

## **Health Canada approves Protopic<sup>®</sup> (tacrolimus ointment) for the prevention of eczema flares.**

**MARKHAM, ON, February 17, 2011** –Astellas Pharma Canada, Inc. has announced that it has received approval from Health Canada for a new indication for its topical eczema therapy, Protopic<sup>®</sup> (tacrolimus ointment 0.03% and 0.1%). The new indication means that tacrolimus ointment can be prescribed for maintenance therapy to prevent flares and prolong flare free intervals in patients with moderate to severe atopic dermatitis (commonly called eczema). These are individuals who experience a high frequency of flares ( $\geq 5$  times per year). Tacrolimus ointment, a steroid-free topical agent, is a topical calcineurin inhibitor (TCI) also indicated for the intermittent-treatment of moderate to severe atopic dermatitis in non-immunocompromised patients.

“We’re excited to be able to offer eczema sufferers an effective option to help prevent the chronic recurrence of eczema flares,” said Michael Tremblay, President of Astellas Pharma Canada, Inc. “Patients can now enjoy being symptom-free for longer periods, ultimately improving their overall quality of life, which is always our primary objective at Astellas.”

“This new indication is an important adjunct to our treatment armamentarium because atopic dermatitis is in so many cases a lifelong episodic skin disorder, and an important goal of treatment is to prevent or delay recurrent skin exacerbations,” said Dr. Harvey Lui, MD, FRCPC, Professor and Head, Department of Dermatology and Skin Science, Vancouver General Hospital, University of British Columbia. “While patients are typically accustomed to using this topical therapy when they are experiencing an eczema flare, our challenge will be to educate them and their health care providers on the new use of tacrolimus ointment on their clear skin for preventing the flare from coming back.”

### **Clinical Trial Results**

The efficacy and safety of tacrolimus ointment in maintenance of moderate to severe atopic dermatitis was assessed in 306 patients in two Phase 3, multi-centre clinical trials of similar design, one in adult patients ( $\geq 16$  years) and one in pediatric patients (2-15 years). Patients were randomized to apply either tacrolimus ointment (0.1% adults; 0.03% children) or vehicle once a day, twice weekly, for example on Mondays and Thursdays.

Both studies showed significant benefit with twice weekly treatment with tacrolimus ointment with regard to primary endpoint over a period of 12 months. The median number of disease exacerbations requiring a substantial intervention (adjusted for length of time at risk) was 1.0 in the tacrolimus arm versus 5.3 in the vehicle arm ( $p$  0.001) in the adult study and 1.0 in the tacrolimus arm versus 2.9 in the vehicle arm ( $p$  0.001) in the pediatric study.

“Treating the chronic and recurring nature of atopic dermatitis has been a source of frustration for most clinicians and patients,” said Dr. Lui. “This new approach now represents a paradigm shift in how patients treat their eczema. Instead of reacting to their disease and treating their flares only when they occur, now patients can take control of their disease by applying tacrolimus twice weekly on cleared skin to significantly reduce the number of flares and the time between flares.”

## **About Atopic Dermatitis (Eczema)**

Eczema is a relapsing, life-altering disease affecting between four to six million Canadians nationwide, and is characterized by painfully red, swollen, itchy, flaky skin. In some cases the itching and redness is so serious and intense that sufferers can scratch themselves until they bleed, increasing the risk of secondary infection. The majority of eczema cases are diagnosed in early childhood. While 85-90 percent of children suffering from eczema outgrow the disease, others live with it throughout their entire lives. For sufferers, especially children and teenagers, the visibility of eczema flares can lead to low self-esteem and often the inability to interact with others.

Eczema develops as a result of a complex relationship of many known and yet to be determined causes, including heredity, environmental allergens, and skin irritants such as wools and fragrances. The disease is often associated with immune system response to environmental irritants and with respiratory allergies and asthma. When an immunologic response to an allergen or irritant is triggered, white blood cells are activated and release substances that cause inflammation. The inflammation causes redness to appear, as well as releasing other substances that can cause itching. It can be very difficult to resist scratching during an eczema flare. Scratching can damage the skin, causing more inflammatory substances to be produced that, in turn, cause more white blood cells to respond to this reaction. This increases the redness and itching, which makes it harder to resist scratching. This is known as the itch-scratch-rash cycle. Emotional factors such as stress can also influence and worsen the condition.

## **About Tacrolimus Ointment**

Tacrolimus ointment, both 0.03% and 0.1% for adults and only 0.03% for children aged 2 to 15 years, was introduced in Canada by Astellas in 2001 as one of a new class of drugs called topical calcineurin inhibitors or TCIs indicated as a second-line therapy for short and long-term intermittent-treatment of moderate to severe atopic dermatitis in non-immunocompromised patients. This topical prescription therapy should be applied twice a day to treat the skin at the site of the immune imbalance to help stop the redness and itching of eczema inflammation. As maintenance therapy, tacrolimus ointment 0.03% and 0.1% should be applied once a day twice a week (e.g. Monday and Thursday) to all affected areas of the skin, including the face, neck and eyelids for preventing flares from coming back if the patient has a high frequency of flares ( $\geq 5$  times per year).

## **Safety Information**

Tacrolimus ointment is contraindicated in patients with a history of hypersensitivity to tacrolimus or to any other component of the preparation. Long-term safety of topical calcineurin inhibitors has not been established. Although a causal relationship has not been established, rare cases of skin malignancy and lymphoma have been reported in patients treated with topical calcineurin inhibitors, including tacrolimus ointment (0.1% and 0.03%). Therefore, continuous long-term use of a topical calcineurin inhibitors including tacrolimus ointment (0.1% and 0.03%) should be avoided, and application limited to areas of involvement with atopic dermatitis. Tacrolimus ointment is not indicated for children less than 2 years of age. Only 0.03% tacrolimus ointment is indicated for use in children 2-15 years of age.

The most common side effects that may be experienced by patients who use tacrolimus ointment include skin burning (burning sensation, stinging, soreness) or pruritus (an itch or sensation that

causes the desire to scratch); however these are localized and tend to be brief, typically lasting a few days following the initial application of tacrolimus ointment and decreasing as the skin heals. Other less common events associated with tacrolimus ointment included acne, allergic reaction, flu-like symptoms, fever, abdominal pain, increased cough, rhinitis, diarrhea and headache.

Researchers agree that because the effect of ultraviolet light on skin treated with tacrolimus ointment is unknown, patients should use safe sun practices to avoid exposure to natural or artificial sunlight.

**About Astellas Pharma Canada, Inc.**

Astellas Pharma Canada, Inc., a Canadian affiliate of Tokyo-based Astellas Pharma Inc., is a pharmaceutical company dedicated to improving the health of people around the world through innovative and reliable pharmaceutical products. Astellas was formed in 2005 through the merger of two companies – Fujisawa and Yamanouchi. Astellas Pharma Canada has an intense focus on five key therapeutic areas – Infectious Disease, Immunology, Cardiology, Urology and Dermatology – and is considered a leader in these fields. Additional corporate information is available at [www.astellas.com/ca](http://www.astellas.com/ca).

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