GALPHARM HAYFEVER AND ALLERGY RELIEF 1MG/ML SYRUP
PL 16028/0098

UKPAR

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GALPHARM HAYFEVER AND ALLERGY RELIEF 1MG/ML SYRUP PL 16028/0098

LAY SUMMARY

The MHRA granted Galpharm Healthcare Limited Marketing Authorisations (licences) for the medicinal products Galpharm Hayfever and Allergy Relief 1mg/ml Syrup on 19th January 2007. This product to be sold to the general public (GSL) contains cetirizine hydrochloride and is to be used to relieve the allergic symptoms (runny and itchy nose, with or without stuffiness) caused by hayfever and other allergies (e.g. house and dust mite allergies. The medicine can also be used for skin allergies, such as rash, itching and urticaria (also known as nettle rash or hives).

The active ingredient cetirizine hydrochloride acts as an antihistamine reducing the symptoms of the allergic reaction.

This application is a duplicate of a previously granted application for Cetirizine Hydrochloride 1mg/ml Oral Solution (PL 00289/0595), granted to Approved Prescription Services in November 2002 (current marketing authorisation holder is Teva UK Ltd).

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Galpharm Hayfever and Allergy Relief 1mg/ml Syrup outweigh the risks, hence a Marketing Authorisation has been granted.

GALPHARM HAYFEVER AND ALLERGY RELIEF 1MG/ML SYRUP
PL 16028/0098

SCIENTIFIC DISCUSSION

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INTRODUCTION

The UK granted marketing authorisations for the medicinal products Galpharm Hayfever and Allergy Relief 1mg/ml Syrup (PL 16028/0098) to Galpharm Healthcare Limited on 19th January 2007. The products are for sale to the public by a General Sales Licence (GSL).

The application was submitted as a simple abridged application according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Cetirizine Hydrochloride 1mg/ml Oral Solution (PL 00289/0595), approved in November 2002 to the marketing authorisation holder Approved Prescription Services Limited.

No new data was submitted nor was it necessary for these simple applications, as the data is identical to that of the previously granted cross-reference product. As the cross-reference products were granted prior to the introduction of current legislation, no PARs were generated for them.

The active ingredient cetirizine hydrochloride acts as an antihistamine reducing the symptoms of the allergic reaction. Galpharm Hayfever and Allergy Relief 1mg/ml Syrup is indicated for the symptomatic treatment of allergic rhinitis (seasonal and perennial), and chronic idiopathic urticaria.

PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 16028/0098
PROPRIETARY NAME: Galpharm Hayfever and Allergy Relief 1mg/ml Syrup
ACTIVE(S): Cetirizine hydrochloride
COMPANY NAME: Galpharm Healthcare Limited
E.C. ARTICLE: Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC
LEGAL STATUS: GSL

1. INTRODUCTION

This is a simple, piggy back application for Galpharm Hayfever and Allergy Relief 1mg/ml Syrup submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Galpharm Healthcare Limited, Hugh House, Galpharm Way, Upper Cliffe Road, Dodworth Business Park, Dodworth, Barnsley, South Yorkshire, S75 3SP.

The application cross-refers to Cetirizine Hydrochloride 1mg/ml Oral Solution (PL PL 00289/0595), approved in November 2002 to the marketing authorisation holder Approved Prescription Services Limited. The current application is considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The proposed name of the product is Galpharm Hayfever and Allergy Relief 1mg/ml Syrup. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

The product contains cetirizine hydrochloride, equivalent to 1mg/ml. It is to be stored in amber glass bottles with a polypropylene screw cap and child-resistant closure. Pack size is 70ml. The proposed shelf-life (3 years) and storage conditions (none) are consistent with the details registered for the cross-reference product.

2.3 Legal status

On approval, the products will be on sale to the general public, under a general sales licence (GSL).

