CASE AUTH/3737/2/23

HEALTH PROFESSIONAL v NOVO NORDISK

Allegations about a Saxenda promotional leavepiece

CASE SUMMARY

This case was in relation to a Saxenda (liraglutide) promotional leavepiece.

The Panel considered that the statement 'Treatment with Saxenda should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight' should have been made clear to the reader as it was an important part of both the licensed indication as stated in Section 4.1 of the SPC and the medicine's benefit/risk profile. Its omission from the indication stated on the front page was compounded by its omission anywhere within the main body of the leavepiece. The indication given in the prescribing information omitted this same statement. The Panel considered that whilst this information appeared in the Posology and administration section of the prescribing information, this was insufficient as the indication given in the prescribing information was not consistent with the SPC. The Panel ruled a breach of the following Clauses of the 2021 Code as the leavepiece was inconsistent with the particulars listed in the Saxenda SPC and the indication given in the prescribing information was not consistent with the SPC. The omission of the statement in question from the main body of the promotional material, and its position under the incorrect heading in the prescribing information, was such that Novo Nordisk had failed to maintain high standards:

Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 11.2	**Material inconsistent with the particulars in the SPC**
Breach of Clause 12.1	**Failing to provide prescribing information with at least one authorised indication consistent with the SPC.**

The Panel ruled a breach of the following Clause of the 2021 Code for the leavepiece citing an 0845 number for reporting adverse events to the company, which the Panel considered might be perceived as a barrier; in that regard Novo Nordisk had failed to maintain high standards:

Breach of Clause 5.1	**Failing to maintain high standards**

The Panel ruled no breach of the following Clause of the 2021 Code as whilst it had concerns about the interaction between Novo Nordisk and the named pharmacy group, there was no evidence that Novo Nordisk had directed the pharmacy group to publish the Saxenda leavepiece on its website nor that Novo Nordisk was aware of the existence of the material on the website. The Panel considered that it had no evidence that Novo Nordisk was responsible for the publication of the leavepiece on the pharmacy group's website:

No Breach of Clause 26.1	**Requirement to not advertise prescription only medicines to the public**

The Panel ruled a breach of the following Clause of the 2021 Code as the lack of clear guidance to the pharmacy group when providing them with the leavepiece, particularly given that the representative and their line manager, who was copied into the email, knew that the pharmacy group engaged in online marketing of its weight management programme and had set up a website with Saxenda in the URL, was such that Novo Nordisk had failed to maintain high standards:

Breach of Clause 5.1	**Failing to maintain high standards**

The Panel ruled no breach of the following Clause of the 2021 Code as it considered, on balance, that its rulings above adequately addressed the complainant's concerns:

No Breach of Clause 2	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**

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 complainant who described themselves as a concerned health professional about a Saxenda (liraglutide) leavepiece.

COMPLAINT

The complainant provided a link and alleged that the promotional item was freely available on the internet to the general public although it should only be for health professionals.

The complainant further alleged that the indication mentioned on page 1 of this item omitted part of the current indication: 'Treatment with Saxenda should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight'. This was thus allegedly promoting off-licence. The entire statement on page 1 was written in small writing and in a light shade of grey.

The complainant further alleged that in the prescribing information, the information for discontinuation at 12 weeks had also been moved from the therapeutic indication to the posology section where it was even less likely to be noticed. The telephone number to report adverse events was also a '0845' number which could discourage people from reporting since there was a cost involved.

In response to a question from the case preparation manager about how the complainant found and accessed the website with the leavepiece, the complainant stated that the link provided was found via Google.co.uk and remained a live link. The complainant asserted that it was therefore

"indexed" by search websites as whoever put the file online had not restricted access and that the only information the complainant had accessed was that available to the general public.

When writing to Novo Nordisk, the Authority asked it to consider the requirements of Clauses 2, 5.1, 11.2, 12.1, 12.2 and 26.1 of the 2021 Code.

