CASE AUTH/3838/10/23 and CASE AUTH/3840/10/23

COMPLAINANTS v LEO

Allegations about tralokinumab data presented at a Leo symposium

CASE SUMMARY

This case was in relation to the presentation of tralokinumab data at a Leo symposium. The allegation was that there was no clear evidence to support the EASI-100 (Eczema Area and Severity Index) data for tralokinumab presented during this symposium.

The outcome under the 2021 Code was:

Breach of Clause 6.1	**Making a misleading claim**
Breach of Clause 6.2	**Making an unsubstantiated claim**

This summary is not intended to be read in isolation.
For full details, please see the full case report below.

FULL CASE REPORT

Two separate complaints, Case AUTH/3838/10/23 and Case AUTH/3840/10/23, were received from anonymous, non-contactable complainants about the presentation of tralokinumab data at a Leo symposium.

The Case Preparation Manager decided to amalgamate the two cases as they were based on essentially the same evidence, in accordance with Paragraph 5.1 of the 2021 Constitution and Procedure. As both complainants were non-contactable there could be no appeal of the decision to amalgamate the complaints.

Case AUTH/3838/10/23

COMPLAINT

The complaint wording is reproduced below:

> "I attended the Leo Symposia at the BDNG this year. I was surprised to see the information on Tralokinumab presented for EASI 100 results.
>
> To date this has never been seen before even with Dupilumab. The speaker seemed to gloss over very thinly and quickly over this information.
>
> I am an HCP with a lot of experience in treating patients and I have not yet come across these types of results."

When writing to Leo, the PMCPA asked it to consider the requirements of Clauses 6.1 and 6.2 of the 2021 Code.

Case AUTH/3840/10/23

COMPLAINT

The complaint wording is reproduced below:

> "I am currently an active Nurse working in the North of the country. I attended the BDNG 2023 at Harrogate where a Leo meeting/symposia took place. Data regarding EASI 100 was presented quickly with no clear evidence to support it. I have not EASI 100 data with dupilumab and concerned the claim that a reputable company was making."

When writing to Leo, the PMCPA asked it to consider the requirements of Clauses 6.1 and 6.2 of the 2021 Code.

LEO'S RESPONSE

Leo provided a joint response to Cases AUTH/3838/10/23 and AUTH/3840/10/23; this is reproduced below:

> "**Background**
>
> The British Dermatological Nursing Group (BDNG) annual conference took place at the Harrogate Conference Centre on 19 – 21st September 2023. LEO Pharma UK and Ireland held a promotional symposium as part of the main conference agenda. This took place on Thursday 21 September 2023, 11:40–12:25. The agenda and presentations for the symposium were certified before the symposium took place.
>
> **LEO Pharma UK and Ireland symposium**
>
> The symposium was aimed at nurses working in dermatology and focussed on the experience of patients with atopic dermatitis (AD) being treated with tralokinumab (Adtralza®) both in clinical trials and also in a real-world setting at one centre within the UK. Tralokinumab is LEO Pharma's monoclonal antibody which is licensed for the treatment of moderate-to-severe atopic dermatitis in adult and adolescent patients 12 years and older who are candidates for systemic therapy.[1] (1. Tralokinumab summary of product characteristics)
>
> The symposium title was "Adtralza®▼ (tralokinumab) long-term perspectives in atopic dermatitis: from trial data to real-world experience."
>
> The agenda was as follows:

11:40–11:50	Unmet needs in atopic dermatitis	[Speaker 1], nurse consultant, chair

11:50-12:05	Long-term efficacy and safety in adults: results from ECZTRA 3 and ECZTEND 2-year data	[Speaker 2], consultant dermatologist
12:05-12:20	Real-world experiences from [named] Hospital	[Speaker 3], lead nurse specialist
12:20-12:25	Questions and Answers	All

Speakers had individual verbal briefings of 30 – 45 minutes, additional individual slide rehearsals of 45-60 minutes and a final group preparation meeting of 40 minutes on the day of the symposium. These sessions included members of the LEO marketing team and the LEO medical team. In addition the speaker agreements cover requirements in the ABPI and IPHA codes of practice and standards expected by the speakers on pages 2, 3 and 4 of the agreement. We have provided the speaker agreements as requested copies provided.

EASI 100 data were presented as part of [Speaker 2's] presentation. [They] covered the pivotal trial data for tralokinumab, including a post hoc analysis of the ECZTRA 3 trial which assessed patients receiving tralokinumab and topical corticosteroid as needed[2] (2. Silverberg JI, *et al*. Am J Clin Dermatol 2022;23:547–559). The analysis included data on EASI scores.

