as described in the package leaflet or as their doctor or pharmacist has told them. They should check with their doctor or pharmacist if they are not sure.

Taking this medicine

- Take this medicine by mouth
- Do not take for longer than 7 days. If the patient’s symptoms worsen or do not improve after 7 days, they should talk to their doctor or pharmacist.

If the patient feels the effect of their medicine is too weak or too strong, they should not change the dose themselves, but ask their doctor.

How much to take

The recommended dose is:

Adults (including the elderly) and children over 16 years of age:

- One or two tablets (25mg-50mg) taken at night.
Use this medicine only as recommended. Do not exceed the recommended dose.

**Exposure to sunlight**
Phenergan Night Time can make the patient’s skin more sensitive to sunlight. Keep out of direct sunlight while taking this medicine.

Please refer to section 3 of the package leaflet for information on how to use this medicine.

This medicine can be obtained without a prescription.

For further information on how Phenergan Night Time is used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

**What benefits of Phenergan Night Time have been shown in studies?**
Phenergan Night Time is considered identical to previously authorised Phenergan 25 mg Tablets (PL 04425/0281), with the same benefits and risks. So no new studies have been provided for Phenergan Night Time but reference is made to the studies for Phenergan 25 mg Tablets (PL 04425/0281).

**What are the possible side effects from Phenergan Night Time?**
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Phenergan Night Time is considered to be identical to the previously authorised application for Phenergan 25 mg Tablets (PL 04425/0281) with the same benefits and risks.

For a full list of all the side effects reported with Phenergan Night Time see section 4 of the package leaflet, available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

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

**Why is Phenergan Night Time approved?**
The MHRA decided that the benefits of Phenergan Night Time are greater than the risks and recommended that it is approved for use.

**What measures are being taken to ensure the safe and effective use of Phenergan Night Time?**
A Risk Management Plan has been developed to ensure that Phenergan Night Time is used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Phenergan Night Time 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 Phenergan Night Time**
A Marketing Authorisation was granted in the UK on 15 February 2017.

The full PAR for Phenergan Night Time follows this summary.

For more information about treatment with Phenergan Night Time read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in March 2017.
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INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Aventis Pharma Limited a Marketing Authorisation for the medicinal product Phenergan Night Time (PL 04425/0700) on 15 February 2017. The product is a pharmacy (P) medicine indicated for short term use in the treatment of insomnia in adults and as a sedative in children over 16 years of age.

This application was submitted as a simple abridged (informed consent) application according to Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to the reference product Phenergan 25 mg Tablets, which was first authorised to the marketing authorisation holder (MAH) May and Baker Limited (PLR 00012/5286) as a Product Licence of Right and subsequently granted a reviewed licence on 29 December 1988 (PL 00012/5286R). The reference product subsequently underwent a change of ownership procedure to the current MAH Aventis Pharma Limited (PL 04425/0281) on 23 January 2003.

Promethazine hydrochloride is a potent, long acting, antihistamine with additional anti-emetic central sedative and anti-cholinergic properties.

Promethazine hydrochloride is distributed widely in the body. It enters the brain and crosses the placenta. Promethazine hydrochloride is slowly excreted via urine and bile. Phenothiazines pass into the milk at low concentrations.

No new data were submitted nor were necessary to be submitted for this application, as the data are identical to the data for the previously granted cross-referenced product.
II QUALITY ASPECTS

II.1 Introduction
This is an abridged application for Phenergan Night Time (PL 04425/0700) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to the reference product Phenergan 25 mg Tablets, which was first authorised to the marketing authorisation holder (MAH) May and Baker Limited (PLR 00012/5286) as a Product Licence of Right and subsequently granted a reviewed licence on 29 December 1988 (PL 00012/5286R). The reference product subsequently underwent a change of ownership procedure to the current MAH Aventis Pharma Limited (PL 04425/0281) on 23 January 2003. The application is considered valid.

II.2 Drug Substance

Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference product.