RESPONSE

Novo Nordisk submitted that the item in question was a leavepiece for Saxenda (UK20SX00030) which was certified on 19 March 2020. The item was described as an 'HCP discussion guide' and the intended audience was noted in the metadata as 'Healthcare practitioners'. It was withdrawn from use on 15 December 2021.

Saxenda indication

Novo Nordisk stated that the complainant appeared concerned that the leavepiece was not clear as to the indication of Saxenda.

Novo Nordisk submitted that the prominent statements at the top of the first page of the leavepiece were clear that Saxenda should be used in the management of weight loss in obese patients. There was also a bold statement at the bottom of the first page referring the reader to the prescribing information for the medicine in which the indication was stated.

The statement in the Saxenda summary of product characteristics (SPC) relating to discontinuation of the medicine after 12 weeks if patients had not lost at least 5% of their initial body weight was known as 'the stopping rule'. As could be seen in the European Public Assessment Report (EPAR) for Saxenda, it was agreed with the European Medicines Agency (EMA) that this statement should be included in Section 4.1 of the SPC, however, Novo Nordisk did not consider that its omission from page 1 of the leavepiece amounted to the promotion of the medicine outside the terms of its marketing authorisation. This statement was included in the prescribing information at the end of the leavepiece. Novo Nordisk refuted the allegation that the leavepiece was in breach of Clause 11.2.

The 'stopping rule' statement appeared in the 'Posology and Administration' section of the prescribing information. Novo Nordisk expected that a health professional would read the prescribing information in its entirety and therefore it did not consider that the statement was 'less likely to be noticed'. Having consulted Novo Nordisk Regulatory Affairs, Novo Nordisk could confirm that during vetting of all Saxenda promotional materials (which contained prescribing information), no comments were received from The Medicines and Healthcare products Regulatory Agency (MHRA) on the prescribing information other than adding a reference sentence to the full SPC.

Novo Nordisk therefore denied a breach of Clauses 12.1 and 12.2.

Availability of leavepiece on a clinic website

It appeared that the leavepiece at issue was placed on a clinic's website which was part of a named pharmacy group. The Novo Nordisk representative covering that clinic at the time that the leavepiece was in use no longer worked for Novo Nordisk. Therefore, Novo Nordisk was not able to speak to the representative in relation to whether the leavepiece was provided

directly to the clinic or, if it was, whether any specific instructions were given to the clinic in relation to its use and intended audience.

The representative's line manager had reviewed emails for any sent by the representative to which they might have been copied. It seemed that in June 2020 the representative sent an email to two pharmacists at the clinic following a virtual meeting with them.

Novo Nordisk submitted that the email indicated that, at the meeting, there was a discussion about the clinic offering Saxenda as part of a weight management programme and the representative stated that they would send to the clinic 'marketing materials' from Novo Nordisk, by which Novo Nordisk assumed that the representative meant the leavepiece at issue as well as a patient booklet (UK20SX00029). Novo Nordisk did not have any evidence that the representative then emailed the material to the clinic but, on the balance of probabilities, this was likely to be the means by which the clinic came to have a copy of the leavepiece in question.

There was no evidence that Novo Nordisk could find that the representative instructed or stated that the leavepiece could be placed on the clinic website or provided it in any other way to patients or members of the public. Therefore, Novo Nordisk denied a breach of Clause 26.1.

Novo Nordisk submitted that the email also copied in another Novo Nordisk employee and indicated that they might be able to provide support for the clinic's marketing team. The response to this email from the clinic requested that this employee review the clinic's website. Having spoken to the employee as part of the investigation into this case, they stated that they did not recall having any discussion with the clinic about their website and had no record of any communication with the clinic. There was no, nor had there ever been, a contract between Novo Nordisk and the clinic for any purpose, including for any supportive activities relating to its website or any other marketing activities. Thus, it seemed that there was no evidence of any relationship between Novo Nordisk and the clinic other than a general representative/healthcare organisation one.