2.4 Marketing authorisation holder/Contact Persons/Company

The proposed Marketing Authorisation Holder, Galpharm Healthcare Limited, Hugh House, Galpharm Way, Upper Cliffe Road, Dodworth Business Park, Dodworth, Barnsley, South Yorkshire, S75 3SP.

The QP responsible for pharmacovigilance is stated and his CV is included.

2.5 Manufacturers

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

2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

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

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

2.10 TSE Compliance
No materials of animal or human origin are included in the product. This is consistent with the cross reference product.

3. EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS
The proposed summary is consistent with the details registered for the cross-reference product.

6. PATIENT INFORMATION LEAFLET/CARTON
PIL
The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.

Carton and Label
The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

7. CONCLUSIONS
The data submitted with the application are acceptable. A Marketing Authorisation should be granted.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

As this is a duplicate application, no new clinical data have been supplied and none are required.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for this application are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
These applications are identical to a previously granted application for Cetirizine Hydrochloride 1mg/ml Oral Solution (PL 00289/0595).

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products which, in turn, have been shown to be interchangeable with the innovator products. Extensive clinical experience with cetirizine hydrochloride is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.

GALPHARM HAYFEVER AND ALLERGY RELIEF 1MG/ML SYRUP
PL 16028/0098

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation application on 14/06/2004.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 06/07/2004.
3	Following assessment of the application the MHRA requested further information on 03/06/2005 and 07/12/2005
4	The applicant responded to the MHRA's requests, providing further information on 07/12/2005 and 19/01/2007
5	The application was determined on 19/01/2007

GALPHARM HAYFEVER AND ALLERGY RELIEF 1MG/ML SYRUP
PL 16028/0098

STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

GALPHARM HAYFEVER AND ALLERGY RELIEF 1MG/ML SYRUP
PL 16028/0098

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Galpharm Hayfever and Allergy Relief 1mg/ml Syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1 ml of solution contains 1 mg of cetirizine hydrochloride.

Excipients:
Galpharm Hayfever and Allergy Relief 1mg/mL Syrup contains 315 mg sorbitol per ml.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Oral solution.
Clear colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Adults and children aged 6 years and over.

Symptomatic treatment of allergic rhinitis (seasonal and perennial), and chronic idiopathic urticaria.

4.2 Posology and method of administration
For oral use.

Adults and children aged 6 years and over: 2 x 5ml once daily or 5 ml taken twice daily (morning and evening).

If drowsiness occurs, the solution can be administered in the evening.

Children under 6 years:
Not recommended

Cetirizine is contraindicated in patients with severe renal impairment. In patients with moderate renal impairment the dose should be adjusted to 5 ml. Caution should be exercised in patients with mild to moderate renal impairment or impaired liver function (see 4.4 Special warnings and precautions for use).

There is no evidence that the dose needs to be modified for healthy elderly patients. The duration of the treatment may vary depending on the symptoms.

4.3 Contraindications
Hypersensitivity to any component of the preparation.

Patients with severe renal impairment.

4.4 Special warnings and precautions for use
In some patients, long term treatment with Cetirizine Solution may lead to an increased risk of caries due to mouth dryness. The patients should therefore be informed about the importance of oral hygiene.

In cases of impaired hepatic function and renal function, the elimination of cetirizine may be impaired. Caution should be exercised when administering cetirizine to these patients. (see section 4.2 posology and section 4.3 contraindications).

Cetirizine may potentiate the effects of alcohol. Therefore caution is recommended at concomitant use of alcohol.

Caution is recommended with concomitant use of CNS depressants.

Contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Allergy testing: Use of cetirizine must be discontinued three days before allergy tests. Cetirizine may potentiate the effects of alcohol. Therefore caution is recommended during concomitant use of alcohol. Caution is recommended during concomitant use of CNS depressants.

4.6 Pregnancy and lactation

Data on a limited number of exposed pregnancies indicate no adverse effects of cetirizine on pregnancy or on health of foetus/new born child. To date no other relevant epidemiological data are available.

