

# PHARMACIST v ASTELLAS PHARMA

## Promotion of Protopic

A pharmacist complained about a Protopic (tacrolimus) leavepiece issued by Astellas Pharma. The front cover featured the claim '142 days without a major eczema flare? That's a whole British summer' above a photograph of a woman standing in a field, wearing sandals, knee-length shorts and a vest top. The weather appeared to be blustery and cold.

The complainant submitted that the Protopic summary of product characteristics (SPC) stated that skin exposure to sunlight should be avoided when using the medicine. In that regard the complainant alleged that the leavepiece promoted Protopic in a manner inconsistent with its SPC and misleadingly implied that it could be used in the summer on skin exposed to sunlight. The complainant further alleged that the promotion failed to maintain high standards.

The detailed response from Astellas is given below.

The Panel noted the photograph on the front cover of the leavepiece and although the weather conditions were largely overcast, images of the same woman's face on pages 2 and 5 appeared to reflect sunlight.

Page 4 of the leavepiece referred to patients with frequently-flaring eczema in visible and delicate areas and page 2 referred to the use of Protopic when there were concerns about stepping up to a more potent corticosteroid. Two photographs in the leavepiece featured only the patient's head and shoulders. In the Panel's view there was thus an implication that at least some of the patient population at issue were those with eczema on the face and neck. An explanation of how to use Protopic specifically referred to the amount of ointment to be applied to the face and neck.

Section 4.4 of the Protopic SPC, Special warnings and precautions for use, stated that exposure of the skin to sunlight should be minimised. Physicians should advise patients on appropriate sun protection methods, such as minimisation of the time in the sun, use of a sunscreen product and covering of the skin with appropriate clothing. The Panel noted that in its response, Astellas had not referred to 'covering of the skin with appropriate clothing'.

The Panel noted Astellas' submission that the patient depicted was demonstrating her well-controlled eczema. The Panel accepted that patients who had achieved 142 days without a major eczema flare might want to demonstrate

such control of the condition but considered that any such depiction in promotional material had to comply with the Code.

The Panel noted that Astellas referred to avoiding extreme summer conditions and overt sunshine and considered that such references did not fairly reflect the special warning in the SPC about minimising exposure of the skin to sunlight. The Panel noted that skin might be exposed to sunlight even in overcast conditions.

The Panel considered that the front cover of the leavepiece implied that the patient did not have to be concerned about exposure to sun and that was not so: this was inconsistent with the particulars listed in the SPC and a breach of the Code was ruled.

Upon appeal by Astellas, the Appeal Board noted that the leavepiece was directed at GPs and pharmacists. Protopic had not been actively promoted to either group in the last five years. The leavepiece was approved for use in May 2011 and would thus be used through the summer. The SPC stated that Protopic treatment should be initiated by physicians with experience in the diagnosis and treatment of atopic dermatitis.

The Appeal Board noted that the advice in the SPC about minimisation of skin exposure to sunlight and the use of sun protection methods was based on a theoretical potential risk of malignant skin changes (skin malignancies had been reported in association with oral tacrolimus treatment).

The Appeal Board noted Astellas's comment that it was not possible to cover the face with appropriate clothing but considered that physicians could advise relevant patients to wear a sun hat. The Astellas representatives agreed that if the leavepiece had depicted overt sunshine then a sun hat would have been appropriate; they stated that the patient depicted might have already applied sunscreen. The Appeal Board noted the three photographs of the patient (on the front cover and pages 2 and 5) were not the same and considered that the photograph on page 5 of the leavepiece reinforced the impression that the patient was wearing minimal clothing on a sunny day.

The Appeal Board was concerned to note that research had shown that prescribers would not ordinarily advise Protopic patients about sun protection. The Appeal Board considered that

such advice was an important aspect to the appropriate use of Protopic. The leavepiece was directed to an audience which might not be wholly familiar with the product and was about patients being able to expose skin in the summer. The Appeal Board considered that companies had a responsibility to ensure that their medicines were correctly used and in that regard it considered that in the circumstances there should be some acknowledgement of the SPC warning. The prescribing information was inadequate in this regard. In the Appeal Board's view the images in the leavepiece were inconsistent with the particulars listed in the Protopic SPC. The Appeal Board thus upheld the Panel's ruling of a breach of the Code. The appeal on this point was unsuccessful.