With the above in mind, Novo Nordisk did not consider that the interaction that they had with the clinic, or the materials that were likely provided to it by a Novo Nordisk representative, amounted to a failure to maintain high standards, and Novo Nordisk denied a breach of Clause 5.1. Further, Novo Nordisk did not consider that there had been any act or omission that could be considered as bringing the industry into disrepute and denied a breach of Clause 2.

PANEL RULING

The Panel noted that whilst Novo Nordisk had been asked to respond in relation to the requirements of the 2021 Code, it appeared that the 2019 Code potentially applied to certain aspects of the complaint; however, in the particular circumstances of this case, the Panel did not consider that there were any substantive relevant differences between the 2019 and 2021 Codes in relation to the subject matters of the complaint and the Panel therefore ruled in relation to the requirements of the 2021 Code.

The Panel noted that the complaint concerned a Saxenda (liraglutide) leavepiece (UK20SX00030) which was described in the electronic copy approval system as an HCP discussion guide. The Panel noted that the front page of the leavepiece read 'I had the will to start a business from scratch. But I still need help to lose weight and keep it off' above an

image of a patient. Adjacent text read 'Your patients with obesity have the will. You can offer them the way.' Text in smaller font size at the bottom of the page read 'Saxenda is indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adult patients with an initial Body Mass Index (BMI) of ≥30kg/m^2 (obese), or ≥27 kg/m^2 to <30 kg (overweight) in the presence of at least one weight-related comorbidity such as dysglycaemia (pre-diabetes or type 2 diabetes mellitus), hypertension, dyslipidaemia or obstructive sleep apnoea.' A statement beneath stated that 'Prescribing information and adverse events reporting information can be found on page 15.' The complainant stated that the indication statement on page 1 was written in small writing and in a light shade of grey.

The Panel noted the complainant's allegation that the indication mentioned on page 1 of the leavepiece omitted part of the indication namely 'Treatment with Saxenda should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight' and was thus promoting off-licence.

The Panel noted that the statement at issue 'Treatment with Saxenda should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight' appeared in Section 4.1 of the Saxenda SPC, Therapeutic indications, Adults, immediately beneath the first part of the licensed indication which was reproduced on the front page of the leavepiece at issue. The Panel noted that the statement at issue was the only part of the therapeutic indication for adults that was omitted from the front page of the leavepiece.

The Panel noted that Section 5.1 of the SPC, Pharmacodynamic Properties, Weight loss response after 12 weeks with liraglutide (3.0 mg) treatment, stated that 'For patients who have achieved a weight loss of < 5% after 12 weeks on treatment dose of liraglutide, the proportion of patients not reaching a weight loss of ≥ 10% after 1 year is 93.4%.' The Panel also noted that Section 2.5.3 of the European Public Assessment Report (EPAR), Discussion on clinical efficacy, Efficacy data and additional analyses, Stopping rule, stated that based on data and the similarity with orlistat, it was agreed to use the 5% cut-off margin and the applicant and the Committee for Medicinal Products for Human Use (CHMP) had agreed on the wording in question for the stopping rule to be included in Section 4.1 of the SPC.

The EPAR made reference within 'Discussion on the benefit-risk assessment' to the stopping rule protecting subjects from long-term use of a non-effective therapy and that the CHMP had concluded that the benefit/risk was positive subject to adherence to the stopping rule. It appeared to the Panel from the benefit-risk assessment in the EPAR, and the wording in Section 4.1 of the SPC, that the stopping rule was an important part of the licensed indication and should be made clear to health professionals.

The Panel noted that the statement at issue 'Treatment with Saxenda should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight' did not appear anywhere within the main body of the promotional material but was referred to in the prescribing information, on page 15.

The Panel noted that Clause 11.2 stated that the promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its summary of product characteristics.

