

ALMIRALL v LEO

Picato advertisement

Almirall complained about a journal advertisement for Picato (ingenol mebutate) gel issued by Leo Pharma. The advertisement employed the image of a high speed train which Almirall submitted reinforced the claims 'Announcing the arrival of... The revolutionary, shortest duration, patient-applied actinic keratosis treatment'. Almirall alleged that the advertisement was misleading and that the claims and the visual imagery were exaggerated and all embracing.

Almirall noted that Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults ie actinic keratosis grade 1. The advertisement implied that Picato was licensed for any type of actinic keratosis and failed to clarify its more restricted indication.

Almirall alleged that the description of Picato as being 'shortest duration, patient-applied treatment' was misleading because it appeared to suggest that the clinically relevant, therapeutic *effect* of treatment (ie complete healing of actinic keratoses), was the most rapid available, which was not so. Whilst the application was over 2 or 3 days, the summary of product characteristics (SPC) stated that optimal therapeutic effect should be assessed after 8 weeks when, if the treatment area showed an incomplete response, the treatment should be carefully re-evaluated and management reconsidered.

The SPC stated that Picato had to be stored between 2 and 8°C; however this was not reflected in the prescribing information. Almirall alleged that this was misleading.

Almirall alleged that high standards had not been maintained.

The detailed response from Leo is given below.

The Panel noted that the advertisement was headed 'Picato Announcing the arrival of...The revolutionary, shortest duration, patient-applied actinic keratosis treatment'. Below the claim were two spiral bound pads one showing '2 DAYS' and the other showing '3 DAYS'. To the left of the pads was the depiction of a high speed train which appeared to be on the move.

The Panel noted that Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults. The headline claim, however, only referred to actinic keratosis without noting the licence restriction. It appeared that Picato could treat any type of actinic keratosis which was not so. The Panel did not consider that the advertisement encouraged rational use and a breach was ruled.

The Panel noted that patients had to apply Picato gel to the affected area once daily for two or three consecutive days depending on the site affected. The Panel noted Leo's submission that this was 'revolutionary' in that other treatment options had to be applied for 21-90 days. The Panel accepted that for patients, only having to apply treatment once daily for two or three consecutive days as opposed to 21-90 days would be seen as a radical change. The Panel considered, however, that from the claim, 'The revolutionary, shortest duration, patient-applied actinic keratosis treatment', it was not entirely clear that 'revolutionary' referred only to 'shortest duration' and not also to the 'patient-applied actinic keratosis treatment'. The claim together with the image of the high speed train might be taken to relate to the speed of effect of Picato. In that regard the Panel noted that the optimum effect of treatment could only be assessed approximately 8 weeks (56 days) after treatment. The Panel considered that the claim was exaggerated as alleged. A breach of the Code was ruled.

The Panel considered that although Picato had to be stored in a refrigerator (2°C-8°C) omission of this information from the prescribing information did not mean that there had been a failure to provide the information required and no breach of the Code was ruled.

The Panel noted its rulings above and in particular its ruling that the advertisement did not encourage the rational use of the medicine. The Panel considered that high standards had not been maintained. A breach of the Code was ruled.

Almirall Ltd complained about an advertisement (ref 4340a/00016(1)) for Picato (ingenol mebutate) gel issued by Leo Pharma and published in the BMJ 26 January 2013. Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults.

COMPLAINT

Almirall noted that the advertisement employed the image of a high speed train to reinforce the claims 'Announcing the arrival of... The revolutionary, shortest duration, patient-applied actinic keratosis treatment'. Almirall alleged that the advertisement was misleading and that the claims and the visual imagery were exaggerated, all embracing and clearly in breach of Clauses 7.10 and 9.1. Almirall also alleged a breach of Clause 4.2.

Almirall noted the requirements of Clause 7.10 and its supplementary information which warned against the use of superlatives, all embracing terms (such as 'the', 'revolutionary' etc) unless they could be clearly substantiated.

Almirall noted that Section 4.1 of the Picato summary of product characteristics (SPC) clearly stated that Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults ie actinic keratosis grade 1. The Picato advertisement implied that Picato was licensed for any type of actinic keratosis and failed to give adequate information, consistent with the SPC, to clarify its more restricted indication.

Picato was described as being 'shortest duration, patient-applied treatment'. Even though the technical dictionary definition of 'treatment' might relate to its time of physical application, Almirall alleged that the claim was misleading because it appeared to suggest that the clinically relevant, therapeutic effect of treatment (ie complete healing of actinic keratoses), was the most rapid available, which was not so. Almirall submitted that inadequate care had been taken to avoid misleading the prescriber on this point; whilst the application was indeed over 2 or 3 days, Section 4.2 of the SPC stated that optimal therapeutic effect should be assessed 8 weeks after treatment, adding that if the treatment area showed an incomplete response at the follow-up examination, the treatment should be carefully re-evaluated and management reconsidered.

