CASE AUTH/3864/12/23

COMPLAINANT v CELLTRION

Alleged false claim about NICE approval status for Remsima (infliximab) SC

CASE SUMMARY

This case was in relation to an alleged false claim made by a Celltrion representative during a meeting, about the NICE approval status of Remsima (infliximab) subcutaneous (SC)

The outcome under the 2021 Code was:

Breach of Clause 17.2	**Representatives failing to comply with all relevant requirements of the Code**
Breach of Clause 18.2	**Failing to provide claim substantiation within ten working days**

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

FULL CASE REPORT

A complaint was received from a lead pharmacist at a University Hospitals NHS Trust about Celltrion Healthcare UK Ltd.

COMPLAINT

The complaint wording is reproduced below:

> "I'd like to report an incident regarding Remsima (infliximab) SC following a false claim about NICE approval status from [a] Celltrion representative [representative 1].
>
> - Myself and [a Lead IBD Specialist Nurse] had a meeting with another representative [representative 2] and with [representative 1] on 10th October 2023 over MS Teams, starting 11am. I'm afraid the meeting was not recorded.
> - The meeting was to discuss options for the company to support our local service and infusion clinic in switching patients from infliximab IV to SC. Discussion included my mention of divergent funding status and approval processes for this drug between local ICBs, hampering uptake.
> - [Representative 1] stated that Celltrion had had a discussion with NICE on this topic. [They] claimed that NICE had stated that infliximab SC falls under the TAG for infliximab IV, on the basis that the pharmacoeconomics are cost neutral when compared to IV.

- I held this statement with a fair degree of scepticism so asked whether [they] had this in writing, and [they] referred me to the BNF. The BNF does not make this claim, so [they] said [they] would forward the communications.
- I chased this as per below, but nothing was forthcoming. On chasing today I'm told that [representative 1] has left the company. I also spoke to [representative 2] again verbally over the phone today, who stated that [they] had chased it from [their] end but found that the statement did not exist ([their] words).

I feel this claim by [representative 1] was likely a breach of ABPI code, so am submitting this for further investigation. To confirm, I have no issue with the conduct of [representative 2] throughout any of this, only [representative 1]/Celltrion."

When writing to Celltrion, the PMCPA asked it to consider the requirements of Clauses 17.2 and 18.2 of the 2021 Code.

CELLTRION'S RESPONSE

The response from Celltrion is reproduced below:

"I hope this message finds you well. We are writing in response to the complaint that was received on the 18th of December 2023, regarding the alleged false claim about the NICE approval status for Remsima® (infliximab) subcutaneous preparation or SC.

We take all concerns seriously and appreciate the opportunity to address the issues you have raised with regards to the clauses, 17.2 and 18.2 of the 2021 ABPI Code of Practice for the Pharmaceutical Industry.

Celltrion Healthcare have reviewed the complaint including the accompanying documentation.

Upon receipt of your complaint, we initiated a thorough investigation to understand the circumstances surrounding the issue. This investigation included reviewing the alleged false claim about the NICE approval status for Remsima® (infliximab) SC and interviewing the named representative, [representative 2], and [their] current manager, as the previous manager, [representative 1], who partook in the aforementioned meeting has since left the business.

Outcomes from interview

As stated earlier, [representative 1], who is mentioned in the complaint left the business on [date provided].

[Representative 2], the second representative present at the call was interviewed. Please see the outcomes of the interview below:

> [Representative 2] acknowledged that the meeting on the 10th of October 2023 did take place as described by the complainant, virtually and not recorded. In this meeting, [representative 1] did state infliximab SC falls under the Technology Appraisal Guidance for infliximab IV. During the meeting, the online BNF, was consulted to highlight that infliximab SC is indeed under the TAG. The

> complainant was, however, allegedly sceptical of the reasoning for the [sic] given. We are unable to confirm or deny the justification [representative 1] provided during the call, regarding the pharmacoeconomics and cost neutrality when compared to IV, however we can confirm that the complainant followed up by email to get confirmation on the NICE substantiation for this claim after the meeting.

We did also review the email thread sent alongside the complaint and confirmed the lack of a response by Celltrion Healthcare within the 10-working days as is standard practice.

Review of alleged claim

The claim that infliximab SC falls under the TAG for infliximab IV is substantiated using the NICE Evidence Review: Remsima® (infliximab biosimilar) for subcutaneous injection for managing Crohn's disease and ulcerative colitis (2021):

'A biosimilar medicine is a biological medicine that has been shown not to have any clinically meaningful differences from the originator medicine in terms of quality, safety and efficacy. Where NICE has already recommended the originator biological medicine, the same guidance will normally apply to a biosimilar of that originator.'