The Panel considered that whether certain information from the SPC needed to

be highlighted within a particular section of promotional material, in addition to its requirement to be included within the prescribing information that was required on all promotional material, depended on a consideration of all of the circumstances including the nature of the information and the content, layout, audience and intended use of the material.

In this regard the Panel noted that an emphasis in the leavepiece was on Saxenda's longer-term use: the front page, in prominent font size, referred to the patient's need to 'keep it [weight] off'; the first bullet point on page 3 referred to the requirement for long-term management of obesity; pages 4 and 5 referred to 1 year data; page 6 referred to 3 year data; page 10 referred to long-term efficacy and 3 year data; and the summary page referred to 1 and 3 year data. The Panel considered, particularly within the context of this leavepiece, that the statement 'Treatment with Saxenda should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight' should have been made clear to the reader as it was an important part of both the licensed indication as stated in Section 4.1 of the SPC and the medicine's benefit/risk profile. The Panel considered that its omission from the indication stated on the front page was compounded by its omission anywhere within the main body of the leavepiece and was such that the material was inconsistent with the particulars listed in the Saxenda SPC; the Panel ruled **a breach of Clause 11.2 of the Code.**

In relation to the allegation about prescribing information, the Panel noted the complainant's concern that the statement in question 'Treatment with Saxenda should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight' appeared in the 'Posology and administration' section of the prescribing information where, in the complainant's view, it was less likely to be noticed. The Panel noted Novo Nordisk's submission that as could be seen in the EPAR for Saxenda, it was agreed with The European Medicines Agency (EMA) that this statement should be included in Section 4.1 of the SPC.

The Panel noted that Clause 12.1 required the prescribing information listed in Clause 12.2 to be provided on all promotional material. Clause 12.2 listed the components of prescribing information; failure to satisfy the requirements of Clause 12.2 would be a breach of Clause 12.1. The Panel noted that Novo Nordisk had been asked to bear in mind the requirements of Clauses 12.1 and 12.2, however, noting its comments above the Panel made its ruling on this matter in relation to Clause 12.1 only.

The Panel noted that Clause 12.2 stated that the prescribing information consists of, amongst other things, at least one authorised indication for use consistent with the summary of product characteristics. Whilst Clause 12.1 did not require the licensed indication as set out in the SPC to be reproduced verbatim, whether the licensed indication as set out in the prescribing information was consistent with the SPC would depend on a number of factors including the nature and relevance of any omitted information. The Panel, noting its comments about the stopping rule and the EPAR above, considered that the indication given in the prescribing information was not consistent with the SPC as it omitted 'Treatment with Saxenda should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight' which was part of the licensed indication as stated in Section 4.1 of the SPC. The Panel considered that whilst this information appeared in the middle of the Posology and administration section of the prescribing information, this was insufficient as the indication given in the prescribing information was not consistent with the SPC and therefore the Panel ruled **a breach of Clause 12.1**.

The Panel considered that the omission of the statement 'Treatment with Saxenda should be discontinued after 12 weeks on the 3.0 mg/day dose if patients have not lost at least 5% of their initial body weight' in the main body of the promotional material and, in addition, its position under the incorrect heading in the prescribing information was such that Novo Nordisk had failed to maintain high standards and **a breach of Clause 5.1 was ruled**.

In relation to the allegation that the telephone number to report adverse events was also a '0845' number which could discourage people from reporting since there was a cost involved, the Panel noted that Novo Nordisk had not responded to this matter. The Panel noted that Novo Nordisk had been provided with relevant details about this allegation when it was notified of the complaint, the Panel therefore considered this matter in the usual way.