The Panel noted that the complainant had also alleged that the leavepiece misleadingly implied that Protopic could be used in the summer on areas of skin exposed to sunlight. The Panel noted that Section 4.2 of the SPC stated that Protopic ointment might be used on any part of the body, including the face, neck and flexure areas, except on mucous membranes. There was no prohibition on using Protopic on areas of skin exposed to sunlight such as the face although of course the special warning in Section 4.4 should be borne in mind. The Panel did not consider the leavepiece was misleading on the narrow point alleged; no breach of the Code was ruled which was upheld upon appeal.

The Panel considered that its ruling of a breach of the Code above adequately covered its concerns about this matter; the circumstances did not warrant a further ruling with regard to high standards. No breach was ruled which was upheld upon appeal.

A pharmacist complained about a leavepiece (ref: PRO11003UK) for Protopic (tacrolimus) issued by Astellas Pharma Ltd. The front cover of the leavepiece featured the claim '142 days without a major eczema flare? That's a whole British summer' above a photograph of a woman standing in a field and wearing strappy sandals, knee-length denim shorts and a vest top. The weather appeared to be blustery and cold.

## COMPLAINT

The complainant noted that the woman had exposed skin on her lower legs, arms and around her neckline as well as her face.

The complainant considered that the wording and picture inferred that Protopic did not carry a specific warning that skin exposure to sunlight should be avoided when using the medicine however, this was a specifically worded precaution in the summary of product characteristics (SPC).

The complainant alleged that the leavepiece promoted Protopic in a manner inconsistent with its

SPC in breach of Clause 3.2. The complainant further alleged a breach of Clause 7.2 because the leavepiece misleadingly implied that Protopic could be used in the summer on areas of skin exposed to sunlight. Finally, the complainant alleged that the promotion failed to maintain high standards in breach of Clause 9.1.

## RESPONSE

Astellas stated that patient safety was its highest priority and the company took its obligations to the letter and spirit of the Code extremely seriously. The company explained that the focus of the campaign was the prevention of eczema flares (two single applications of Protopic per week to areas usually affected). The leavepiece, to be given to health professionals by sales representatives, supported this message. Care was taken when composing the scene on the front of the leavepiece to incorporate noticeably dark clouds and dull tones to generate overcast conditions, avoiding overt sunshine. This was balanced by the presence of several people in the background who were dressed in line with those readily recognisable poor weather conditions (supporting the use of the ironic statement: 'That's a whole British summer'). The patient featured in the photograph was taking the opportunity to demonstrate her well-controlled eczema at a time of year when her attire would ordinarily be deemed more appropriate to summer conditions. Astellas noted that the patient was not wearing minimal clothing eg swimwear or necessarily demonstrating excessive sun exposure eg through sunbathing.

Astellas noted the complainant's submission that the Protopic SPC stated that skin exposure to sunlight should be avoided. This was incorrect. The SPC actually stated 'Exposure of the skin to sunlight should be minimised'; it did not state that exposure of the skin to sunlight should be avoided.

If the depicted weather included extreme summer conditions, Astellas considered that the patient featured would still not necessarily be demonstrating irresponsibly excessive sun exposure through either her attire or associated activities.

Astellas considered that it was unreasonable to expect eczema sufferers (treated with Protopic) to be dressed in clothing covering the entire body when outdoors, regardless of the season/climate.

Astellas noted that Section 4.2 of the SPC stated 'Protopic ointment may be used on any part of the body, including face, neck and flexure areas, except on mucous membranes'.

The use of topical calcineurin inhibitors such as Protopic on the face was specifically referred to in a National Institute for Health and Clinical Excellence (NICE) guideline. TA82 'Tacrolimus and pimecrolimus for atopic eczema' stated: 'Tacrolimus is applied as a thin layer to affected areas of the skin twice daily and may be used on any part of the body, including the face, neck and flexural areas'.

The Protopic SPC further stated 'Physicians should advise patients on appropriate sun protection methods, such as the minimisation of time in the sun, use of a sunscreen product...' and Astellas submitted that it always advocated this course of action.

The focus of the campaign was the prevention of eczema flares in particular, on visible, delicate areas such as the face where the use of sunscreen application and minimisation of time in the sun were the only practical options for minimisation of skin exposure to sunlight.

Astellas refuted the allegation that the campaign implied that Protopic could be used during the summer on areas of sun exposed skin. There was no contraindication to the use of Protopic, either during the summer or on areas of sun exposed-skin. As noted above, the Protopic SPC stated 'Exposure of the skin to sunlight should be minimised'. It did not state that exposure of the skin to sunlight should be avoided. Similarly, there was no contraindication to the use of the product either in the summer or on sun exposed areas of skin.

In summary, Astellas denied a breach of Clauses 3.2, 7.2 or 9.1.

