CASE AUTH/3258/10/19

COMPLAINANT AND EX-EMPLOYEE v NOVO NORDISK

Promotion of Ozempic

A contactable complainant complained about the promotion of Ozempic (semaglutide) by Novo Nordisk Limited. The complainant originally acted alone but subsequently stated that an ex-employee of Novo Nordisk had agreed to join him/her to help and possibly lead the complaint.

The complainant stated that a Novo Nordisk representative approached him/her to submit Ozempic to the local hospital formulary which Novo Nordisk medical and market access personnel helped to write and should not have and for which they received a commission. A former medical liaison divulged that he/she received incentive upon acceptance, for assisting the writing of faster acting insulin as part of formulary applications. The complainant stated that he/she could not distinguish medical personnel from representatives. The complainant stated that he/she was given the guidelines in practice formulary decision guide (UK/SM/0818/0304) but was disappointed to note that Novo Nordisk had deliberately misled formulary applicants with regard to the safety of semaglutide by omitting that it caused a significant (76%) increase in retinopathy, including blindness. The complainant referred to the post-authorisation safety study (PASS) that the regulators had imposed on Novo Nordisk specifically in retinopathy hence the grave concerns about this but this vital information on safety was deliberately omitted in this critical piece for formulary application. The representatives were not able to provide a summary of product characteristic (SPC) or a detailed explanation about retinopathy when requested. The complainant queried whether representatives (sales, market and medical) were briefed to downplay retinopathy, to coax/seek formulary champions and to help write the formulary application.

The complainant further stated that the costs in the prescribing information were misleading. The formulary leavepiece and another leavepiece were given by 2 separate representatives at the end of 2018 but the complainant stated that he/she was explicitly told not to prescribe Ozempic until 1/1/2019 as it was not in supply until then.

The complainant explained that a named employee told him/her at the European Association for the Study of Diabetes (EASD) conference that he/she should 'save' patients from then, knowing that semaglutide was coming which was outrageous behaviour and there were prescribing issues in January- April 2019 that caused patients to be without medication. Further, the complainant was informed that direct switching from GLP-1 was allowed ie switching from dulaglutide 1.5mg directly to semaglutide 0.5mg the following week; but this caused many issues with hypoglycaemia in 4 of his/her patients. The complainant alleged that the named employee had given advice outwith the Ozempic licence and had no evidence to support that advice and clearly Novo Nordisk had no regard for patient safety let alone cost implications of hypoglycaemia. Many months following his/her complaint to the company and reporting of these adverse effects, the employee had since changed his/her response to state switching involved starting at semaglutide 0.25mg dose. Unfortunately, many patients suffered as a result of negligence by pharma. These behaviours and disregarding safety

continued to draw that divide/trust amongst pharmaceutical companies. The complainant stated that the 'semaglutide discussion was at a GLP-1 advisory board in 2017. The question and discussions were around interclass switching ie from one GLP-1 to semaglutide where the employee stated that 'direct' switching from another GLP-1's (dulaglutide) maintenance dose to semaglutide lowest maintenance dose of 0.5mg'. The complainant subsequently confirmed that the advisory board was not at the EASD conference. It was in London where the subsequent discussions took place.

The complainant stated that he/she requested information from the representative and the response had taken more than ten days.

The detailed response from Novo Nordisk is given below.

The complainant had not named the representative nor any of the other staff to which the complaint referred other than the one named employee. The complainant appeared to use the term representative to describe employees of Novo Nordisk, referring to market access, medical and sales. The Panel considered the allegations as follows

1 Role of Novo Nordisk employees in formulary applications

The Panel noted that it was not necessarily a breach of the Code for a company or its staff to provide information and material to support a health professional in an application for its medicine/s to be included on formulary. It was important that the role of the company be made clear in such circumstances.

The Panel noted that Novo Nordisk provided two documents. Firstly the Ozempic Supporting Information Formulary Application document (ref UK/OZS/0618/0025(1)), the objective of which was to support clinicians or prescribing decision making committee members in submitting a formulary application. The second document was the Ozempic Formulary Decision Guide (UK/SM/0818/0304), the objective of which was an overview of key information required to make a formulary submission in the UK. It included the 'Guidelines in Practice' logo. It was for UK payers and health professionals.

It appeared from the objection handler (ref UK/SM/1118/0395, November 2018) that representatives were asked to call upon health professionals who were 'important stakeholders in the formulary submission process' as Ozempic was not currently available for prescribing and the company was focussed on getting formulary submissions prepared and submitted. The objection handler did not include any instructions about writing formulary applications. It encouraged health professionals to use Victoza whilst waiting for Ozempic to become available.

The Panel noted Novo Nordisk's submission that it was not the role of representatives, market access or medical staff to write formulary applications or complete formulary applications on behalf of a health professional. The role of the representatives was to support the formulary applicants either by introducing them to the local diabetes outcomes director (field based market access role) or providing information directly as appropriate.

The key purpose of the market access role was provided. The Panel considered that it was difficult to see that the market access role was anything other than promotional as defined in the Code.

