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National Center of Pharmacovigilance
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To: Health Professionals

INFORMATIONAL NOTE

Case of adverse reactions associated with the inappropriate use of products containing the active ingredients finasteride, spironolactone and minoxidil in combination with retinoids for the treatment of alopecia in women

THE NATIONAL PHARMACOVIGILANCE CENTER OF THE NATIONAL DIRECTORATE OF PHARMACY AND DRUGS OF THE MINISTRY OF HEALTH, CONSIDERS PERTINENT TO PRESENT YOU THE FOLLOWING CASE:

Case description

A 55-year-old female patient who, to treat hair loss, was prescribed the following medications: spironolactone 25 mg (dose schedule not indicated), finasteride 1 mg 3 times a week, and biotin 5000 µg one capsule every day. In addition, two magisterial formulas were indicated. Formula "A" contained: minoxidil 5%, biotin 0.005% and vitamin E 1000 Ulo/o, while formula "B" contained: minoxidil 5% and retinol 50,000 Ulo/o. Formula "A" was applied in the morning and formula "B" in the afternoon.

Approximately a month and a half after being under this therapy, the patient developed hair growth on the face, arms, tear ducts and in the inguinal area. Due to these adverse reactions, the patient suspended the use of the prescribed medications, but the adverse reactions did not disappear. For this reason, the suspected drugs were not readministered and the hair growth in the areas described above were removed by depilation.

Information for health professionals

Finasteride

- Finasteride is an inhibitor of the enzyme 5-a-reductase type II. This enzyme is responsible for the conversion of testosterone to dihydrotestosterone, a hormone involved in androgenetic alopecia.

- Finasteride 1 mg is only indicated for the treatment of androgenetic alopecia in men.

- Both in Panama and in other countries of the world, the active ingredient finasteride is contraindicated in women. This is due to the ability of inhibitors of the enzyme 5-a-reductase type II to inhibit the

conversion of testosterone to dihydrotestosterone (the hormone responsible for the differentiation of the external genitalia during pregnancy) and produce malformations in the external genitalia of male fetas when administered to pregnant women.

- Lack of efficacy has been demonstrated in postmenopausal women with androgenetic alopecia who were treated with 1 mg finasteride in a 12-month placebo-controlled study (n=137). These women showed no improvement in either hair count, patient self-assessment, investigator assessment, or standardized photo assessment, compared to the placebo group.

Spironolactone

- Spironolactone is an aldosterone antagonist, which is not indicated for the treatment of androgenetic alopecia 11-18. However, it has been reported that due to its affinity for other steroid receptors, spironolactone can cause hypertrichosis 10 with a frequency of occurrence between uncommon (~1/1000 to <1/100) and very rare (<1/10,000).

- Spironolactone, being a potassium-sparing medication, could cause hyperkalaemia, exposing the patient to the appearance of more adverse reactions.

Minoxidil

- Topical solutions of 5% minoxidil should not be used in women, given the possibility of the appearance of hypertrichosis (excessive growth of body hair) in other body areas. Cases of severe hypertrichosis have been reported in 5 of 5o women who applied a 5% minoxidil solution topically for the treatment of androgenetic alopecia. Cases of facial, arm, and leg hypertrichosis were reported 2 to 3 months after starting minoxidil treatment. The hypertrichosis disappeared 5 months after discontinuing minoxidil19-20.

- The recommended daily dose of 5% minoxidil is 1 ml every 12 hours applied to the scalp starting in the center of the area to be treated and the maximum recommended daily dose is 2 ml, so the recommended daily dose must be respected regardless of the extension of the alopecia.

- Minoxidil should not be administered in other parts of the body.

- It should not be applied concomitantly with other topical products such as corticosteroids, retinoids or occlusive ointments, since they can increase the absorption of minoxidil. In the particular case of this patient, formula “B” containing retinal could increase the absorption of minoxidil, enhancing the appearance of systemic adverse reactions, such as hypertrichosis or cardiovascular effects 19· 21-23.

- Although studies with minoxidil have not shown significant systemic absorption, there is the possibility of small local absorption through the scalp, so regular monitoring of blood pressure and heart rate is recommended in patients taking minoxidil. have a heart or cardiovascular problem such as: coronary heart disease, congestive heart failure and/or valve disease, potential risk of hydrosaline retention, local and generalized edema, pericardial effusion, pericarditis, cardiac tamponade, tachycardia, angina.

- If systemic effects or severe dermatological alterations appear, treatment should be interrupted.

- In patients with dermatoses or skin lesions of the scalp, greater percutaneous absorption of the active ingredient may occur, so it must be ensured that these do not exist before application.

Recommendations for health professionals

- In this case, drugs whose uses have not been approved in Panama have been selected, ineffective and unsafe drugs in the treatment of alopecia in women, which is why health professionals who adhere to the prescription and dispensing of medicines under the indications approved in the inserts of the products registered in Panama.

- Reinforce the information provided by the doctor through pharmaceutical care.

- Report your suspected adverse reactions, pharmaceutical failures and therapeutic drug failures to the National Pharmacovigilance Center. Fax 512-9404 or email fvigilancia@minsa.gob.pa

Recommendations for patients

- Do not self-medicate.

- Consult a doctor about your hair loss problem, since in this situation it is necessary to carry out a medical history and a complete physical examination.

- Do not buy or acquire medicines or treatments in establishments not authorized for that purpose.

- Remember that only qualified doctors can prescribe medication. Do not follow advice or use treatments recommended by people who are not suitable for this purpose.

- Report your suspected adverse reactions, pharmaceutical failures and therapeutic drug failures to the National Pharmacovigilance Center. Telefax 512-9404 or email fviqilancia@minsa.gob.pa

To conclude, we thank you for complying with the recommendations issued in this information note and we ask you to extend this information to other health professionals and patients.

Sources of information consulted:

1. Monograph of the product Finapel 1 mg Coated Tablets. Prepared by Chalver de Colombia, S. A. for Pharmaderm, S. A. de Colo_mbia. Sanitary Registry 80505, et. al.