European Medicines Agency

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# QUESTIONS AND ANSWERS ON PROTOPIC/PROTOPY AND ELIDEL

Following a request from the European Commission and Denmark, the Committee for Medicinal Products for Human Use (CHMP) has reviewed the safety data on medicines containing tacrolimus and pimecrolimus, used topically (on the skin) for the treatment of atopic dermatitis. They concluded that the benefits of these products still outweigh the risks, but recommended some changes to the prescribing information.

## Which medicines have been reviewed?

The CHMP has reviewed the data for all topical medicines containing tacrolimus and pimecrolimus, authorised in the European Union for the treatment of atopic dermatitis (eczema, an itchy red rash - atopic means that it is linked to an allergy). These medicines are:

- **Protopic/Protopy**: a medicine containing tacrolimus, authorised EU-wide to treat moderate to severe atopic dermatitis in patients who cannot use or do not respond to standard treatments, such as topical corticosteroids,
- **Elidel**[1]: a medicine containing pimecrolimus, authorised first in Denmark then in other European countries, for the treatment of mild or moderate atopic dermatitis.

Both tacrolimus and pimecrolimus are immunomodulators. This means that they work on the immune system (the body's natural defences). In atopic dermatitis, an over-reaction of the skin's immune system causes skin inflammation (itchiness, redness, dryness). These substances calm the immune system down, and this helps relieve the skin inflammation and itching.

## Why did the CHMP review these medicines?

As for all medicines marketed in the EU, the use of Protopic/Protopy and Elidel is being continuously monitored. During such monitoring, a 'safety signal' (a sign of a potential side effect) was identified indicating a potential risk of skin cancer and lymphoma (another type of cancer) with these medicines. The European Commission and Denmark requested the CHMP to review all available data, to see if there was a potential link between the use of Protopic/Protopy or Elidel and the skin cancers or lymphomas, to see how this impacted on the benefit/risk profile of these medicines, and to give an opinion on whether any action was necessary.

## What data has the CHMP reviewed?

The companies who market Protopic/Protopy and Elidel gave to the CHMP the scientific data relevant to the safety and effectiveness of Protopic/Protopy and Elidel. This included data from preclinical studies, clinical trials, reports of side effects, epidemiological studies (studies of causes of diseases in the population) and information published in scientific journals.

[1] Elidel, also marketed under the tradenames Aregen, Douglan, Ombex, Rizan and Velov

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 86 68
E-mail: mail@emea.eu.int http://www.emea.eu.int

**What are the conclusions of the CHMP?**

The CHMP concluded that the benefits of the use of topical tacrolimus and pimecrolimus still outweigh the risks. But they could not on the basis of the available data prove nor disprove that Protopic/Protopy or Elidel were associated with the reported cancers and lymphomas.
The CHMP requested the companies to gather more data on the long-term safety profile to ensure that it remains acceptable but the results will not be known for a number of years. Meanwhile, the CHMP recommended that Protopic/Protopy and Elidel should be used with greater caution than currently. Prescribers and patients need to be aware of the need to monitor patients being treated for atopic dermatitis and that suspected adverse reactions including tumours should be reported.

The CHMP recommended changes to the product information (the information that is made available to doctors and to patients) for Protopic/Protopy and Elidel.

The CHMP recommended that the product information for Elidel be modified to reflect that this product should only be used in patients with mild or moderate atopic dermatitis, only when they cannot use or do not respond to treatment with topical corticosteroids.

**What are the recommendations for patients?**

Patients who are using Protopic/Protopy or Elidel should not stop or modify their treatment without first speaking with the doctor who prescribed it to them.

**What are the recommendations for prescribers?**

When prescribing Protopic/Protopy or Elidel, doctors should be aware that:

- These medicines should only be used in patients over the age of 2 years with mild or moderate disease (in the case of Elidel) and moderate to severe disease (in the case of Protopic/Protopy), when treatment with topical corticosteroids should not or cannot be used. This can be because the areas to be treated are not suitable for corticosteroid treatment (such as the face and neck), because corticosteroids don't work, or because the patient cannot tolerate them.
- Only doctors with experience in the diagnosis and treatment of atopic dermatitis should start the treatment.
- Protopic /Protopy and Elidel should be applied to affected skin surfaces only using a thin layer of product.
- Continuous long-term use should be avoided. Treatment should be carried out until the eczema clears, then stopped.
- If the disease does not get better, or even worsens, the diagnosis of atopic dermatitis should be re-evaluated and further therapeutic options considered
- These medicines should not be used in immunocompromised adults or children (people whose immune system is weakened, because of a disease such as AIDS or because they have received special medicines that suppress the immune system, such as those used in people who have received a transplant).
- These medicines should not be applied to lesions that are cancerous or pre-cancerous.
- Cases of cancers, including cutaneous and other types of lymphoma, and skin cancers, have been reported in patients using these medicines.

In addition, for Protopy/Protopic:

- If a patient has lymphadenopathy (enlarged lymph nodes, or ‘glands’) at the start of treatment, the doctor should investigate it and keep it under review.
- The lowest strength of the medicine should be used whenever possible.
- Once daily application should be used whenever possible

For further information, please check the Summary of Product Characteristics for Protopic/Protopy and Elidel adopted by CHMP on 23 March 2006.