The Panel noted Novo Nordisk's submission that the regional medical advisors' role with regard to formulary support was the provision of clinical data upon request by a health professional to support a formulary application.

The Panel key purpose of the regional medical advisor role was provided. The Panel considered that this role appeared to include the promotion of medicines.

The Panel did not consider that the complainant had established that any Novo Nordisk employee had written a formulary application as alleged or had not been appropriately briefed in relation to the company's role with regard to formulary applications. The Panel noted that the complainant had not detailed why in his/her view the activity constituted disguised promotion; it was not for the Panel to make out a complainant's allegations. The Panel noted its comments above and therefore ruled no breaches of the Code.

2 Alleged incentives for formulary applications

With regard to the allegation that staff including medical were incentivised upon acceptance of formulary applications that they helped to write, the Panel noted its rulings above; the complainant had not established that any Novo Nordisk employee wrote formulary applications on behalf of health professionals.

The Panel noted that it appeared that market access and sales staff were incentivised to obtain formulary status for products which was not necessarily a breach of the Code. Medical staff were not included in the incentive scheme. The Panel did not accept that paying a bonus which appeared to be capped and did not appear to constitute an undue proportion of the representatives remuneration meant that Novo Nordisk had failed to maintain a high standard and no breach of the Code was also ruled.

3 Content of Ozempic Formulary Decision Guide (Guidelines in Practice document)

The Panel noted its comments above regarding the printed material. The first document (not the subject of this allegation), (ref UK/OZS/0618/0025(1), included proposed formulary wording, clinical evidence including comparisons with other medicines in relation to glycaemic control, weight loss and cardiovascular benefits. The adverse events and tolerability section included information about diabetic retinopathy. Early worsening of retinopathy symptoms was reported in a small proportion of a subset of patients with a previous history of diabetic retinopathy.

The second document, the formulary decision guide (UK/SM/0818/0304) included an overview of the key information required for a formulary submission in the UK. This two-page document did not specifically refer to diabetic retinopathy other than a reference in the prescribing information. The Panel considered that the failure to mention diabetic retinopathy in the formulary decision guide was concerning, particularly given the company was required to do a further study at the request of the regulatory authorities in this regard. The available evidence was not reflected in the formulary decision guide and the Panel therefore ruled a breach of the Code. The Panel considered that the absence

amounted to a failure to maintain high standards and a breach of the Code was ruled. On balance the Panel did not consider that its ruling above meant that in addition the material was misleading as alleged and therefore ruled no breach of the Code.

The Panel noted that whilst the information on retinopathy was only in the prescribing information in the summary document, fuller information was provided in the detailed supporting information for formulary application and other materials. On balance the Panel decided that the circumstances did not amount to a breach of Clause 2.

4 Provision of the summary of product characteristics and detailed explanation of retinopathy

The Panel considered that the lack of detailed information from the complainant including who he/she had asked for the SPC, meant that he/she had not provided evidence to show that the SPC had not been provided upon request. The Panel therefore ruled no breach of the Code.

With regard to the allegation concerning the failure of the representative to provide a detailed explanation about retinopathy, the Panel noted that the two current leavepieces (ref UK19OZM00122 and UK19OZM00181) and an e-detailer (ref UK/OZS/0318/0001) provided by Novo Nordisk included information in sections headed 'diabetic retinopathy'. A leavepiece used in 2018(ref UK/OZS/0318/0005) included very brief details in a general paragraph headed 'common side effects'. The objection handler gave further information including encouraging representatives to proactively discuss diabetic retinopathy upfront when describing the safety and tolerability profile. Regional medical advisers were also available to discuss diabetic retinopathy. It was not known what materials the medical advisers used in such circumstances. However, the Panel considered that the lack of detailed information from the complainant including who he/she had asked for information on retinopathy, meant that he/she had not provided evidence to show on the balance of probabilities that there was a breach of the Code. The Panel therefore ruled no breach of the Code.

5 Cost and promotion prior to availability

The Panel considered that the complainant was not clear with regard to the allegations about the cost of the medicine. Novo Nordisk submitted that the costs in the prescribing information were accurate. The Panel did not consider that the complainant had shown on the balance of probabilities that the information about costs was misleading. The Panel therefore ruled no breach of the Code.

The Panel noted that it appeared that Ozempic received its marketing authorization in February 2018 (according to information on the eMC). It was not available until January 2019 according to the complainant and various documents provided by Novo Nordisk. The objection handler encouraged health professionals to use Victoza whilst waiting for Ozempic to become available.

The Panel did not consider it was necessarily a breach of the Code to promote a licensed medicine before that medicine was available for supply. Obviously in such circumstances companies needed to be clear about the position. The Panel considered

that the complainant had not shown that Novo Nordisk had been misleading in this regard and no breach of the Code was ruled.

6 Alleged conversations with named employee

The Panel noted that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. The complainant had provided no supporting evidence in relation to his/her allegations.