#### **PANEL RULING**

The Panel noted that the front cover of the leavepiece depicted a woman dressed in a vest top, long shorts and flat strappy sandals, holding a pair of binoculars whilst standing in front of a large, open field that appeared to be a campsite. Figures in the background also wore long shorts but were each wearing long sleeved jackets. The woman was thus wearing less clothing and consequently exposing more skin than those around her. The sky was overcast with rain clouds threatening to the right of the picture but with much lighter clouds on the horizon to the left, to which the figure was facing. The accompanying text '142 days without a major eczema flare? That's a whole British summer' made clear that the photograph depicted the variable weather conditions of a British summer. An image of the same woman's face on pages 2 and 5 of the leavepiece appeared to reflect sunlight although the background was still slightly overcast.

Page 4 of the leavepiece referred to patients with frequently-flaring eczema in visible and delicate areas and page 2 referred to the use of Protopic when there were concerns about stepping up to a more potent corticosteroid. Two photographs in the leavepiece featured only the head and shoulders of the depicted patient. In the Panel's view there was thus an implication that at least some of the patient population at issue were those with eczema on the face and neck. A diagram on page 3 explaining how to use Protopic specifically referred to the amount of ointment to be applied to the face and neck.

Section 4.4 of the Protopic SPC, Special warnings and precautions for use, stated that exposure of the

skin to sunlight should be minimised. Physicians should advise patients on appropriate sun protection methods, such as minimisation of the time in the sun, use of a sunscreen product and covering of the skin with appropriate clothing. The Panel noted that in its response, Astellas had not referred to 'covering of the skin with appropriate clothing'.

The Panel noted Astellas' submission that the patient depicted in the leavepiece was taking the opportunity to demonstrate her well-controlled eczema. The Panel accepted that patients who had achieved 142 days without a major eczema flare might want to demonstrate such control of the condition but considered that any such depiction in promotional material had to comply with the Code.

The Panel noted that Astellas referred to avoiding extreme summer conditions and overt sunshine and considered that such references were not a fair reflection of the special warning about minimising exposure of the skin to sunlight in Section 4.4 of the SPC. The Panel noted that skin might be exposed to sunlight even in overcast conditions.

The Panel considered that the front cover of the leavepiece implied that the patient did not have to be concerned about exposure to sun and that was not so: this was inconsistent with the particulars listed in the Protopic SPC and a breach of Clause 3.2 was ruled.

The Panel noted that in addition the complainant had also alleged that the leavepiece misleadingly implied that Protopic could be used in the summer on areas of skin exposed to sunlight. The Panel noted that Section 4.2 of the SPC stated that Protopic ointment might be used on any part of the body, including the face, neck and flexure areas, except on mucous membranes. There was no prohibition on using Protopic on areas of skin exposed to sunlight such as the face although of course the special warning in Section 4.4 should be borne in mind. The Panel did not consider the leavepiece was misleading on the narrow point alleged; no breach of Clause 7.2 was ruled.

The Panel noted its rulings above and considered that its ruling of a breach of Clause 3.2 adequately covered its concerns about this matter and the circumstances did not warrant a further ruling in relation to Clause 9.1; no breach of Clause 9.1 was ruled.

#### **APPEAL BY THE COMPLAINANT**

The complainant noted that although a breach of Clause 3.2 had been ruled Astellas had defended the leavepiece noting careful composition of the background to the front page image to include 'overcast conditions, avoiding overt sunshine'. This, however, was not the case in the image on the reverse of the leavepiece on the section titled 'References' where the face of the woman was apparently in direct sunlight. The overcast

conditions were therefore inconsistent throughout the piece.

The complainant understood the ironic use of 'British summer' however, just as there were periods of inclement weather there were often long, warm, sunny spells. Clinicians were not warned anywhere in the leavepiece, other than in the prescribing information, that exposure of the skin to sunlight should be minimised. In the complainant's view, it was imprudent to link the promotion of a product that contained such a warning to 'summer'.

The complainant noted that the Panel ruled that the leavepiece was not misleading by implication as the SPC included no prohibition to use on areas of skin exposed to sunlight. The complainant noted that the SPC contained a specific special warning advising that exposure of the skin to sunlight should be minimised and that physicians should advise patients on sun protection methods such as minimisation of time in the sun, sunscreen and appropriate clothing.

Although the leavepiece did not depict an individual with a less than appropriate level of clothing there was no mention or indication of sunscreen or sunlight exposure limitation by time. For example, the woman depicted could have been portrayed walking from outdoors to indoors or applying sunscreen. The complainant also noted that in the entry for tacrolimus, the BNF stated in the cautions section 'UV light (avoid excessive exposure to sunlight and sunlamps)'.

