Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

Pharmacy to General Sales List Reclassification

Pirinase Hayfever Relief for Adults 0.05% Nasal Spray

(Fluticasone)

PL 00079/0688

Glaxo Wellcome UK Limited

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1. INTRODUCTION

Pirinase Hayfever Relief for Adults 0.05% Nasal Spray (Pirinase Hayfever) is a medicine to be used to treat the symptoms of hayfever, such as sneezing, runny or itchy nose, and burning or itchy eyes.

The active ingredient in the product is fluticasone propionate.

The Licence holder Glaxo Wellcome UK Limited applied to make this product available as a General Sales List medicine (GSL) for sale through general retail outlets.

The Medicines and Healthcare products Regulatory Agency (MHRA) considers this product is safe enough to be sold on general sale. This report outlines the evidence that the MHRA reviewed which led to the decision to approve the application.

2. BACKGROUND

A nasal spray containing fluticasone propionate with the product name Flixonase Aqueous Nasal Spray has been authorised as a Prescription Only Medicine (POM) since 1990. In March 2002, the nasal spray was reclassified to a Pharmacy (P) medicine under the name Flixonase Allergy Nasal Spray. A P medicine can be sold without prescription from pharmacies under the supervision of a pharmacist. Flixonase Allergy Nasal Spray has subsequently been renamed Pirinase Allergy 0.05% Nasal Spray and may be used for the prevention and treatment of seasonal allergic rhinitis (hayfever) and perennial rhinitis (indoor allergy).

Fluticasone propionate is in the class of medicines known as glucocorticosteroids, often referred to as steroids. It works by helping to reduce the symptoms of inflammation (sneezing, runny nose and or nasal congestion) following exposure to an allergen (trigger), such as pollen, dust mites, fungus spores or pets.

This is the first application for GSL availability for this product in the UK.

2.1 Use of fluticasone propionate

Nasals sprays containing fluticasone may be used for both the prevention and treatment of seasonal allergic rhinitis (hayfever) and perennial rhinitis (indoor allergy). The products are effective in helping to provide relief of sneezing, itchy and runny nose, itchy and watery eyes, nasal congestion and associated sinus discomfort.

Fluticasone propionate is also used as the active ingredient in other medicines including nasal drops, skin preparations, and products for inhalation (either as a dry powder or liquid).

2.2 Legal Status of other medicines in this class

Another nasal spray containing the glucocorticosteroid beclometasone is already available as a GSL medicine for the treatment of hayfever.

2.3 Legal status of other hayfever treatments

Other types of product are available GSL in the UK for the treatment of hayfever. These include tablets containing either cetirizine or loratadine which are non-sedating antihistamines.

3. PROPOSED TERMS OF RECLASSIFICATION

The applicant has proposed the following conditions for the GSL supply.

- For treatment of seasonal allergic rhinitis (hayfever)
- Strength: 0.05% fluticasone
- Maximum dose: two sprays per nostril once a day
- Maximum daily dose: two sprays per nostril
- Maximum pack size: 60 sprays

Use of Pirinase Hayfever as a General Sales List medicine is limited to symptoms of hayfever. The dosage for the GSL product has been set at the lowest effective dose, two sprays per nostril once a day.

The approved Summary of Product Characteristics (SmPC) and patient information leaflet are available on the MHRA website.

4. GENERAL SALES LIST CRITERION

Under the provisions of The Human Medicines Regulations 2012, regulation 62(5), General Sales List is appropriate for medicines which can, with reasonable safety, be sold or supplied by someone other than a pharmacist. The term “with reasonable safety” has been defined as: “where the hazard to health, the risk of misuse, or the need to take special precautions in handling is small and where wider sale would be a convenience to the purchaser."

5. ASSESSMENT OF SUITABILITY FOR GENERAL SALES LIST AVAILABILITY

The MHRA assessed the application against the General Sales List criterion, stated in Section 4.

5.1 Hazard to health

5.1.1 Safety Profile

The safety profile of nasal sprays containing fluticasone is well established and predictable. The most commonly reported Adverse Events (AEs) are nasal symptoms associated with local irritation related to the use of an aqueous spray formulation. These are usually mild and reversible.