The Panel noted that the complainant had not detailed why in his/her view the medical lead in allegedly stating that the complainant should 'save' patients from knowing that semaglutide was coming, was in breach of the Code. Nor did the complainant provide evidence of the prescribing issues referred to in his/her complaint. The objection handler for some staff was clear that they were to encourage health professionals to consider Victoza whilst waiting for Ozempic to become available. It would be concerning if a company employee had suggested deferring treatment for patients with diabetes until Ozempic was available. The Panel did not consider that the complainant had provided evidence to show that on the balance of probabilities that there was a breach of the Code or that high standards had not been maintained. The Panel therefore ruled no breaches of the Code in this regard including Clause 2.

In relation to the advice regarding switching from other GLP-1 receptor agonists to Ozempic, the Panel was concerned that the complainant alleged he/she was given different advice to that set out in the undated medical information document and that allegedly following that advice had led to patients having problems with hypoglycaemia. The complainant had initially stated the advice was given at one meeting and then that it was at a different meeting, an advisory board meeting. Novo Nordisk denied that the topic had been raised at the advisory board meeting. The Panel noted that no evidence was provided by the complainant to support the allegations and therefore ruled no breach of the Code.

7 Medical information enquiry

The Panel did not have the details with regard to the allegation concerning the failure of Novo Nordisk to respond to a medical information query within 10 days. The Panel did not know what the query was, when it had been asked or if or when a response had been received. It considered that the complainant had not provided evidence to show on the balance of probabilities that there was a breach of the Code. The Panel therefore ruled no breach of the Code.

8 Cummulative effect

In relation to the allegation that Novo Nordisk's conduct was in breach of Clause 2, the Panel noted its rulings above. It did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use. The Panel therefore ruled no breach.

A contactable complainant complained about the promotion of Ozempic (semaglutide) by Novo Nordisk Limited. The complainant originally acted alone but subsequently stated that a good

friend, an ex-employee of Novo Nordisk had agreed to join him/her to help and possibly lead the complaint.

Ozempic was indicated for the treatment of type 2 diabetes, either as a monotherapy or in addition to other treatments for the condition.

COMPLAINT

The complainant alleged that it was disappointing that Novo Nordisk was trying to hide the side effects of Ozempic. The complainant explained that the Novo Nordisk representative approached him/her to submit Ozempic to the local hospital formulary which the medical and market access personnel in Novo Nordisk helped to write (even though rightfully they should not have). The complainant had no doubt they all got a commission for it, even the medical person (a former medical liaison with Novo Nordisk who was a good friend) divulged that he/she received incentive upon acceptance, for assisting the writing of faster acting insulin as part of formulary applications. The complainant stated that he/she could not distinguish medical personnel from representatives. The complainant stated that he/she was given the guidelines in practice formulary decision guide (UK/SM/0818/0304) but found it very disappointing that Novo Nordisk had deliberately misled formulary applicants with regard to the safety of semaglutide by omitting that it caused a significant (76%) increase in retinopathy, including blindness. The complainant noted that the post-authorisation safety study (PASS) that the regulators had imposed on Novo Nordisk specifically in retinopathy hence the grave concerns about this but in such a critical piece for formulary application vital information on safety was deliberately omitted by the company and its representatives (sales, market access and medical). The representatives were not able to provide a summary of products characteristic (SPC) when requested or a detailed explanation about retinopathy. Were the representatives (sales, market and medical) briefed to downplay retinopathy? Were they briefed to coax/seek formulary champions (as they label us!)? Were they briefed to help write the formulary application?

The complainant noted, the costs in the prescribing information were misleading, costs were crucial for formulary application - the piece compared to dulaglutide [Lilly's product Trulicity] (the complainant provided a copy of the leavepiece showing the SUSTAIN 7 trial as detailed by representatives) which was a use-and-throw device hence leading the complainant to think that the pricing was skewed and semaglutide £73.25 x4 for each month. The formulary piece and leavepiece were given by 2 separate representatives at the end of 2018 but the complainant stated that he/she was explicitly told not to prescribe Ozempic until 1/1/2019 as it was not in supply until then.

The complainant explained that a named employee told him/her at the European Association for the Study of Diabetes (EASD) conference that he/she should 'save' patients from then knowing that semaglutide was coming. This was outrageous behaviour and it turned out there were massive prescribing issues in January- April 2019 that caused patients to be without medication. Further, the complainant was informed that direct switching from GLP-1 was allowed ie switching from dulaglutide 1.5mg directly to semaglutide 0.5mg the following week; but this caused many issues with hypoglycaemia in 4 of his/her patients, in hindsight unsurprising due to the potency of semaglutide. The employee had given advice outwith the Ozempic licence and had no evidence to support that advice and clearly Novo Nordisk had no regard for patient safety let alone cost implications of hypoglycaemia. Many months following his/her complaint to the company and reporting these adverse effects, the employee had since changed his/her response to state switching involved starting at semaglutide 0.25mg dose. Unfortunately, many

patients suffered as a result of negligence by pharma and this too was worryingly the direction from the employee's department. These behaviours and disregarding safety and quite blatantly pulling the wool over the eyes of the practitioner, thereby impacting patient safety, continued to draw that divide/ trust amongst pharmaceutical companies. Not much had changed since thalidomide days!