The complainant therefore alleged that the spirit of the photographs in the leavepiece was inconsistent with the safety message that skin exposure to sunlight (and other sources of UV light) should be minimised and that physicians needed to advise patients using these products to employ protective measures such as reduce skin exposure time, cover up with clothing and apply sunscreen.

The complainant noted that the Panel ruled that a breach of Clause 3.2 adequately covered this complaint and as such it did not rule a breach of Clause 9.1.

The complainant was not entirely familiar with PMCPA procedures but he wondered why this clause was not examined further with acceptance that a breach of Clause 3.2 was adequate. It would be more appropriate to rule that high standards had been maintained or otherwise independently of a review of other clauses. However, as the complainant had already stated he was not fully aware of the PMCPA's inner workings so this might be common practice, in which case the complainant noted that Astellas asserted that it made patient safety its highest priority and also stated that it would always advocate that physicians advised patients on appropriate sun protection methods. While the complainant could not dispute either of these assertions in general terms, in specific regard to this leavepiece there was no explicit mention

anywhere in the leavepiece, other than in the prescribing information, that this medicine had any cautions on use relating to UV light, which seemed at odds with the use of a promotional theme based on the British summer (albeit ironically). As noted above it seemed the Panel noted too, there was an overt picture of a woman's face bathed in sunlight within this leavepiece.

In summary, the complainant stated that since Astellas had appealed the ruling of a breach of Clause 3.2, there was perhaps room to review all three clauses originally alleged to be in breach.

### COMMENTS FROM ASTELLAS

With respect to the ruling of a breach of Clause 3.2, Astellas submitted that it had responded fully to the complainant's allegations and the findings of the Panel in its original response and subsequent appeal.

In relation to the appeal of no breach of Clause 7.2 (promotion which misleadingly implied that Protopic could be used during summer months on areas of sun exposed skin) and Clause 9.1 (failure to maintain high standards), Astellas submitted that it had responded to these allegations in detail previously. Astellas again noted that the SPC did not state that exposure of the skin to sunlight should be avoided. Similarly, there was no contraindication to the use of Protopic, either in the summer or on sun-exposed areas. Astellas submitted that the imagery used in this case was fully consistent with the SPC, specifically in relation to Section 4.4, 'Special warnings and precautions for use'.

### FINAL COMMENTS FROM THE COMPLAINANT

The complainant had no further comments.

### APPEAL BY ASTELLAS

Astellas considered that the imagery used in the leavepiece was consistent with the SPC, specifically in relation to Section 4.4, 'Special Warnings and Precautions for Use'.

In relation to the specific 'Special Warning or Precaution for Use' the Protopic SPC stated the following: 'Physicians should advise patients on appropriate sun protection methods, **such as** minimisation of time in the sun, use of a sunscreen product and covering of the skin with appropriate clothing' (emphasis added). It did not state that exposure of the skin to sunlight should be avoided, rather that these methods should be recommended as examples of measures to minimise exposure to sunlight. Obviously, it was not possible to apply all of these measures, in particular appropriate clothing, in cases where the treated area was the face.

As noted by the Panel, the focus of the campaign at issue was the treatment of sensitive areas such as

the face and neck where potent steroids might not be tolerated due to potential side effects. In this respect, the only practical sun protection methods which could be applied to the face were, as stated in the Protopic SPC, the use of sunscreen or minimisation of time in the sun. These measures were not necessarily practical steps which could be depicted in the imagery. Similarly, other additional specific 'Special warnings and precautions for use' were not necessarily possible to address in the imagery.

Astellas submitted that the imagery was not inconsistent with the SPC in this respect.

Astellas noted the Panel's observation that the image of the woman's face on pages 2 and 5 of the leavepiece appeared to reflect sunlight. It was important to clarify that this image was the same image as used on the front cover of the leavepiece on the background of the dull, overcast conditions and dark clouds.

Specifically, the composition of the scene on the front cover included the following intentional elements:

- dark clouds and dull tones to generate overcast conditions
- no depiction of the sun
- the inclusion of several reference figures dressed appropriately for the poor weather conditions. The Panel noted that 'the woman was thus wearing less clothing and consequently exposing more skin than those around her'. The bystanders in the scene were covered up because of the poor weather, not to minimise exposure to sunlight. They would not require this degree of weatherproof clothing if the conditions matched the attire of the woman in focus. Indeed, this was the ironic basis for the headline on the front cover 'That's a whole British summer'
- the Panel noted that 'skin might be exposed to sunlight even in overcast conditions'. Following implementation of the appropriate outlined sun protection measures, eczema patients treated with Protopic were at liberty to go outdoors though not necessarily in full length items of clothing irrespective of the climate/conditions. Once again, the SPC did not state that sunlight should be avoided.

