

# **Risk of psychiatric adverse drug reactions to inhaled and intranasal corticosteroids and risk of non-psychiatric systemic adverse drug reactions to intranasal corticosteroids**

**Final SmPC and PL wording Agreed by the PhVWP in November 2010**

*Doc.Ref.: CMDh/PhVWP/027/2010  
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## **KEY PRINCIPLES**

The following key principles for inclusion in updates to product information are recommended:

### **1. For inhaled steroids:**

- In section 4.4 and 4.8, a specific reference to psychiatric and behavioural ADRs (particularly in children), including examples of such reactions. This would be in addition to any existing warnings and examples of other systemic ADRs which may occur

### **2. For intranasal steroids:**

- In section 4.4, specific examples of psychiatric and other systemic ADRs which may occur with some nasal corticosteroids
- In section 4.4, a warning to monitor growth in children, for any products which are licensed for use in children
- In section 4.8, a warning that systemic ADRs may occur, particularly at high doses when used for prolonged periods
- In section 4.8 for intranasal products supplied in a bottle and licensed for use in children, an additional warning that growth retardation has been reported in children receiving intranasal steroids

Given the wide number of products and broad variation in existing labelling, final SmPC wording in line with the key principles above could be agreed at a national level. However, psychiatric ADRs are currently listed in product information for only some inhaled products and no intranasal products, and specific examples of systemic ADRs to intranasal steroids are currently not included in any product information. We therefore suggest the following wording for these issues:

## **Inhaled Corticosteroids**

### **SUMMARY OF PRODUCT CHARACTERISTICS**

#### **• Section 4.4**

It is proposed that a short statement should be included in section 4.4 of the SmPC for all inhaled steroids to alert prescribers to the potential for psychological and behavioural effects (alongside any warnings on systemic side-effects)

Proposed additional wording: (**bold and underlined** below)

#### Section 4.4 (Special warnings and precautions for use)

*Systemic effects of inhaled corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract, glaucoma, **and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children)**. It is important therefore that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control of asthma is maintained.*

- **Section 4.8**

For section 4.8 of the SmPC, it is proposed that psychological and behavioural side-effects should be included for all inhaled steroids amongst other listed ADRs, as follows.

Section 4.8 (undesirable effects)		
System Organ Class	Adverse Event	Frequency
Psychiatric Disorders	<b><u>Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (predominantly in children)</u></b>	unknown*

*\*unless the MAH can designate a suitable frequency category according to the Guideline on Summary Of Product Characteristics*

## **PATIENT INFORMATION LEAFLET**

The warnings on psychological and behavioural adverse reactions in the SmPC should be reflected in the Patient Information Leaflet using suitable lay terms and with information on the rarity of these reactions, if available.

It is also proposed that a general reminder to patients not to exceed the prescribed dose should be included in the leaflet, if not already included.

**Note:** *wording for the PIL varies widely amongst products and the wording suggested below is largely based on patient-friendly wording taken from PILs which have undergone successful user-testing.*

### **Section 3**

**If you use more [product] than you should:**

**It is important that you take your dose as stated on the pharmacist's label or as advised by your doctor. You should not increase or decrease your dose without seeking medical advice.**

### **Section 4**

*Frequency not known, but may also occur:*

**• Sleeping problems, depression or feeling worried, restless, nervous, over-excited or irritable. These effects are more likely to occur in children**

## Intranasal corticosteroids

### SUMMARY OF PRODUCT CHARACTERISTICS

- **Section 4.4**

Section 4.4 of the UK SmPC for intranasal products already includes a statement on the risk of systemic side-effects, without specific examples of systemic ADRs. It is proposed to include examples of systemic ADRs to nasal steroids (including psychiatric effects) as a class effect in section 4.4, using wording which makes it clear these are less likely to occur with intranasal than oral steroids.

#### **Section 4.4 (Special warnings and precautions for use)**

*Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. **These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).***

### PATIENT INFORMATION LEAFLET

The general warnings on systemic side-effects in section 4.8 of the SmPC should be reflected in the Patient Information Leaflet using suitable lay terms and with information on the rarity of these reactions. Since specific examples of effects which may occur are described in section 4.4 of the SmPC only, and are not proposed for inclusion in section 4.8, specific examples should not be included in section 4 of the Patient Information Leaflet as side-effects.

It is also proposed that a general reminder to patients not to exceed the prescribed dose should be included in the leaflet, if not already included.

***Note:** wording for the PIL varies widely amongst products and the wording suggested below is largely based on patient-friendly wording taken from PILs which have undergone successful user-testing.*

#### **Section 3**

**If you use more [product] than you should:**

**It is important that you take your dose as stated on the pharmacist's label or as advised by your doctor. You should use only as much as your doctor recommends; using more or less may make your symptoms worse.**