The complainant asked the PMCPA to investigate and listed Clauses 1.5, 1.7, 2, 3.1, 3.2, 4.2, 7.1, 7.2, 7.3, 7.4, 7.5, 7.10, 8.1, 9.1, 15.1, 15.2,15.7, 15.8, 15.9, 15.10 and 16.

In supplementary correspondence with the complainant, the case preparation manager queried why he/she had listed Clauses 7.1 and 7.5. The complainant explained that he/she requested information from the representative who referred to the regional medical affairs who referred to the department of medical information. The complainant noted that response had taken more than ten days when enquiring about semaglutide.

In relation to a request for further clarity around the conversations with the named employee, the complainant stated that the 'semaglutide discussion was at a GLP-1 advisory board in 2017. The question and discussions were around interclass switching ie from one GLP-1 to semaglutide where he/she stated that 'direct' switching from another GLP-1's (dulaglutide) maintenance dose to semaglutide lowest maintenance dose of 0.5mg'. The first complainant subsequently confirmed that the advisory board was not at the EASD conference. It was in London where the subsequent discussions took place.

When writing to Novo Nordisk, the PMCPA asked it to consider the requirements of various clauses as set out below:

1 In relation to the role of the representative, market access staff and medical staff in relation to the formulary applications including briefing of relevant staff: Clauses 2, 9.1, 12.1, 15.2 and 15.9. To bear in mind the definition of a representative at Clause 1.6 when commenting on the role of the market access and medical staff.
2 Incentivisation and formulary applications: Clauses 9.1 and 15.7.
3 Content of Guidelines in Practice and Formulary Decision Guide: Clauses 2, 7.2, 7.9 and 9.1.
4 Failure of representative to provide SPC and detailed explanation on retinopathy: Clauses 15.1, 15.8 and 15.9.
5 Cost in prescribing information: Clauses 4.2 and 7.2.
6 Conversations with the named employee: Clauses 2, 7.2, 7.9 and 9.1.
7 Medical information enquiry raised with representative: Clause 7.1 and 7.5
8 Cumulative effect of all matters: Clause 2.

RESPONSE

Novo Nordisk noted that the complainant alleged that a representative approached him/her to submit semaglutide to their local hospital formulary and that Novo Nordisk medical and market access personnel helped to write the formulary application.

Novo Nordisk submitted that the complaint did not contain enough information for it to take proportionate steps to investigate what specific discussions, if any, might have taken place between Novo Nordisk staff and the first complainant in relation to formulary applications.

However, it was not the role of Novo Nordisk representatives, market access staff or medical staff to write formulary applications and staff were trained on and required to comply with the ABPI Code.

The primary purpose of the field-based market access staff (diabetes outcome directors (DODs)) was to influence key local healthcare decision-makers around the value of Novo Nordisk's portfolio of medicines to secure funding within local diabetes care pathways. This was outlined in the role profile (copy provided). One way to do this was to provide key health professionals with information they requested in order to support their formulary applications. Neither market access, nor any Novo Nordisk staff, completed the formulary applications on behalf of a health professional. Novo Nordisk had provided an example of a Supporting Information Formulary Application (SIFA) document. The front page, and accompanying certificate, clearly stated that this was to support a health professional who was developing a formulary application and was to be provided to the health professional. This complied with the Code.

The role of the representatives in the above process was to support the formulary applicants either by introducing them to the local market access staff or providing information directly as appropriate.

The field-based medical team (regional medical affairs (RMAs)) was non-promotional and the team's key accountability was to exchange credible scientific and medical information with health professionals and ensuring they were aware of, and understood the scientific basis for, and clinical usefulness of, Novo Nordisk products. With regard to formulary support, the team provided clinical data upon request from a health professional to support a formulary application. The role profiles for a diabetes representative and a member of the field based medical team were provided.

Novo Nordisk noted the complainant's speculation that medical staff and market access staff received a commission for writing formulary applications and alleged that a former medical liaison at Novo Nordisk said he/she 'received incentive upon acceptance, for assisting the writing of faster acting insulin as part formulary applications'. Novo Nordisk refuted this claim absolutely. As explained above, staff did not write or assist in the writing of formulary applications.

A bonus was currently available for market access staff and diabetes representatives in connection with inclusion of Ozempic onto local formularies ie once the local NHS committee had assessed the application and agreed that it was to be available for prescription within that area. This bonus was capped, it was not linked to writing formulary applications and did not contribute an undue proportion of remuneration. Details of the bonus scheme were provided. Regional Medical Advisors (RMAs) were not included in this incentive scheme; they were a non-promotional team and were not remunerated based on sales of medicines in their region or the inclusion of Novo Nordisk medicines onto formularies in their region.

Novo Nordisk noted that the complainant alleged that the Formulary Decision Guide (document UK/SM/0818/0304) was misleading in that it omitted 'the fact that semaglutide causes a significant (76%) increase in retinopathy, including blindness'.