Eczema Area and Severity Index (EASI) is a validated scale and can be used in the assessment of severity and extent of AD. The total EASI score ranges from 0 to 72 points, with the highest score indicating worse severity of AD and a score of 0 indicating clear skin. Improvement in EASI scores is expressed as percentage improvement from baseline; EASI 50 indicates ≥ 50% improvement from baseline, EASI 75 indicates ≥ 75% improvement from baseline, EASI 90 indicates ≥ 90% improvement from baseline and EASI 100 indicates 100% improvement from baseline.

[Speaker 2] presented data on the proportion of patients achieving 50%, 75%, 90% and 100% improvement in EASI (EASI-50, EASI-75, EASI-90 and EASI-100). The data were presented as waterfall plots adapted from figure 3 in the post hoc analysis.[2] (2. Silverberg JI, *et al*. Am J Clin Dermatol 2022;23:547–559) Slides 7, 8 and 9 presented the waterfall plots from weeks 4, 16 and 32 respectively. Waterfall plots represent the number of patients achieving the different percentage improvement in EASI scores. We have enclosed the analysis of the EASI 100 data which formed the waterfall plots (enclosure 3) copy provided. The absolute figures were not published in the Silverberg publication, however as enclosure 3 shows there were a small number of patients who achieved EASI-100. We note there is a discrepancy of 1 patient at weeks 16 and 32. Therefore, there is clear evidence to support the data in the presentation.

When presenting the waterfall plots, [Speaker 2] made reference to the EASI-100 scores achieved by the small number of patients. [They] did this within the context of the other scores and did not place particular emphasis on the achievement of the EASI-100 scores. [They] focused on the other EASI scores from the post-hoc analysis. This can be seen in the recording provided. [They] did not make any further reference to EASI-100 data within [their] presentation outside the 3 slides with the waterfall plots.

[Speaker 3] presented four case studies from [their] centre for 16 patients with atopic dermatitis treated with tralokinumab. Case studies 3 and 4 included patients who had an improvement in their EASI scores post treatment to an EASI score of 0, however [they] [do] not specifically mention EASI-100. There is no undue emphasis placed on the improvement of EASI scores for those two case studies compared with the other two case studies.

We have provided the recording of the symposium as requested.

[Speaker 2's] presentation started at 09:30 minutes within in the recording, EASI 100 was mentioned at the following minutes:
14:25 number of patients with EASI-100 at week 4
14:54 number of patients with EASI-100 at week 16
15:46 number of patients with EASI-100 at week 32.

In [Speaker 3's] presentation:
34:00 Case Study 3 – patient achieves an EASI score of 0
35:00 Case study 4 – patient achieves an EASI score of 0

To conclude, the focus of the symposium was the experience of patients with atopic dermatitis (AD) being treated with tralokinumab, both in clinical trials and in the real world. EASI-100 data were presented as a small part of one of the presentations and were not the focus of the symposium. Whilst the two complaints received did not give much detail regarding the concerns of the complainants, they appear to be questioning whether any patients had actually achieved clear skin (i.e. an EASI-100 score). The data are substantiable, they are present within waterfall plots within the published post-hoc analysis and the absolute figures have been provided. Therefore, LEO Pharma denies a breach of clause 6.2. In addition, the data were not given undue emphasis in the presentation, as seen in the recording provided, therefore LEO Pharma denies a breach of clause 6.1.

We have enclosed all references as requested along with a copy of the summary of product characteristics for tralokinumab. We have enclosed certified copies of the agenda and all three presentations, and the speaker contracts. The signatory qualifications are;

[signatories' qualifications provided]"

PANEL RULING

The symposium at issue was a Leo-sponsored promotional symposium, at the British Dermatological Nursing Group (BDNG) annual conference in September 2023. It proposed to cover 'Adtralza (tralokinumab) long-term perspectives in atopic dermatitis (AD): from trial data to real-word experience' and was scheduled to last 45 minutes, including five minutes for Q&A. Based on the enclosures provided by Leo, the symposium consisted of 45 slides delivered by three speakers. The complaints related to the EASI-100 (Eczema Area and Severity Index) data presented, which appeared within the second section covering the long-term efficacy and safety [of Adtralza] in adults: results from ECZTRA 3 and ECZTEND 2-year data. This section consisted of 23 slides, covering initially the primary and secondary endpoints of the ECZTRA 3

trial followed by the results from a post-hoc analysis (Silverberg JI, et al. Am J Clin Dermatol 2022;23:547–559.)