The Panel noted that an outlined box beneath the prescribing information stated, 'Adverse events should be reported'; reporting details and information were provided followed by 'Adverse events should also be reported to Novo Nordisk Limited (Telephone Novo Nordisk Customer Care Centre [0845 number])'. In general terms the Panel considered that given the potential deterrent effect that the use of an 0845 number might have on potential callers it was particularly important that any associated charges were made clear in all written material. The Panel considered that taking all the circumstances into account, the use of an 0845 number might be perceived as a barrier to reporting adverse events to the company. In that regard Novo Nordisk had failed to maintain high standards and the Panel ruled a **breach of Clause 5.1 of the Code.**

The Panel noted that the complainant alleged that the leavepiece was freely available on the internet to the general public although it should only be for health professionals. The Panel noted Novo Nordisk's submission that the leavepiece at issue was on the website of a pharmacy group.

The Panel further noted Novo Nordisk's submission that it was not able to speak to the relevant representative in relation to this matter but that in June 2020 the representative sent an email to two pharmacists at the pharmacy group in question following a virtual meeting with them. The email indicated, amongst other things, that the representative stated they would send to the pharmacy group 'marketing materials' from Novo Nordisk, by which Novo Nordisk assumed that the representative meant the leavepiece at issue as well as a patient booklet. Novo Nordisk stated that it did not have any evidence that the representative subsequently emailed the material to the pharmacy group but, on the balance of probabilities, this was likely to be the means by which the pharmacy group came to have a copy of the leavepiece in question. Novo Nordisk submitted that there was no evidence that the representative instructed or stated that the leavepiece could be placed on the pharmacy group website or provided it in any other way to patients or members of the public.

The Panel accepted Novo Nordisk's admission that, on the balance of probabilities, the representative had provided the leavepiece to the pharmacy group and considered the complaint on that basis. The issue the Panel had to determine was whether Novo Nordisk was responsible for the publication of the leavepiece on the pharmacy group website.

The Panel noted the email in June 2020 from the representative to the two pharmacists and was particularly concerned that electronic and hard copy materials, for what appeared to be differing audiences (health professionals and members of the public), had been offered and, on the balance of probabilities, provided to the pharmacists without any detailed guidance regarding

their use. This was concerning given that the response from the pharmacy group the same day was clear that the clinic engaged in online marketing activity about its weight management programme and had asked Novo Nordisk to review its two websites including one which bore the product name Saxenda as part of its URL. The Panel noted Novo Nordisk's submission that there was no record of any follow-up discussions with the pharmacy group about its websites. The Panel further noted Novo Nordisk's submission that there was no contractual relationship between it and the pharmacy group and no evidence of a relationship beyond that of a representative/healthcare organisation. Whilst the Panel had concerns about the interaction between Novo Nordisk and the pharmacy group, there was no evidence that Novo Nordisk had directed the pharmacy group to publish the Saxenda leavepiece in question on its website nor that Novo Nordisk was aware of the existence of the material on the pharmacy group's website. The Panel considered that it had no evidence that Novo Nordisk was responsible for the publication of material on the pharmacy group's website and **no breach of Clause 26.1** was ruled in that regard.

The Panel was concerned about the exchange between the representative and the pharmacy group. The representative's line manager was copied into the exchange yet did not appear to provide any clarification to the pharmacy group about the use of the materials that were being offered by the Novo Nordisk representative. This was particularly concerning given that it was abundantly clear that the pharmacy group engaged in online marketing activity of its weight management programme and had set up a website with Saxenda in the URL. The Panel considered that the lack of clear guidance to the pharmacy group when providing them with 'electronic marketing materials' was such that Novo Nordisk had failed to maintain high standards and **a breach of Clause 5.1 was ruled**.

The Panel noted the narrow allegation in relation to the licensed indication and its rulings of breaches of the Code above, including breaches of Clause 5.1, and considered that these adequately addressed the complainant's concerns, which in the Panel's view, and on balance, did not warrant a ruling of a breach of Clause 2, which was used to indicate particular censure and reserved for such use; **no breach of Clause 2** was ruled accordingly.

Complaint received **13 February 2023**

Case completed **27 November 2023**