As explained in the Ozempic SPC:

> ‘A 2-year clinical trial investigated 3,297 patients with type 2 diabetes, with high cardiovascular risk, long duration of diabetes and poorly controlled blood glucose. In this trial, adjudicated events of diabetic retinopathy complications occurred in more patients treated with semaglutide (3.0%) compared to placebo (1.8%). This was observed in insulin-treated patients with known diabetic retinopathy. The treatment difference appeared early and persisted throughout the trial. Systematic evaluation of diabetic retinopathy complication was only performed in the cardiovascular outcomes trial. In clinical trials up to 1 year involving 4,807 patients with type 2 diabetes, adverse events related to diabetic retinopathy were reported in similar proportions of subjects treated with semaglutide (1.7%) and comparators (2.0%)’.

Novo Nordisk stated that it was conducting a post authorisation safety study (PASS) at the request of the authorities. There had been no change in the SPC with regard to retinopathy data since marketing authorisation was granted.

Novo Nordisk did not accept that the Formulary Decision Guide was misleading and noted that it had been vetted by the Medicines and Healthcare products Regulatory agency (MHRA) together with other Ozempic promotional materials, prior to the launch of the product.

Novo Nordisk was clear that the document complied with the Code. A copy of the guideline was provided. UK/SM/0818/0304 was no longer the current version of the document and had not been in use since March 2019.

Novo Nordisk noted that the complainant stated; ‘… it is very disappointing that Novo Nordisk has deliberately misled formulary applicants with regard to their safety data by omitting the fact that semaglutide causes a significant (76%) increase in retinopathy, including blindness’ and stated that the statement was grossly misleading and stated without context. An assessment of diabetes retinopathy across the SUSTAIN trial program (Visiboll *et al* 2018) showed there was no imbalance in diabetic retinopathy adverse events across the SUSTAIN 1 to 5 trials and Japanese trials. SUSTAIN 6 included 3296 patients and showed that 50 patients in the semaglutide group (3%) vs 29 in the placebo group (1.8%) experienced diabetic retinopathy ie a 76% increase in the semaglutide group. Unlike other GLP1 trials, SUSTAIN 6 did not exclude patients with pre-existing retinopathy but was also not designed to adequately assess diabetic retinopathy as was discussed within the publication. The analysis further showed that the increase in diabetic retinopathy was seen in a specific group of patients; those with pre-existing retinopathy, poorly controlled diabetes and treated with insulin. This group of patients had been specified within the SPC precautions. With respect to blindness, 5 patients in the semaglutide group vs 1 in the placebo group met the criteria for events of diabetes-related blindness. All 5 semaglutide-treated patients had pre-existing proliferative diabetes retinopathy. Information was available for 3 of the 5 semaglutide treated patients post event, none of whom continued to fulfil the criteria for diabetes-related blindness.

This information was within Section 4.4 Special warnings and precautions of the Ozempic SPC which stated:

> ‘In patients with diabetic retinopathy treated with insulin and semaglutide, an increased risk of developing diabetic retinopathy complications has been observed (see section 4.8). Caution should be exercised when using semaglutide in patients with diabetic retinopathy treated with insulin. These patients should be monitored closely and treated according to clinical guidelines. Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy, but other mechanisms cannot be excluded.’

Novo Nordisk provided a copy of a leavepiece which was available at the end of 2018 (UK/OZS/0318/0005). This material was also no longer available. The company also provided copies of the current leavepieces which were used specifically with GPs (UK19OZM00122 and UKOZM00181). The company submitted that the incidence of diabetic retinopathy, and the relevant warnings and precautions for use were clearly included in those pieces. A copy of the electronic sales aid (UK/OZS/0318/0001) which was used by representatives with GPs was also provided and page 31 had information about retinopathy.

Novo Nordisk submitted that all Ozempic representatives were fully briefed and trained on the information outlined above about diabetic retinopathy; and to raise that information proactively in discussions. A copy of the Ozempic Objection Handling and Best Practice document (UK/SM/1118/0395) were provided.

Novo Nordisk refuted the allegation that the representatives were not able to provide the SPC when requested or detailed explanation about retinopathy. The first complainant was anonymous and the email dated 2 October 2019 did not specify to what time period this allegation related, where the alleged communication with the Novo Nordisk representative(s) took place or the identity of the relevant representative(s).

Novo Nordisk stated that it had checked the call reports into its customer care centre and had not found any complaints about representatives not providing an SPC when requested.

Novo Nordisk noted that pages 8 and 9 of the Ozempic Objection Handling and Best Practice document (UK/SM/1118/0395) gave direction to representatives about how to discuss diabetic retinopathy. The section starts with the following:

> "Proactively discussing diabetic retinopathy upfront when you are describing the safety and tolerability profile will help to reduce any confusion the clinician may have heard about diabetic retinopathy with Ozempic."

Further, representatives were trained on and required, to comply with the requirement in the Code, to provide or have available to provide if requested, a copy of the SPC.

Novo Nordisk stated that the prescribing information for Ozempic included the following information about costs:

> **MA numbers and Basic NHS Price:**
>
> Ozempic 0.25mg pre-filled pen EU/1/17/1251/002 £73.25
>
> Ozempic 0.5mg pre-filled pen EU/1/17/1251/003 £73.25
>
> Ozempic 1 mg pre-filled pen EU/1/17/1251/005 £73.25
>
> **Each pre-filled pen delivers 4 doses and includes 4 disposable NovoFine Plus needles**

The first complainant alleged however that 'the costs in the prescribing information were misleading' and asserted 'the pricing is skewed and semaglutide £73.25 x 4 for each month'. It was not clear why the complainant alleged that the costs in the prescribing information were

misleading, particularly as he/she appeared to suggest that the cost for 4 doses of semaglutide was £73.25, as stated in the prescribing information.