Astellas was conscious of the impact of any chronic condition on patients who were prescribed its products. In devising this campaign, Astellas undertook market research to understand the impact of eczema upon patients' lives. As a result of the many associated negative psychological consequences, in depicting the typical patient and their surroundings, Astellas was keen to emphasise the importance of patient confidence and to avoid the exclusion of this patient group from the usual activities of daily life including the freedom to wear clothing which would (ordinarily) be appropriate to the conditions, and not exceptional to the clothing of those around them.

Astellas submitted that it was not a requirement of the Code to list all precautions and special warnings in an SPC on advertisements other than in the prescribing information. Astellas took patient safety extremely seriously and care had been taken with the imagery to ensure it was consistent with the SPC. Astellas considered that it was not the case that 'the leavepiece implied that the patient did not have to be concerned about exposure to the sun'. As described in detail above, the scene was neither sunny, nor was the patient dressed in minimal clothing or necessarily failing to adhere to the sun protection advice deemed appropriate for her treatment and as recommended in the SPC to be advised by the physician.

In summary therefore, the essence of this case was a difference of opinion between Astellas and the Panel. Astellas submitted that the imagery did not promote the use of Protopic ointment in a manner inconsistent with the SPC. Astellas had taken reasonable care to depict a dull and overcast day and it hoped the Appeal Board agreed with its view and rule no breach of Clause 3.2.

#### **COMMENTS FROM THE COMPLAINANT**

The complainant referred to their letter of appeal and had nothing further to add.

#### **APPEAL BOARD RULING**

The Appeal Board noted from the Astellas representatives that the leavepiece was directed at general practitioners and pharmacists. Protopic had not been actively promoted to either group in the last five years. The leavepiece was approved for use in May 2011 and would thus be used through the summer months. The SPC stated that Protopic treatment should be initiated by physicians with experience in the diagnosis and treatment of atopic dermatitis.

The Appeal Board noted the statement in the SPC that 'Exposure of the skin to sunlight should be minimised ... Physicians should advise patients on appropriate sun protection methods, such as minimisation of the time in the sun, use of a sunscreen product and covering of the skin with appropriate clothing'. The Appeal Board noted from the Astellas representatives that the SPC advice was based on a theoretical potential risk of malignant skin changes (skin malignancies had been reported in association with oral tacrolimus treatment).

The Appeal Board noted Astellas' comment that it was not possible to cover the face with appropriate clothing but considered that physicians could advise relevant patients to wear a sun hat. The Astellas representatives agreed that if the leavepiece had depicted overt sunshine then a sun hat would have been appropriate. The Astellas representatives stated that the patient depicted might have already applied sunscreen. The Appeal Board noted the three photographs of the patient (on the front cover and pages 2 and 5) were not the same and considered

that the photograph on page 5 of the leavepiece reinforced the impression that the patient was wearing minimal clothing on a sunny day.

The Appeal Board was concerned to note from the company representatives that according to its research, prescribers would not ordinarily advise Protopic patients about sun protection methods. The Appeal Board considered that sun protection advice was an important aspect to the appropriate use of Protopic. The leavepiece at issue was directed to an audience which might not be wholly familiar with the product and was all about patients being able to expose skin in the summer months. The Appeal Board considered that companies had a responsibility to ensure that their medicines were correctly used and in that regard it considered that in the circumstances there should be some acknowledgement of the SPC warning. The prescribing information was inadequate in this regard. In the Appeal Board's view the images in the leavepiece were inconsistent with the particulars listed in the Protopic SPC. The Appeal Board thus upheld the Panel's ruling of a breach of Clause 3.2 of the Code.

The Appeal Board noted that the complainant had alleged that the leavepiece misleadingly implied that Protopic could be used in the summer on areas of skin exposed to sunlight. The Appeal Board noted that exposure to sunlight was not prohibited although patients should be advised about minimisation of exposure to the sun. The Appeal Board did not consider the leavepiece was misleading on this narrow point as alleged. The Appeal Board upheld the Panel's ruling of no breach of Clause 7.2. The appeal on this point was unsuccessful.

The Appeal Board noted its rulings above and considered that it did not warrant a further ruling in relation to Clause 9.1. The Appeal Board upheld the Panel's ruling of no breach of Clause 9.1. The appeal on this point was unsuccessful.

**Complaint received**                      **24 June 2011**

**Case completed**                              **10 October 2011**

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