The Panel noted that the Constitution and Procedure stated that the complainant had the burden of proving their complaint on the balance of probabilities. All complaints are judged on the evidence provided by the parties. Although both complaints were brief, the Panel understood the complaints to be that there was no clear evidence to support the EASI-100 data for tralokinumab, that was presented in this symposium.

In its response, Leo explained that EASI is a validated scale used in the assessment of severity and extent of AD and that improvement in EASI scores is expressed as percentage improvement from baseline; EASI-50 indicates ≥ 50% improvement from baseline, EASI-75 indicates ≥ 75% improvement from baseline, EASI-90 indicates ≥ 90% improvement from baseline and EASI-100 indicates 100% improvement from baseline.

The Panel was provided with copies of the slides presented at the symposium as well as a recording of the symposium. The Panel viewed the slides and noted that the slides displaying data from the post-hoc analysis featured a prominent green box on the top right corner of each slide, within which white bold text stated 'Post-Hoc Analysis'. The Panel noted that three slides in the post-hoc analysis section referred to EASI (Eczema Area and Severity Index) 100, the claim at issue. These three slides demonstrated EASI improvements, including EASI-100, over time with Adtralza (plus topical corticosteroid as needed). The three slides displayed data at three separate time points; at weeks 4, 16 and 32. The distribution of EASI improvement at each time point was displayed by means of a waterfall plot, where each vertical bar represented a patient and their EASI improvement. The panel noted that on the symposium slides it was stated that these figures were adapted from Silverberg JI et al. 2022. In addition to the waterfall charts, the Panel noted that each slide had a light green text box located above and to the right of the waterfall plot which stated the number (or approximate number) of patients achieving EASI-50 and EASI-100 at week 4 (on the week 4 slide), EASI-50, EASI-75, EASI-90 and EASI-100 at week 16 (on the week 16 slide) and EASI-75, EASI-90 and EASI-100 at week 32 (on the week 32 slide). The EASI-50, EASI-75 and EASI-90 figures provided in this text box were referenced to Silverberg JI et al. 2022. No reference number was provided next to the statements regarding the EASI-100 patient numbers.

The Panel noted Leo's explanation that absolute figures for EASI-100 were not provided in the Silverberg JI et al. 2022 publication. On reviewing the publication, the Panel considered that it may be possible, with a higher resolution and enlarged version of the waterfall plot displayed within the paper, to ascertain the absolute number of patients experiencing EASI-100; however, the Panel was reliant on the information provided by Leo. The Panel considered that within a symposium setting, it was unlikely that health professionals would be able to distinguish the absolute EASI-100 patient figures from the waterfall plots due to the busy nature of the display with a separate bar for each patient (252 in total). Instead, they would likely rely on the EASI-100 numbers stated in text on the slide and provided verbally by the speaker.

The Panel was provided with the analysis of the EASI-100 data which formed the waterfall plots as part of Leo's response. This analysis provided absolute figures for the number of patients experiencing EASI-100. The Panel noted Leo had highlighted a discrepancy of one patient at weeks 16 and 32 between the analysis they provided, and the figures stated on the symposium slides. At week 16, the symposium slides and speaker stated that 17 out of 252 patients achieved EASI-100, whereas the supporting analysis provided by Leo stated that 16 patients

out of 252 had achieved EASI-100. At week 32, the symposium slides and speaker stated that 34 out of 252 patients achieved EASI-100, whereas the supporting analysis provided by Leo stated that 33 patients out of 252 had achieved EASI-100.

Clause 6.1 of the 2021 Code stated that information, claims and comparisons must be accurate, balanced, fair, objective and unambiguous and must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. Based on the evidence provided, the discrepancy between the EASI-100 patient numbers presented at the symposium and those provided in the supporting analysis, meant that the EASI 100 figures presented in the Leo promotional symposium were not an accurate reflection of the supporting data, and as such were misleading. The Panel ruled **a breach of Clause 6.1**.

The Panel disagreed with Leo's assertion that there was clear evidence to support the EASI-100 data in the symposium. The cited paper did not provide EASI-100 figures, and due to the discrepancy noted above, the number of patients experiencing EASI-100 stated in the symposium slides could not be substantiated based on the evidence provided. The Panel ruled **a breach of Clause 6.2**.

Complaint AUTH/3838/10/23 received **12 October 2023**
Complaint AUTH/3840/10/23 received **24 October 2023**

Case completed **3 February 2025**