Novo Nordisk noted that it had been alleged that the named employee had asked the complainant to:

(i) ‘‘save’ patients from then [sic] knowing that semaglutide was coming’;

(ii) had informed the complainant that ‘direct switching from glp-1 is allowed i.e switching from dulaglutide 1.5mg directly to semaglutide 0.5mg the following week’ and that he/she ‘had since changed his/her response to state switching involved starting at semaglutide 0.25mg dose’.

Novo Nordisk stated that it was not clear what the complainant's allegation was in relation to point (i) above.

In relation to point (ii), the complainant initially stated that the alleged conversations referred to above took place at an EASD conference but later contradicted this and said that the alleged discussions took place in London at a GLP-1 advisory board in 2017.

Novo Nordisk noted that its GLP-1 advisory board took place in London on 9 October 2017. There was no discussion about switching from dulaglutide to semaglutide. Furthermore, there was no UK launch date for semaglutide at that time. There were a limited number of attendees at the advisory board and as the complainant was anonymous, Novo Nordisk did not know if he/she was one of the health professionals present.

Novo Nordisk confirmed that the named employee attended the advisory board but he/she categorically refuted that there were discussions regarding semaglutide and dosing, or semaglutide and switching from dulaglutide, either as part of the formal agenda or in one to one conversation during the breaks. The employee did not recall being asked about switching from another medicine to semaglutide, either before Ozempic was available in the UK or after. He/she was fully aware of the dosing information which was appropriate when switching a patient to Ozempic, and in addition was the primary approver for the standard medical information response which gave dosing and switching information for Ozempic. The standard response in relation to switching from other glucagon like peptide-1 receptor agonists (GLP-1 RAs) to semaglutide, stated that:

(i) ‘the switch from other once-weekly GLP-1 RAs (such as dulaglutide) to semaglutide has not yet been evaluated, and the impact on potential side effects and glycaemic control are unknown;

(ii) when considering initiating a new patient on semaglutide, including those who are on other GLP-1 RA therapies, you should follow the dosing escalation steps and safety considerations detailed within the Summary of Product Characteristics;

(iii) regardless of prior antidiabetic therapy, patients should always start semaglutide at an initiation dose of 0.25mg once-weekly for 4 weeks.’

Novo Nordisk stated that it took its responsibilities to comply with the Code extremely seriously. It was categorically clear that the allegations were unfounded and it denied breaches of Clauses 2, 4.2, 7.1, 7.2, 7.4, 7.5, 7.9, 12.1, 15.1, 15.2, 15.7, 15.8, 15.9 and 9.1.

PANEL RULING

The Panel noted that the Constitution and Procedure stated that the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties.

The complainant had not named the representative nor any of the other staff to which the complaint referred other than the medical lead. The complainant appeared to use the term representative to describe employees of Novo Nordisk, referring to market access, medical and sales.

1 Role of Novo Nordisk employees in formulary applications

The Panel noted that it was not necessarily a breach of the Code for a company or its staff to provide information and material to support a health professional in an application for its medicine/s to be included on formulary. It was important that the role of the company be made clear in such circumstances. The Panel considered that most of those on a formulary decision making body would expect the company to have some involvement in the provision of information etc.

With regard to the printed material for formulary applications, the Panel noted that Novo Nordisk provided two documents. Firstly the Ozempic Supporting Information Formulary Application document (ref UK/OZS/0618/0025(1)), the objective of which was to support clinicians or prescribing decision making committee members in submitting a formulary application. This included prescribing information and was clearly promotional. It was described as being available in person or by email upon request from a health professional. The second document was the Ozempic Formulary Decision Guide (UK/SM/0818/0304), the objective of which was an overview of key information required to make formulary submission in the UK. It included the 'Guidelines in Practice' logo as well as prescribing information and was clearly promotional. It was for UK payers and health professionals.

It appeared from the objection handler (ref UK/SM/1118/0395, version 1.1 approved in November 2018) that representatives were asked to call upon health professionals who were 'important stakeholders in the formulary submission process' as Ozempic was not currently available for prescribing and the company was focussed on getting formulary submissions prepared and submitted. The objection handler did not include any instructions about writing formulary applications. It encouraged health professionals to use Victoza whilst waiting for Ozempic to become available.

The Panel noted Novo Nordisk's submission that it was not the role of representatives, market access or medical staff to write formulary applications or complete formulary applications on behalf of a health professional. The role of the representatives was to support the formulary applicants either by introducing them to the local diabetes outcomes director (field based market access role) or providing information directly as appropriate.