Fluticasone nasal spray has been approved for non-prescription use in nine countries including the UK, Australia, China, Denmark, Ireland, and New Zealand. In the UK, approximately 4.1 million units have been sold since 2002 when the P product was approved. The estimated non-prescription use in the three years from March 2008 to February 2011 has been approximately 245.7 thousand patient years (assuming four sprays per day and 60 sprays per inhaler). During this period 200 AE reports are likely to have been associated with non-prescription use of the nasal spray. Of these, 187 were non-serious and there were no fatal case reports.

The majority of reported AEs relate to local effects related to the use of an aqueous spray formulation, such as nasal irritation, dryness of the nose, sore or irritated throat, epistaxis, or headache, unpleasant taste/ smell and allergic reactions.

For GSL supply, use of the product is for hayfever symptoms only, in adults aged 18 years and over, with a dose of two sprays into each nostril once a day and for a maximum period of use of 1 month continuously. Healthcare professional advice should be sought if use beyond 1 month is required. The pack size is 60 sprays which is sufficient for 1 month’s use at the recommended dosage.

These specific uses and dosage for Pirinase Hayfever have been introduced to help ensure that the product is not used at too high a dose or for too long a period of time

without healthcare professional advice. High doses and long periods of use may be linked to unwanted side effects such as Cushing's syndrome (a collection of symptoms caused by very high levels of a hormone called cortisol in the body), adrenal suppression (where the adrenal glands do not produce adequate amounts of steroid hormones), growth retardation in children and glaucoma (a build-up of pressure in the eye which can affect sight).

In very rare circumstances, use of the nasal spray may have caused nasal septum perforation (a hole in the structure between nostrils). Usually this has occurred when there has been previous nasal surgery or injury. In order to reduce the risk of this occurring, the product information includes advice: "Talk to your doctor or pharmacist if you have recently had surgery, an injury or ulcers in your nose".

5.1.2 Drug Interactions

Clinically important interactions of fluticasone nasal spray with commonly used medicines are considered unlikely.

AEs such as Cushing's syndrome, adrenal suppression, growth retardation in children and glaucoma may also occur if Pirinase Hayfever Nasal Spray is used in patients already taking other corticosteroid medicines. The patient information leaflet recommends that patients should speak to a doctor before using the nasal spray if they are taking any other corticosteroid products, such as tablets, creams, ointments, asthma medications, and similar nasal sprays or eye/ nose drops.

During the period of public consultation on GSL availability of Pirinase Hayfever Relief for Adults 0.05% Nasal Spray (ARM 83, see Section 8 of this report) a concern was highlighted that the symptoms of overuse of corticosteroids (as outlined above) may arise if the nasal spray is used in patients already taking medicines to treat HIV infection (Human Immunodeficiency Virus), and medicines containing ritonavir in particular. In order to ensure that patients on HIV medicines do not use the nasal spray the product information includes a warning "Do not to use if you are taking medicines for HIV"

5.1.3 Special Populations

The product is not intended for use during pregnancy and lactation without advice from a healthcare professional and the patient information leaflet includes advice to, "talk to your doctor or pharmacist before using the product if you are pregnant, trying to become pregnant or are breast feeding".

To avoid any risk that growth rate in children and adolescents may be affected, the product is not for use in children and adolescents under 18 years.

There is sufficient information in the packaging and patient leaflet, without the need for pharmacist intervention, to ensure people take appropriate action during pregnancy and lactation or avoid use in those under the age of 18 years.

5.2 Risk of misuse

5.2.1 Ability to self-diagnose and treat hayfever

Hayfever (seasonal allergic rhinitis) is already established as a condition which is suitable for self-diagnosis and treatment using GSL medicines such as non-sedating antihistamines tablets and liquids and beclometasone aqueous nasal spray. Considering the characteristic symptoms of hayfever, and the association with seasonal pollen and its recurring nature (usually annually) the chance of incorrect

self-diagnosis is extremely small. Patients may also have been first diagnosed with hayfever by a doctor and then find it more convenient to treat themselves afterwards.

Use in perennial allergic rhinitis (indoor allergies) is not proposed for this product as it can take longer than a month to treat these allergies and advice from a pharmacist is important to help ensure correct and safe use.