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or post natal development (see 5.3). Caution should be exercised when prescribing to pregnant women.

Breast feeding
No data concerning the excretion of cetirizine into human milk are available. Cetirizine should be avoided during lactation.

4.7 Effects on ability to drive and use machines

Cetirizine may have minor or moderate influence on the patient's ability to react. This should be considered when extra alertness is required e.g. when driving. Cetirizine may potentiate the effects of alcohol and CNS depressants.

4.8 Undesirable effects

Mouth dryness, headache, dizziness, drowsiness, somnolence in children and adults, agitation, abdominal complaints and digestive disorders.
Exceptionally, cases of allergic reactions such as cutaneous reactions and angioedema (Quincke's Oedema) have been reported.

4.9 Overdose

Toxicity: Limited experience of overdosing. 20 mg to a 2 year old, 30 mg to a 3 year old and 40 mg to an 11 year old did not give any symptoms. 60 mg to a 4 year old gave mild intoxication, 400 mg to a 14 year old gave mild symptoms while 400-500 mg to an adult gave no symptoms at all.

Symptoms of overdosage reported with antihistamine substances: Somnolence, unconsciousness and/or excitation (principally in children). Ataxia, tremor, headache, hallucinations, seizures, dry mouth, flush, hyperthermia, mydriasis, urine retention tachycardia and in the case of massive doses, possible fall in blood pressure and arrhythmias. Nausea and vomiting. Also extrapyramidal symptoms are possible. Cetirizine has a low sedative and anticholinergic effect. Sedation can be a symptom of overdose, it can occur after a single dose of less than 50 mg.

Treatment: At the present time there is no specific antidote. Experience of overdosing is limited and no severe intoxication has been reported to date. Primary treatment should be gastric lavage, if justified and charcoal. Symptomatic treatment should be instituted in the case of acute intoxication, such as diazepam for seizures or acute dystonias.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: RO6AEO7
Pharmacotherapeutic group: Antihistamine piperazine derivatives
Cetirizine hydrochloride is a racemate and an anti-allergic with specific histamine H1 - receptor blocking characteristics.

Cetirizine inhibits cutaneous reactions in allergic individuals by VIP (Vasoactive Intestinal Polypeptide) and substance P, neuropeptides that are considered involved in the allergic reaction. Effect is reached within 2 hours with a maximum effect after 4 hours, and remains for at least 24 hours. In allergic individuals, cetirizine inhibits the recruitment of eosinophils after stimulation with allergens and non selective histamine liberators, by a mechanism that is not primarily explained by the H1-receptor blocking characteristics of the pharmaceutical.

5.2 Pharmacokinetic properties

Cetirizine is absorbed with small inter-individual variations. Cetirizine has not been given intravenously, therefore the bioavailability, clearance and volume of distribution (Vd) are unknown. Maximum plasma concentration is achieved within 1 hour and the terminal half-life is about 10 hours in adults and 6 hours in children between the age of 6-12 years. The grade of protein binding in plasma is about 93%. Cetirizine is metabolised to a small extent with a known inactive main metabolite. 60% of a dose of cetirizine is eliminated in unchanged form via the kidneys within 96 hours. Repeated administration does not lead to any accumulation, nor is the absorption or elimination affected. In cases of impaired kidney function, the elimination is slower and the half-life is prolonged. Elimination will also be decreased in cases of hepatic impairment.
There is no evidence that the pharmacokinetics of cetirizine is altered in elderly patients unless renal or hepatic function is reduced.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction, genotoxicity or carcinogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol
Propylene glycol
Liquid Sorbitol (non-crystallising) (E420)
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Sodium acetate
Acetic acid
Saccharin sodium
Banana flavour
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

70ml fill bottle.