The key purpose of the market access role was to achieve market access across Novo Nordisk's portfolio through the implementation of corporate and market access strategies aligned with brand marketing strategies. According to Novo Nordisk the purpose of the role was to influence key decision makers around the value of Novo Nordisk's portfolio of medicines, demonstrating outcomes and using value propositions to secure funding within local diabetes care pathways. One way to do this was to provide key health professionals with information

they requested in order to support their formulary applications. Market access staff worked in collaboration with sales, medical and marketing to develop local business plans and ensure implementation of the plan as appropriate to their role. The Panel considered that it was difficult to see that this role was anything other than promotional as defined in Clause 1.2 of the Code.

The Panel noted Novo Nordisk's submission that the regional medical advisors' role with regard to formulary support was the provision of clinical data upon request by a health professional to support a formulary application.

The Panel noted that the key purpose of the regional medical advisor role included leading the development of services for medics and other healthcare professionals in support of new business opportunities and strategic objectives taking into account local and national business needs. The main outcome was to ensure that health professionals were aware of and understood the scientific basis for and clinical benefits of Novo Nordisk compounds. The key accountabilities included maintaining relations with key customers/influencers and institutions building local credibility personally and on behalf of Novo Nordisk. As well as contributing to medico-marketing strategy and providing support for local business plans to promote the achievement of targets. The Panel considered that this role appeared to include promotion of medicines as defined by Clause 1.2 of the Code.

The Panel did not consider that the complainant had established that any Novo Nordisk employee had written a formulary application as alleged or had not been appropriately briefed in relation to the company's role with regard to formulary applications. The Panel noted that the complainant had not detailed why in his/her view the activity constituted disguised promotion; it was not for the Panel to make out a complainant's allegations. The Panel noted its comments above and therefore ruled no breach of Clauses 12.1, 15.2, 15.9, 9.1 and 2.

2 Alleged incentives for formulary applications

With regard to the allegation that staff including medical were incentivised upon acceptance of formulary applications that they helped to write, the Panel noted its comments and rulings above; the complainant had not established that any Novo Nordisk employee wrote formulary applications on behalf of health professionals.

The document describing the bonus payment scheme for market access and sales dated September 2018 set out the scheme rules. Medical staff were not included in the incentive scheme. The Panel noted that it appeared that market access and sales staff were incentivised to obtain formulary status for products which was not necessarily a breach of the Code. Details were provided.

Clause 15.7 required that representatives were paid a fixed basic salary and any addition proportion to sales of medicines must not constitute an undue proportion of their remuneration. Clause 15.7 did not prevent the provision of a bonus to representatives and thus the Panel ruled no breach of Clause 15.7 based on the allegation. The Panel did not accept that paying a bonus which appeared to be capped and did not appear to constitute an undue proportion of the representatives remuneration meant that Novo Nordisk had failed to maintain a high standard and no breach of Clause 9.1 was also ruled.

3 Content of Ozempic Formulary Decision Guide (Guidelines in Practice document)

The Panel noted its comments above regarding the printed material. The first document (not the subject of this allegation), (ref UK/OZS/0618/0025(1), included proposed formulary wording, clinical evidence including comparisons with other medicines in relation to glycaemic control, weight loss and cardiovascular benefits. The adverse events and tolerability section included information about diabetic retinopathy. Early worsening of retinopathy symptoms was reported in a small proportion of a subset of patients with a previous history of diabetic retinopathy.

The second document, the formulary decision guide (UK/SM/0818/0304) which was the subject of this allegation, included an overview of the key information required for a formulary submission in the UK. This two-page document did not specifically refer to diabetic retinopathy other than a reference in the prescribing information. The Panel noted that the formulary decision guide at issue had to be capable of standing alone with regard to the requirements of the Code and could not rely on the inclusion of relevant safety information being included in the prescribing information. The Panel considered that the failure to mention diabetic retinopathy in the formulary decision guide was concerning, particularly given the company was required to do a further study at the request of the regulatory authorities in this regard. The available evidence was not reflected in the formulary decision guide and the Panel therefore ruled a breach of Clause 7.9. The Panel considered that the absence amounted to a failure to maintain high standards and a breach of Clause 9.1 was ruled. On balance the Panel did not consider that its ruling above meant that in addition the material was misleading as alleged and therefore ruled no breach of Clause 7.2.

The Panel noted that whilst the information on retinopathy was only in the prescribing information in the summary document, fuller information was provided in the detailed supporting information for formulary application and other materials. On balance the Panel decided that the circumstances did not amount to a breach of Clause 2.

4 Provision of the summary of product characteristics and detailed explanation of retinopathy

With regard to the allegation concerning the failure of the representative to provide the SPC when requested, the Panel considered that the lack of detailed information from the complainant including who he/she had asked for the SPC, meant that he/she had not provided evidence to show that the SPC had not been provided upon request. The Panel therefore ruled no breach of Clause 15.8.