If symptoms do not improve in 7 days, it is possible patients may have bacterial rhinosinusitis (when a bacterial infection develops in the nose). So if symptoms do not improve after 7 days patients are advised to stop using the product or see their doctor or pharmacist for advice about whether to continue using it. If patients think they may have bacterial rhinosinusitis they should see their doctor or pharmacist before use, although, nasal steroids are unlikely to have unexpected effects if used in that condition.

5.2.2 Prolonged or excessive use

To ensure correct use as a medicine that people can choose themselves without advice or supervision from a pharmacist, there are clear instructions about the dose and length of treatment and when to seek advice from a healthcare professional on the outer carton and in the patient leaflet, and the pack size is limited to 60 sprays (1 month's supply). These measures are considered satisfactory to help avoid the risk of intentional/unintentional over dose or prolonged treatment.

To help avoid use in age groups less than 18 years, the name, label and patient information leaflet clearly indicate that the product is for adults only. There is no evidence of a problem of overuse in age groups less than 18 years.

5.3 Special Precautions in Handling

There are clear instructions in the patient information leaflet on how to put the product into the nose and no further special precautions in handling are required.

5.4 Wider sale would be a convenience

Hayfever is a common condition, readily self-diagnosed by a sufferer who usually experiences the same condition each year. GSL availability enables a hayfever sufferer to obtain the product as soon as the symptoms appear. This ready availability has been recognised as an advantage when other medicines for hayfever have been approved as GSL.

In general, people are used to obtaining hayfever treatments from general sales outlets and Pirinase Hayfever represents an additional choice to treat hayfever symptoms.

6. RISK MANAGEMENT PLAN

A comprehensive risk management plan has been approved. The plan identifies important risks and potential risks and outlines how they will be prevented or minimised.

A post authorisation Drug Utilisation Study has been agreed. Otherwise, routine pharmacovigilance measures are considered sufficient to address the identified and potential risks. Safety information will be collected and presented to MHRA and other Health Authorities in accordance with the regulations.

6.1 Specific Risk Minimisation Measures

6.1.1 Product Information

The SmPC has been revised to ensure the product is safe for use when supplied as a general sales medicine without the supervision of a pharmacist. Certain patients are advised not to use the product and to talk to their doctor. User testing of the patient information leaflet and label has shown that people can understand what the product is for, when not to use it and how to use it. The label is designed to clearly distinguish the product from other similar products.

6.1.2 Survey of Usage

A post authorisation study will be conducted to establish if people properly follow the key warnings and instructions for use on the outer label, when selecting the product themselves and using the product, following purchase as a GSL medicine. The survey may be accessed via a QR code on the carton label, which also includes the website address.

7. CONSULTATION ON GSL AVAILABILITY OF FLUTICASONE NASAL SPRAY

Consultation ARM 83 proposing General Sale availability of **Pirinase Hayfever Relief for Adults 0.05% Nasal Spray** was issued on 7 January 2013, with a deadline for comments of 1 February 2013. A copy of the consultation document is available on the MHRA website.

8. RESPONSES TO CONSULTATION ARM 83

There were 11 responses of which 4 were in favour, 4 did not support the reclassification and 3 had no comment. The individual responses are available alongside this report.

Those responding to the consultation highlighted an issue of concern in relation to the risk of an interaction between fluticasone containing products and ritonavir, used to treat HIV, which can on rare occasions lead to increased concentrations in the blood stream of fluticasone propionate in people using these products together. High concentrations of fluticasone in the blood stream could result in a risk of AEs, such as such as Cushing's syndrome, adrenal suppression, growth retardation in children and glaucoma. The risk for this product is low as it is for short term (hayfever season) use and the pack size is small (1 month's use). To help further reduce the risk, the product information advises people not to use the nasal spray if they are taking medicines for the treatment of HIV infection. Also a post authorisation study of Pirinase Hayfever Nasal Spray will be conducted to establish how the nasal spray is used as a GSL medicine.

9. ADVICE FROM THE COMMISSION ON HUMAN MEDICINES

In light of the steps taken for safe use as a GSL medicine, the Commission on Human Medicines advised in favour of GSL supply.

10. CONCLUSION

The issues raised in the responses to consultation on the application have been addressed and CHM were reassured that GSL supply was acceptable. Following the advice from the Commission on Human Medicines the Licensing Authority has taken the decision to approve GSL legal classification for Pirinase Hayfever Relief for Adults 0.05 % Nasal Spray.

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