Amber glass bottle with child-resistant polypropylene screw cap incorporating a tamper evident seal (yellow polyethylene)

Measuring device: 5 ml plastic PP measuring spoon graduated at 2.5 ml

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
Galpharm Healthcare Limited
Hugh House
Upper Cliffe Road
Dodworth Business Park
Dodworth
Barnsley
South Yorkshire S75 3SP

8 MARKETING AUTHORISATION NUMBER(S)
PL 16028/0098

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
19/01/2007

10 DATE OF REVISION OF THE TEXT
19/01/2007

GALPHARM HAYFEVER AND ALLERGY RELIEF 1MG/ML SYRUP
PL 16028/0098

Patient Information Leaflet
Galpharm Hayfever & Allergy Relief 1mg/ml Syrup
cetirizine hydrochloride

Read this leaflet carefully because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must see your doctor if your symptoms worsen or do not improve.

In this leaflet:

This solution contains cetirizine hydrochloride as the active ingredient. It also contains glycerol, propylene glycol, liquid sorbitol (E420), methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216), sodium acetate, acetic acid, saccharin sodium, banana flavour and purified water.

PL Holder: Galpharm Healthcare Ltd., South Yorkshire S75 3SP, England.

Manufactured by: TEVA UK Limited, Eastbourne BN22 9AG, England.

1. What this medicine is and what it is used for

Each 1ml of oral solution contains 1mg of cetirizine hydrochloride. Cetirizine belongs to a group of drugs called antihistamines, which help to relieve the symptoms of some allergies.

The product is available in bottles of 70ml.

Your medicine is used to relieve the allergic symptoms (runny and itchy nose, with or without stuffiness) caused by hayfever and other allergies e.g. pet and house dust mite allergies.

Your medicine can also be taken for skin allergies such as rash, itching and urticaria (also known as nettle rash or hives). Urticaria can occur as a persistent condition and is recognised by the formation of raised white or reddish lumps surrounded by red inflamed areas which itch or sting.

Many things in everyday life can start allergies in certain people. These include:
- Pollen
- Animals
- House dust mites
- Moulds

Other things which do not themselves generate an allergic response, but which can make the symptoms of allergies worse include:
- Pollution
- Poor air conditioning
- Central heating / hot weather

You can help reduce allergic reactions by minimizing contact with those factors which can cause the reactions:
- If you suffer from hayfever, try to ensure low exposure to pollen when hayfever symptoms are expected. For example, keep windows closed, do not cut grass, stay indoors as much as possible etc.
- Try to avoid contact with animals if they normally cause you to have allergic symptoms.

2. Before you take this medicine

Do not take this solution if you:
- are sensitive to any of the ingredients in your medicine.
- have severe kidney problems.

Take special care with this solution if you have:
- liver problems
- mild or moderate kidney problems.

Tell your doctor if you are taking any of the following:
- Sedatives e.g. nitrazepam, as their effects may be increased by cetirizine.

Taking this medicine with food and drink:
• As with other antihistamines, it is advisable to avoid drinking large amounts of alcohol whilst using this syrup.

Pregnancy and Breast feeding:
• Talk to your doctor before taking if you are pregnant.
• Do not take if you are breast feeding.

Driving and using medicines:
• This medicine at the recommended dose does not cause drowsiness in the majority of people. However as with all antihistamines, rare cases of drowsiness have been reported. If affected do not drive or operate machinery. As with all antihistamines you should avoid excessive alcohol consumption when taking this medicine.

Other precautions you must take:
• The medicine must be discontinued 3 days before any allergy testing
• If you take your medicine for a long time there is an increased risk of tooth decay due to mouth dryness. It is important to brush your teeth regularly.

Important information about some of the ingredients of this medicine:
• This product contains liquid sorbitol (E420).
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
• Methyl parahydroxybenzoate (E218) and propyl parahydroxybenzoate (E216) may cause allergic reactions (possibly delayed).

3. How to take this medicine

For oral use.
Use the spoon provided to make sure you have the correct dose.
Adults and children aged 6 years and over: Two 5ml spoonfuls once daily or one 5ml spoonful morning and evening.
If drowsiness occurs, take the medicine in the evening.
If you have kidney problems, you may only need half the recommended dose.
Children under 6 years: not recommended.