With regard to the allegation concerning the failure of the representative to provide a detailed explanation about retinopathy, the Panel noted that the two current leavepieces (ref UK19OZM00122 and UK19OZM00181) and an e-detailer (ref UK/OZS/0318/0001) provided by Novo Nordisk included information in sections headed ‘diabetic retinopathy’. A leavepiece used in 2018 (ref UK/OZS/0318/0005) included very brief details in a general paragraph headed ‘common side effects’. The objection handler gave further information including encouraging representatives to proactively discuss diabetic retinopathy upfront when describing the safety and tolerability profile. Regional medical advisers were also available to discuss diabetic retinopathy. It was not known what materials the medical advisers used in such circumstances. However, the Panel considered that the lack of detailed information from the complainant including who he/she had asked for information on retinopathy, meant that he/she had not provided evidence to show on the balance of probabilities that there was a breach of the Code. The Panel therefore ruled no breach of Clauses 15.1 and 15.9.

5 Cost and promotion prior to availability

The Panel considered that the complainant was not clear with regard to the allegations about the cost of the medicine. Novo Nordisk submitted that the costs in the prescribing information were accurate. The Panel did not consider that the complainant had shown on the balance of probabilities that the information about costs was misleading. The Panel therefore ruled no breach of Clause 7.2 of the Code. The Panel noted that Clause 4.1 of the Code stated that prescribing information listed in Clause 4.2 must be provided in a clear and legible manner. Clause 4.2 listed the components of prescribing information which required the cost to be included. Failure to provide the required information listed in Clause 4.2 would be a breach of Clause 4.1. The Panel noted that although Clause 4.2 had been raised by the complainant it decided that in these particular circumstances Clause 4.1 was the appropriate clause to consider and thus it ruled no breach of Clause 4.1.

The Panel noted that it appeared that Ozempic received its marketing authorization in February 2018 (according to information on the eMC). It was not available until January 2019 according to the complainant and various documents provided by Novo Nordisk. The objection handler encouraged health professionals to use Victoza whilst waiting for Ozempic to become available.

The Panel did not consider it was necessarily a breach of the Code to promote a medicine before that medicine was available for supply. Obviously in such circumstances companies needed to be clear about the position. The Panel considered that the complainant had not shown that Novo Nordisk had been misleading in this regard and no breach of Clause 7.2 was ruled.

6 Alleged conversations with named employee

With regard to the allegations about the named employee, the Panel noted that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. The complainant had provided no supporting evidence in relation to his/her allegations.

The Panel noted that the complainant had not detailed why in his/her view the employee in allegedly stating that the complainant should 'save' patients from knowing that semaglutide was coming, was in breach of the Code; it was not for the Panel to make out a complainant's allegations. Nor did the complainant provide evidence of the prescribing issues referred to in his/her complaint. The objection handler for some staff was clear that they were to encourage health professionals to consider Victoza whilst waiting for Ozempic to become available. It would be concerning if a company employee had suggested deferring treatment for patients with diabetes until Ozempic was available. The Panel did not consider that the complainant had provided evidence to show that on the balance of probabilities that there was a breach of the Code. The Panel therefore ruled no breach of Clauses 7.2 in this regard and consequently ruled no breach of Clauses 2 and 9.1.

Novo Nordisk referred to the advice regarding switching from other GLP-1 receptor agonists to Ozempic in the undated medical information document which stated that there was no data on switching from any other GLP-1RAs to Ozempic and that Novo Nordisk could not provide specific recommendations. The document also stated that regardless of prior antidiabetic therapy patients should start semaglutide at an initiation dose of 0.25mg once weekly for 4 weeks after which the dose should be increased to 0.5mg once-weekly. This initiation and dose increase was intended to mitigate potential gastrointestinal side effects. Health professionals

considering transitioning from other products to Ozempic were advised to exercise clinical judgement taking into account the patient's glycaemic control, concomitant medications, particularly insulin and/or sulphonylureas and hypoglycaemic risk.

The Panel was concerned that the complainant alleged he/she was given different advice to that set out in the medical information document and that allegedly following that advice had led to patients having problems with hypoglycaemia. The complainant had initially stated the advice was given at one meeting and then that it was at a different meeting, an advisory board meeting. Novo Nordisk denied that the topic had been raised at the advisory board meeting. The Panel noted that no evidence was provided by the complainant to support the allegations and therefore ruled no breach of Clauses 7.2, 9.1 and 2.

The Panel noted that the case preparation manger raised Clause 7.9 in relation to the above two allegations which stated that information and claims about adverse reactions must reflect available evidence or be capable of substantiation by clinical experience. It must not be stated that a product had no adverse reactions, toxic hazards or risks of addiction or dependency. The word 'safe' must not be used without qualification. The Panel did not consider that the complainant had made an allegation with regard to Clause 7.9 in this regard and therefore made no ruling.

7 Medical information enquiry

With regard to the allegation concerning the failure of Novo Nordisk to respond to a medical information query within 10 days, the Panel did not know what the query was, when it had been asked or if or when a response had been received. It considered that the lack of detailed information from the complainant meant that he/she had not provided evidence to show on the balance of probabilities that there was a breach of the Code. The Panel therefore ruled no breach of Clauses 7.1 and 7.5.

8 Cummulative effect

In relation to the allegation that Novo Nordisk's conduct was in breach of Clause 2, the Panel noted its rulings above. It did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure and reserved for such use. The Panel therefore ruled no breach of Clause 2.

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Complaint received **10 October 2019**

Case completed **18 May 2020**