Almirall noted that Clause 4.2 required prescribing information to contain a succinct statement of the information in the SPC which related to the dosage and method of use relevant to the indications quoted in the advertisement. The SPC stated that Picato had to be stored between 2 and 8 degrees Celsius; however this was not reflected in the prescribing information. Almirall alleged that this was misleading and had the potential to lead to improper storage and usage of Picato which could compromise both its claimed efficacy and safety.

In view of the shortcomings described above, Almirall alleged that there had been a serious failure to maintain high standards in the creation and review of this advertisement against Code requirements, with scant regard shown to the special nature of the audience to which the advertisement was targeted.

RESPONSE

Leo stated that Picato was indicated for all actinic keratosis, with the exception of hyperkeratotic and hypertrophic actinic keratosis, in adults and this was clearly stated in the prescribing information on the advertisement; thus it did not consider that this part of the advertisement was misleading. In addition, the prescribing information was clearly displayed as part of the advertisement. Leo therefore disputed the allegation that the advertisement implied that Picato was licensed for any type of actinic keratosis and failed to give adequate information, consistent with the SPC, to clarify its more restricted indication.

With regard to the claim 'shortest duration, patient-applied treatment', Leo submitted that the technical definition of treatment related to the time of its physical application, ie the number of days of administration (2 or 3 days). Therefore, Picato was the shortest duration, patient-applied treatment for actinic keratosis.

With regard to the word 'revolutionary' and the context in which it was used, Leo noted that the Oxford English Dictionary defined the word as 'involving or causing a complete or dramatic change'. Leo stood by this claim, as it believed this patient-applied topical treatment, with a duration of just 2 or 3 days (depending on the site of treatment), was considerably shorter than the current treatment duration of 21-90 days. Hence, the word 'revolutionary' was substantiated. Leo submitted that during pre-vetting, the Medicines and Healthcare Products Regulatory Agency (MHRA) had asked the company to make it clear that 'revolutionary' related to the short treatment duration. Leo submitted that this was clear from the advertisement.

Leo did not consider that there was a point to answer in relation to Clause 4.2 as the prescribing information did not usually contain information on the pharmaceutical precautions, but focused on the clinical information. Leo submitted that this was in line with PMCPA guidance. The Picato prescribing information included information about the dosage and method of use consistent with Section 4.2, Posology and Method of Administration, of the SPC, as per the Code requirements.

The SPC, referred to in the prescribing information, included information on storage and the instruction 'Store in a refrigerator' was clearly indicated on the front of the product carton.

In view of the above, Leo did not consider that it had breached the Code and it had therefore maintained high standards.

PANEL RULING

The Panel noted that the advertisement was headed 'Picato Announcing the arrival of...The revolutionary, shortest duration, patient-applied actinic keratosis treatment'. Below the claim were two spiral bound pads one showing '2 DAYS' and the other showing '3 DAYS'. To the left of the pads was the depiction of a high speed train which appeared to be on the move.

The Panel noted that Picato was indicated for the cutaneous treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults. The headline claim, however, only referred to actinic keratosis without noting the licence restriction. It appeared that Picato could treat any type of actinic keratosis which was not so. In that regard the Panel did not consider that the advertisement encouraged the rational use of the medicine. The provision of the indication in full in the prescribing information did not negate the otherwise misleading impression. A breach of Clause 7.10 was ruled.

The Panel noted that for the treatment of actinic keratosis on the trunk or extremities, patients had to apply one tube (0.47g) of Picato 500mcg/g to the affected area once daily for two consecutive days. If the patient had actinic keratosis on the face and scalp then one tube (0.47g) of Picato 150mcg/g had to be applied to the affected area once daily for three consecutive days. The Panel noted Leo's submission that Picato treatment was 'revolutionary' in that other treatment options had to be applied for 21-90

days. The Panel noted that the dictionary defined something as being 'revolutionary' if it involved or constituted radical change. The Panel accepted that for patients, only having to apply treatment once daily for two or three consecutive days as opposed to 21-90 days would be seen as a radical change. The Panel considered, however, that from the claim, 'The revolutionary, shortest duration, patient-applied actinic keratosis treatment', it was not entirely clear that 'revolutionary' referred only to 'shortest duration' and not also to the 'patient-applied actinic keratosis treatment'. The claim together with the image of the high speed train might be taken to relate to the speed of effect of Picato. In that regard the Panel noted that the optimum effect of treatment could only be assessed approximately 8 weeks (56 days) after treatment. The Panel considered that the claim was exaggerated as alleged. A breach of Clause 7.10 was ruled.

The Panel noted that tubes of Picato had to be stored in a refrigerator (2°C-8°C). This was not stated in the

prescribing information included in the advertisement. The Panel noted that Clause 4.2 listed the components of prescribing information; storage conditions of the medicine were not included. The Panel thus did not consider that in omitting the storage requirements for Picato from the prescribing information there had been a failure to provide the information listed in Clause 4.2. Clause 4.1 required the prescribing information listed in Clause 4.2 to be provided and so the Panel ruled no breach of Clause 4.1.

The Panel noted its rulings above and in particular its ruling that the advertisement did not encourage the rational use of the medicine. The Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled.

Complaint received **4 March 2013**

Case completed **4 April 2013**