II.3 Medicinal Product

Name
The proposed product name for this application is Phenergan Night Time 25 mg Film-coated Tablets. The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Each film-coated tablet contains 25 mg of the active substance promethazine hydrochloride. The finished product is packed in blisters formed from opaque white 250µm polyvinyl chloride (PVC) coated with 40gsm polyvinylidene chloride (PVdC) sealed to 20µm hard temper aluminium foil (coated with vinyl heat seal lacquer) and is available in a pack size of 14 tablets.

The proposed shelf life of the unopened product is 3 years with the storage conditions ‘Store below 30°C. Store in the original carton in order to protect from light.’

The proposed packaging, shelf-life and storage conditions are consistent with the details registered for the cross-reference product.

Legal status
Pharmacy (P) medicine.

Marketing Authorisation Holder/Contact Persons/Company
Aventis Pharma Limited, One Onslow Street, Guildford, Surrey, GU1 4YS, UK.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.
**Manufacturing process**
The proposed manufacturing processes are consistent with the details registered for the cross-reference product and the maximum batch size is stated.

**Finished product/shelf-life specification**
The proposed finished product specification is in line with the details registered for the cross-reference product.

**TSE Compliance**
None of the excipients contain materials of animal or human origin.

**Bioequivalence**
No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula utilising the same processes as the cross-reference product, Phenergan 25 mg Tablets (PL 04425/0281).

**Expert Report**
The applicant cross-refers to the data for Phenergan 25 mg Tablets (PL 04425/0281) to which this application is claimed to be identical. This is acceptable.

**Product Name and Appearance**
See Section II.3 ‘Medicinal Product; Name’ for details of the proposed product name. The appearance of the product is identical to that of the cross-reference product.

**II.4 Discussion on chemical, pharmaceutical and biological aspects**
The data submitted with the application is acceptable. The grant of a Marketing Authorisation is recommended.
III NON-CLINICAL ASPECTS

Introduction
As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Ecotoxicity/environmental risk assessment (ERA)
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

Discussion on the non-clinical aspects
The grant of a Marketing Authorisation is recommended.

IV CLINICAL ASPECTS

Introduction
As this is an abridged application submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

Risk Management Plan (RMP)
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 Phenergan Night Time.

A summary of safety concerns and planned risk minimisation activities, as approved in the RMP, are listed below:

Summary table of safety concerns:

<table>
<thead>
<tr>
<th>Important identified risks</th>
<th>Severe hypersensitivity reactions</th>
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<tbody>
<tr>
<td></td>
<td>Severe blood disorders such as agranulocytosis</td>
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<td></td>
<td>CNS depression, including sedation and drowsiness</td>
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<td></td>
<td>Respiratory depression, including in &lt;2 years old</td>
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<tr>
<td></td>
<td>Severe cardiovascular effects, including arrhythmias and hypotension</td>
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<td>Anticholinergic effects</td>
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<td>Seizures, especially in overdose</td>
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<td>Hepatic disorders such as jaundice</td>
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<td></td>
<td>Masking of intestinal obstruction or raised intracranial pressure</td>
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<td>Extrapyramidal symptoms</td>
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<td>Concomitant use with ototoxic drugs</td>
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<td></td>
<td>Use in pregnancy</td>
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<tr>
<td>Important potential risks</td>
<td>None</td>
</tr>
<tr>
<td>Missing information</td>
<td>None</td>
</tr>
</tbody>
</table>

Routine pharmacovigilance and routine risk minimisation are proposed for all safety concerns.
Discussion on the clinical aspects
The grant of a Marketing Authorisation is recommended.

V User consultation
A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to the product for Phenergan 25 mg Tablets (PL 04425/0281). The bridging report submitted by the applicant is acceptable.

VI Overall conclusion, benefit/risk assessment and recommendation
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with promethazine hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.
Summaries of Product Characteristics (SmPC), Patient Information Leaflets (PIL) and Labels

The SmPC and PIL are consistent with the details registered for the cross-reference product.

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for this medicine is presented below:
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)

<table>
<thead>
<tr>
<th>Scope</th>
<th>Procedure number</th>
<th>Product information affected</th>
<th>Date of start of the procedure</th>
<th>Date of end of procedure</th>
<th>Approval/ non approval</th>
<th>Assessment report attached Y/N (version)</th>
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