

## **Important patient information about the topical medications Elidel and Protopic**

The U.S. Food and Drug Administration (FDA) recently added a “boxed” warning to the topical medications Elidel and Protopic, both of which are used in the management of the skin problem known as atopic dermatitis, or eczema. A boxed warning is used to indicate that the long-term safety of a medication is not known. Both Elidel and Protopic are known as **topical calcineurin inhibitors**. They work differently than steroids although both steroids and these medications suppress the inflammation which occurs in atopic dermatitis.

HealthyAirways would like to provide you with further information about the safety of these medications. We hope that this information helps to clarify any questions you might have about these medications and the FDA warning which has been issued.

### **Why did the FDA place a “box” warning on Elidel cream and Protopic ointment?**

There are three reasons we believe the FDA chose to place this warning on Elidel and Protopic.

1. Shortly after these medications were released there was a rapid increase in their use due to a perception that these medications were “safer” than topical steroids which have traditionally been used to treat atopic dermatitis. This alarmed the FDA as these medications had only been approved for use for a short period of time. The long term safety of these medicines had not been established. The FDA also found that these medications were being prescribed “off-label” in that they were being used in children under the age of 2 years.
2. The FDA is investigating a small number of cases of cancer in children and adults who have used these medications. One of the functions of our immune system is to survey our body and stop cancer from developing. Because Elidel and Protopic work by suppressing parts of the immune system (as do steroids) it seemed possible that the use of these medicines contributed to the development of cancer. A study in monkeys revealed that an oral form of Elidel given at 30 times the maximum recommended human dose resulted in an increased risk of lymphoma (a type of cancer affecting the immune system).
3. A final answer regarding the risk of cancer associated with the use of these medications will not be known for years. The FDA does not want to be caught in the dilemma of having told patients these medications are safe only to learn later that they are associated with an increased risk of cancer or other problems.

### **What does currently available data say about the safety of Elidel, Protopic, and other currently available treatments for atopic dermatitis?**

1. These medicines are not absorbed into the body when used on the skin. Blood levels of these drugs are either very low or undetectable. Oral forms of these medications (as used in the monkey study) cause much higher blood levels. These levels cannot be reached when these medicines are used on the skin.
2. Studies in mice reveal that Elidel and Protopic only increase the risk of cancer when they are used at 26 to 47 times the maximum recommended human concentration.
3. **Despite the use of these medications in 7 million people, there has been no evidence that there is an increased risk of developing cancer associated with their use.** The

rates of skin cancer and lymphoma are higher in the general population than they are in patients who have used these medications. For example the rate of skin cancer in patients who used Protopic was less than 1 person per 100,000. The rate of the same kind of cancer in the general population was 533 people per 100,000. Similar results are seen when we look at other types of cancer or if we look at Elidel.

4. Certain features are seen in cancers that occur due to the use of drugs that suppress the immune system. None of these features were seen in the cases of cancer that have been reported in patients who used Elidel or Protopic. An independent panel of experts (dermatology, oncology, pediatric oncology, and epidemiology) concluded there was no link between the use of Elidel or Protopic and the risk of developing cancer.
5. We can measure a person's ability to produce good immunity by their response to vaccines with simple tests. Children who received these medications responded to vaccines just as well as children who did not receive these medications.
6. Atopic dermatitis itself is occasionally (but very rarely) associated with cancer even in the absence of the use of these medications.
7. There is an increased risk of side-effects and cancer among chronic users of oral steroids (like prednisone) and other systemic therapies that are sometimes used for patients who have eczema that is difficult to manage. The long term risks (including the risk of cancer) associated with the use of topical steroids have not been established.

#### **What does HealthAirways recommend?**

- It is important that you discuss how to best treat your (or your child's) atopic dermatitis with your allergist or physician. The liberal use of moisturizers, evaluation for hidden food or environmental allergies, treatment of infections, or referral to an eczema specialist may be helpful in managing this chronic condition.
- Current FDA guidelines recommend that Elidel and Protopic should be used for the short-term or intermittent long-term treatment of atopic dermatitis in patients 2 years of age or older who may need an alternative to topical steroids. In some cases "off-label" use in children under the age of 2 may be necessary or indicated. Most medications (including topical corticosteroids) are not approved for use in this age group.

Although we disagree with the FDA's decision to place a "boxed" warning on these medicines, we do agree with their concern for patient safety. Ultimately the potential risk associated with the use of any drug must be balanced with the potential benefit. Please do not hesitate to contact us should you have any further questions regarding you or your child's atopic dermatitis.