'This evidence review considers Remsima, a biosimilar of infliximab, for subcutaneous injection (Celltrion Healthcare Hungary). Remsima (subcutaneous) received a marketing authorisation for managing rheumatoid arthritis in December 2019 and received a license extension for Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis, and psoriasis in July 2020. This evidence review focuses on the license extension for Crohn's disease and ulcerative colitis only.'

Response to complaint, based on our investigation

We wanted to highlight that the complainant complained specifically about the conduct of [representative 1], so we will be addressing this in our response, with respect to the two clauses highlighted below:

> *17.2 Representatives must maintain a high standard of ethical conduct in the discharge of their duties and comply with all relevant requirements of the Code.*

and,

> *18.2 Substantiation for any information, claim or comparison must be provided as soon as possible, and certainly within ten working days, at the request of health professionals or other relevant decision makers. The validity of indications approved in the marketing authorisation can be substantiated by provision of the summary of product characteristics.*

We at Celltrion understand and fully respect the ABPI Code of Practice and strive to ensure that all activities are in adherence with the Code. We expect our representatives to maintain high standards and comply with all relevant requirements of the Code.

We acknowledge the complainant's timeline of events; our investigation did however highlight the use of the BNF during the time of the meeting to substantiate the claim made during the call. Please note that NICE provides a website providing the content of the BNF to the public. Again, due to lack of the meeting recording, we are unable to investigate in what context, the BNF and/or NICE was used to substantiate the alleged claim.

The PMCPA Constitution and Procedure does require a complainant to prove their complaint on the balance of probabilities. The complainant must be able to show that the requirements set forth in the aforementioned clauses had not been complied with, e.g. maintaining a high standard of ethical conduct during the meeting. Based on the information provided within this response, both from the BNF and the NICE Evidence Review, the claim that infliximab SC falls under the TAG for infliximab IV is substantiable. However, we have no way of knowing how the claim was referenced during the meeting on the 10th of October as no recording was provided.

We do however appreciate the failure to respond to the complainant within 10 working days of the receipt of the enquiry as is standard practice. This is mainly due to the departure of the sales representative, [representative 1] on [date provided] and the timelapse caused during the handover of responsibilities between the representatives. We therefore accept that we are in breach of clause 18.2 of the 2021 ABPI Code of Practice.

We are committed to adhering to the high standards set by the Prescription Medicines Code of Practice Authority and continually strive to improve our practices. We assure you that the necessary steps have been taken to prevent a recurrence of such an issue."

Further response from Celltrion

Further information was provided by Celltrion in response to a request for additional information. The response from Celltrion is reproduced below:

"We appreciate the opportunity to provide the additional information requested. Please find below our responses to your queries:

1. The NICE Technology Appraisal Guidance (TAG) referred to by the representative in the meeting with the complainant, and by Celltrion in our initial response:

We do not know which specific TAG was discussed during the call, but the principles laid out in our initial response letter from January 2024 would apply to any TAG listed on the BNF online page, for any indication in which Remsima SC has received marketing authorization.

2. Any record or documentation of the discussion with NICE that the representative referred to in the meeting with the complainant, in which NICE confirmed the above TAG applies to Remsima SC:

> We regret to inform you that we do not have specific records or documentation of a direct discussion with NICE regarding the application of the TAG to Remsima SC that would have been shared with our representative. The statement was based on the understanding of NICE's general guidance for biosimilars, as referenced in the NICE Evidence Review (Attachment B from our initial response). We do not have additional documents beyond what was previously provided that directly confirm this specific discussion with NICE."

PANEL RULING

This complaint, received from a health professional from their NHS email account, related to an alleged false claim regarding Remsima (infliximab) Subcutaneous (SC) made by a Celltrion sales representative during a virtual, non-recorded meeting. The meeting was reported by the complainant to be to discuss options for Celltrion to support the complainant's local service and infusion clinic in switching patients from infliximab intravenous (IV) to infliximab SC. The meeting was attended by two health professionals including the complainant, and two Celltrion sales representatives. During the meeting, in response to the complainant's discussion of divergent funding status and approval processes for infliximab hampering uptake, one of the Celltrion sales representatives was alleged to have claimed that Celltrion had had a discussion with NICE on this topic and that NICE had stated that infliximab SC falls under the same Technology Appraisal Guidance (TAG) for infliximab IV on the basis that the pharmacoeconomics were cost neutral when compared to IV. The complainant requested substantiation for this and was referred to the British National Formulary (BNF). The complainant did not feel that the BNF supported this claim and so requested further substantiation be sent following the meeting but had yet to receive any further substantiation at the time of complaint.