If you take more solution than you should:
• If you (or someone else) swallow a lot of the syrup all together, or if you think a child has accidentally swallowed any of the syrup, contact your nearest hospital casualty department or your doctor immediately.
• Overdose can cause drowsiness, unconsciousness, dry mouth, loss of co-ordination, shaking, headache, dilated pupils, feeling flushed, a very high temperature, hallucinations, fits, tics, dizziness or fainting, problems urinating, changes in heart rhythm, feeling and being sick. In children, agitation may occur.

If you forget to take a dose:
If you forget to take a dose, take one as soon as you remember, unless it is nearly time to take the next one. Never take two doses together. Take the remaining doses at the correct time.

4. Possible side effects

Like all medicines, Galpharm Hayfever & Allergy Relief 1mg/ml Syrup can have side effects.
Tell your doctor if you notice any of the following:
• Headache
• Dizziness
• Agitation
• Dry mouth
• Drowsiness
• Stomach or intestinal discomfort

These are all temporary, mild side effects of this medicine.
Stop taking this medicine and tell your doctor or go to your nearest hospital casualty department urgently if you experience a severe but rare allergic reaction (rash, swelling of the face, lips, mouth or throat which may cause difficulty swallowing or breathing).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. Storing your medicine

Do not transfer to another container. Do not use after the expiry date shown on the carton.
Keep all medicines out of the reach and sight of children.
Return all unused medicines to your pharmacist for safe disposal.

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Text prepared: December 2006 34C9161350903


Galpharm Hayfever & Allergy Relief 1mg/ml Syrup cetirizine hydrochloride
To relieve the symptoms (e.g. sneezing, runny nose and burning, itchy eyes) of hayfever and other allergies e.g. pet or house dust mite allergies. Can also be taken for skin allergies such as rash, itching and hives.
Please read the enclosed leaflet carefully before use.
Dosage
For oral use. Use the spoon provided to make sure you have the correct dose.
Adults and children aged 6 years and over: Two 5ml spoonfuls once daily or one 5ml spoonful morning and evening. If drowsiness occurs, take the medicine in the evening.
Children under 6 years: Not recommended.
WARNINGS
DO NOT EXCEED THE STATED DOSE
KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN
Do not take if you:
• are sensitive to any of the ingredients in the medicine.
• have severe kidney problems.
• are breast feeding.
Consult your doctor:
• if you are pregnant.
• if symptoms persist.
• if you have liver or kidney problems.
This medicine at the recommended dose does not cause drowsiness in the majority of people. However as with all antihistamines rare cases of drowsiness have been reported. If affected do not drive or operate machinery. As with all antihistamines you should avoid excessive alcohol consumption when taking this medicine.
Ingredients: Each 1ml of oral solution contains 1mg of cetirizine hydrochloride. Also contains: methyl parahydroxybenzoate (E218), propyl parahydroxybenzoate (E216) and liquid sorbitol (E420). See leaflet for further information.
Product Licence Holder: Galpharm Healthcare Ltd, South Yorkshire, S75 3SP, England.
galpharm
PL 16028/0098
GSL
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0903
galpharm
Hayfever & Allergy Relief
1mg/ml Syrup
cetirizine hydrochloride
Hayfever ✓
Skin Allergies ✓
Dust Allergies ✓
Pet Allergies ✓
Sugar-Free • 70ml
63626-A
FPO Barcode
5017353502872


Read the enclosed leaflet carefully before use.
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Children under 6 years: Not recommended.
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DO NOT EXCEED THE STATED DOSE
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KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN.
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PL Holder: Galpharm Healthcare Ltd, South Yorkshire, S75 3SP, England.
PL 16028/0098
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galpharm
Hayfever & Allergy Relief
1mg/ml Syrup
cetirizine hydrochloride
Sugar-Free • 70ml