Direct Healthcare Professional Communication

<Date>

Finasteride, dutasteride – New measures to minimise the risk of suicidal ideation

Dear Healthcare professional,

<Local marketing authorisation holder> in agreement with the European Medicines Agency and <insert the name of the regulatory authority, who have approved the communication> would like to inform you of the following:

Summary

- **Suicidal ideation is an adverse reaction of oral finasteride-containing products, mainly reported in patients treated for androgenetic alopecia.**
- **Advise patients treated with oral finasteride for androgenetic alopecia to stop treatment and seek medical advice if they experience depressed mood, depression or suicidal ideation.**
- **Sexual dysfunction that may contribute to mood alterations, including suicidal ideation, has been reported in some patients treated for androgenetic alopecia. Inform patients to seek medical advice in case of experiencing sexual dysfunction and consider discontinuation of treatment.**
- **A patient card will be available in the package of medicinal products containing finasteride 1 mg to highlight the risks of depressed mood, depression, suicidal ideation and sexual dysfunction reported with finasteride.**
- **Despite the insufficient evidence to establish a direct association of suicidal ideation with dutasteride, and based on the common mechanism of action for medicinal products of the class of 5-alpha reductase inhibitors, patients treated with dutasteride should be recommended to seek prompt medical advice if symptoms of mood alterations occur.**

Background on the safety concern

Finasteride and dutasteride are 5-alpha-reductase inhibitors (5-ARIs). Finasteride is an inhibitor of the enzyme 5-alpha-reductase types 1 and 2 with a greater affinity for type 2. Dutasteride targets both isoforms of this enzyme.

Lower dose oral formulations of finasteride (1 mg) are indicated for the treatment of male pattern hair loss in an early stage (androgenetic alopecia). A cutaneous spray solution of finasteride 2.275 mg/mL (topical) is authorised in the same indication. Higher dose oral formulations of finasteride (5 mg) including combinations with either tadalafil or tamsulosin are indicated for the symptomatic treatment of benign prostatic hyperplasia and for the prevention of urologic events. Dutasteride. available only as oral formulations, including combinations with tamsulosin are indicated for the management of symptomatic benign prostatic hyperplasia. For finasteride- and dutasteride-containing medicinal products, some psychiatric disorders are known risks and are already reflected in the product information.

Following an EU-wide review by the European Medicines Agency (EMA) of the available data regarding suicidal ideation and behaviours reported with 5-ARIs, it was concluded that the level of

evidence for these events differs according to the respective indications, active substances and formulations.

Within the review, 325 relevant cases of suicidal ideation have been identified in EudraVigilance, the European database of suspected adverse drug reaction reports. 313 cases were reported for finasteride and 13 for dutasteride (1 case reported the use of both finasteride and dutasteride). Most of the cases were reported for patients treated for alopecia, while a 10-times lower number of cases were reported for patients treated for benign prostate hyperplasia. These numbers should be considered in the context of the estimated exposure for finasteride of approximately 270 million patient years, and for dutasteride, approximately 82 million patient years.

Finasteride 1 mg (androgenetic alopecia)

Following the review of the available data, the EMA confirms that suicidal ideation is an adverse drug reaction with the frequency not known, meaning that it cannot be estimated from the available data. The current product information of these formulations already contains a warning on mood alterations including suicidal ideation, together with a recommendation to stop treatment and seek prompt medical advice if these symptoms occur. In addition, the review identified cases of suicidal ideation in which sexual dysfunction (a known adverse drug reaction of finasteride) contributed to the development of mood alterations, including suicidal ideation. Warnings and precautions for use will be updated to advise patients to consult their doctor if they experience sexual dysfunction, and discontinuation of the treatment should be considered.

A patient card will be included in the package to inform about the risks of mood alterations, including suicidal ideation, and of sexual dysfunction and to advise on the appropriate actions to be taken.

Finasteride 5 mg (benign prostatic hyperplasia) including combinations with tadalafil or tamsulosin

The review also confirmed that suicidal ideation is an adverse drug reaction with the frequency not known (cannot be estimated from the available data). The current product information of these formulations already contains a warning on mood alterations, including suicidal ideation, together with the recommendation to seek prompt medical advice if these symptoms occur.

Topical finasteride (androgenetic alopecia)

The product information already contains information about the risks of mood alterations associated with the use of oral finasteride**.** There is currently insufficient evidence to support a causal association between topical finasteride and the risk of suicidal ideation. Therefore, no product information update is introduced.

Dutasteride 0.5 mg (benign prostatic hyperplasia) including combinations with tamsulosin

Although there is insufficient evidence to establish a risk of suicidal ideation with dutasteride, as a precautionary measure, and based on the evidence for another oral 5-ARI, warnings and precautions for use will be updated to inform about the potential risk of suicidal ideation, with a recommendation that patients should seek prompt medical advice if symptoms of mood alterations occur.

Call for reporting

Please report any suspected adverse reactions associated with the use of finasteride- and dutasteride-containing products in accordance with the national requirements via the national spontaneous reporting system, to:

<Details (e.g., name, postal address, fax number, website address) on how to access the national spontaneous reporting system>

Company contacts point

<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>