Substantiation for NICE approval claim

The introduction to the PMCPA Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The Panel considered, however, that a high degree of dissatisfaction was usually required before an individual was moved to complain. With regard to the representative call at issue, the Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened. However, the Panel noted that in this case, whilst the representative alleged to have made the claim had since left the business, Celltrion had conducted an interview with the second representative present in the call who had confirmed that the meeting had taken place as described by the complainant, and the first representative had stated that infliximab SC falls under the TAG for infliximab IV.

Celltrion submitted that the claim that infliximab SC falls under the TAG for infliximab IV could be substantiated by the BNF and a NICE Evidence Review, copies of which were available to the Panel. However, it was unable to confirm in what context these documents were used to substantiate the claim during the meeting due to the lack of meeting recording. The Panel noted that the BNF attachment provided appeared to be the BNF listing for Infliximab with reference to both IV and SC use and contained a section with the heading "National funding/access decisions" which listed nine NICE TAG decisions in relation to infliximab in different disease states and conditions.

The NICE Evidence Review provided by Celltrion was entitled "Evidence Review: Remsima (infliximab biosimilar) for subcutaneous injection for managing Crohn's disease and ulcerative colitis". The Panel observed that this Evidence Review made reference to certain NICE TAGs: "Infliximab is recommended as an option for treating moderately to severe active ulcerative colitis (see NICE's technology appraisal guidance on infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy) and severe active Crohn's disease (see NICE's guideline on Crohn's disease: management) in adults whose disease has not responded to conventional therapy, or who are intolerant of or have contraindications to conventional therapy including steroids and immunosuppressive therapies". The Evidence Review also stated: "Remsima for subcutaneous injection is a biosimilar of infliximab…As a biosimilar medicine, Remsima is highly similar to another biological medicine (the 'reference medicine') that is licensed for use in Crohn's disease and ulcerative colitis. The reference medicine for Remsima is Remicade (infliximab)". It further stated "A biosimilar medicine is a biological medicine that has been shown not to have any clinically meaningful differences from the originator medicine in terms of quality, safety and efficacy. Where NICE has already recommended the originator biological medicine, the same guidance will normally apply to a biosimilar of that originator" as highlighted by Celltrion in their response.

Celltrion submitted that they had no records or documentation of a direct discussion with NICE regarding the application of the TAG, but the claim was based on their understanding of NICE's general guidance for biosimilars as referred to in the Evidence Review cited above.

The complainant had not specified which NICE TAG was referenced during the meeting, and Celltrion could also not confirm which TAG document was referred to. Neither party had submitted a TAG document as evidence, so the Panel did not have a copy of any before it. However, based on the evidence it did have before it and on the balance of probabilities, given that Remsima was identified as a biosimilar of infliximab (Remicade) and that NICE guidance would normally apply to a biosimilar of the originator, the Panel concluded it was likely that a NICE TAG covering Remicade (infliximab IV) would also apply to Remsima (infliximab SC). A complainant had the burden of proving their complaint on the balance of probabilities and the complainant had provided no evidence that this was not the case.

The Panel was concerned to note that Celltrion could neither confirm or deny the justification provided by the representative in the call for why the NICE TAG covered both infliximab IV and SC, in that the pharmacoeconomics were cost neutral when compared to IV. The Panel noted that the NICE Evidence Review provided by Celltrion stated in a section titled "Resource Implications": "The cost of prescribing Remsima (subcutaneous) for managing ulcerative colitis and Crohn's disease will vary by locality. Therefore, it is not possible to show the overall resource impact". This appeared to the Panel to not support the justification of cost neutrality provided by the representative during the call. No further evidence had been provided to the Panel to support the representative's claim of cost neutrality.

Clause 17.2 requires that representatives must maintain a high standard of ethical conduct in the discharge of their duties and to comply with all relevant requirements of the Code. In providing a justification that cost neutrality was the reason that a NICE TAG applied to both infliximab IV and SC, a claim that could not be substantiated based on the evidence before the Panel, the representative had failed to comply with all relevant requirements of the Code and the Panel ruled **a breach of Clause 17.2**.

Timeline for providing substantiation

The Panel noted that as the complainant was not happy with the substantiation for the claim provided during the meeting (which took place on 10 October 2023), the representative allegedly agreed to send further substantiation. This request for substantiation was followed up by an email from the complainant on 12 October 2023, as acknowledged by Celltrion. Having not received a response, the complainant again emailed chasing substantiation on 28 November 2023, at which time they submitted their complaint to the PMCPA [email chain provided].

Clause 18.2 states that substantiation for any information, claim or comparison must be provided as soon as possible, and certainly within ten working days, at the request of health professionals or other relevant decision makers. Substantiation for the claim in question had not been provided to the complainant within ten working days of request and so the Panel ruled **a breach of Clause 18.2**, as acknowledged by Celltrion.

Complaint received **28 November 2023**

Case completed **04 March 2025**