**CASE AUTH/3299/1/20**

# COMPLAINANT v NOVO NORDISK

## Promotion of Saxenda

**A named individual complained about the promotion of Saxenda (liraglutide) by Novo Nordisk at the annual British Fertility Conference, in January 2020.**

**Saxenda was indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adults who were either obese or were overweight with at least one weight-related comorbidity. Saxenda was a glucagon-like peptide-1 (GLP-1) analogue. The Saxenda summary of product characteristics (SPC) stated in Section 4.6, Fertility, pregnancy and lactation, that the medicine should not be used during pregnancy or breastfeeding and that if a patient wished to become pregnant or pregnancy occurred, treatment with liraglutide should be discontinued. It was also stated that apart from a slight decrease in the number of live implants, animal studies did not indicate harmful effects with respect to fertility.**

**The complainant explained that the objective of the British Fertility Conference was to discuss fertility and reproduction. The complainant alleged that the representative quite confidently promoted Saxenda to help with weight loss in order to help women get pregnant but never stated that Saxenda was contraindicated in pregnancy or fertility. Everyone at the conference worked in fertility clinics/centres with the objective to assist reproduction; therefore, it was well known that pregnant women at these fertility clinics/centres would be on a host of medicines to help with reproduction such as clomifene and progesterone. Fertility clinicians were not familiar with GLP-1 analogues or the associated warnings and a few believed that it could be used for their patients already on clomifene and progesterone. The representative did not warn against this or tell health professionals about the warnings/contraindications associated with Saxenda. The complainant alleged that this was off-label promotion and dangerous.**

**The complainant stated that it was clear that the representative had not been trained specifically for promotion in fertility and he/she did not refer to safety in this area which was very worrying.**

**The complainant stated that the representative gave out two items from the stand (zapper from demo pens) and these were also left for delegates to take when the stand was not manned. The complainant was very concerned about a promotional piece which deliberately targeted women (at a fertility conference) with no regard for safety issues, specifically the warning not to use in the patients that conference delegates would be treating! The 'benefits beyond weight loss' section did not mention anything about a woman's ability to get pregnant. The complainant queried the relevance of what was promoted at the conference. The complainant stated that the leaflet and the representative iterated that the 'safety' of Saxenda was well investigated but queried how this was so given that pregnant women were excluded.**

**The complainant queried whether Novo Nordisk had the data to substantiate the claim that the safety of Saxenda was well investigated in the fertility space and queried why the suspected unexpected serious adverse reactions with regard to pregnancy, fertility and lactation from the trials were not shared in the leavepiece. It was very clear from the SPC that if a patient wished to become pregnant that liraglutide should be stopped (or clearly not initiated. The promotion of Saxenda at a fertility conference could not be more controversial. Such promotion was so harmful to fertility patients.**

**The complainant also noted that patient material was given out from the exhibition stand to delegates along with the promotional leavepiece. The patient brochure was also left out for delegates to take when no representative was there. The 'eating healthy' section was not appropriate for a pregnant woman or one trying to become pregnant. Cutting down calories was not advised in pregnancy. Similarly, the 'increased activity' described was too generic and not appropriate for pregnant women. The complainant alleged that the patient brochure, approved in 2016, was too old.**

**The complainant alleged that the Novo Nordisk stand was unmanned for a period of time and this was detrimental when delegates took material from the stand which did not explain the Saxenda safety warning, with a view to treating women seeking assisted fertility.**

**The detailed response from Novo Nordisk is given below.**

**The Panel noted Novo Nordisk's submission that obesity was strongly associated with the failure of assisted reproduction techniques and it was not uncommon for clinicians to advise patients about the importance of weight management before starting a cycle of treatment in order to maximise success.**

**The Panel considered that it was not necessarily unacceptable for Novo Nordisk to promote Saxenda at the fertility conference providing the way in which it was done complied with the Code.**

**The Panel noted Novo Nordisk's submission that pregnancy, fertility and lactation were not listed in Section 4.3 Contraindications, of the Saxenda SPC as stated by the complainant and that the relevant details were included in the prescribing information at the end of the leavepiece about women's health. The Panel also noted the content of Sections 4.6 and 5.3 of the Saxenda SPC.**

**The Panel noted that the materials on the stand were general and had not been tailored to the audience. Although the health professionals attending the fertility meeting would be aware of the need for care when prescribing medicines in women hoping to become pregnant, in the Panel's view, on balance, it was not sufficient to rely on the prescribing information to provide the highly relevant information about the use of Saxenda in patients hoping to become pregnant or who became pregnant. In the Panel's view, it would have been prudent to include a more prominent, clear reference to the relevant information within the Saxenda SPC considering the product was being promoted at a fertility conference. Delegates should be in no doubt about the use of Saxenda prior to fertility treatment. The Panel considered that failure to do so meant that Novo Nordisk had not maintained high standards and a breach of the Code was ruled.**

**With regard to the allegation that the representative on the stand promoted Saxenda for weight loss in order to help women get pregnant but did not state the warnings/contraindications in relation to pregnancy or fertility, the Panel noted Novo Nordisk's submission that Saxenda was promoted in accordance with the licensed indication and was not inconsistent with the SPC and that none of the material on the stand referred to Saxenda as a treatment to improve fertility or to increase the chances of becoming pregnant. The Panel noted the that the parties' accounts differed. The Panel did not consider that the complainant had established, on the balance of probabilities, that the promotion of Saxenda by the Novo Nordisk representatives or the materials available on the stand were such that they were inconsistent with the particulars listed in the Saxenda SPC and therefore no breach of the Code was ruled. This ruling was upheld by the Appeal Board following an appeal from the complainant.**

**With regard to patients already on clomifene and progesterone, the complainant provided few or no details of why, in his/her view, this was in breach of the Code. According to the SPC there did not appear to be any interactions with these medicines. It was not for the Panel to make out a complainant's allegations and the Panel therefore made no ruling in this regard.**

**There was no evidence before the Panel that either of the representatives had failed to maintain a high standard of ethical conduct or had not complied with all of the relevant requirements of the Code when manning the stand at the fertility conference and no breach of the Code was ruled. This ruling was upheld by the Appeal Board following an appeal from the complainant.**

**The Panel considered that the complainant had not established, on the balance of probabilities, that the representatives had not been given adequate training in relation to Saxenda as alleged and no breach of the Code was ruled. This ruling was appealed by the complainant.**

**The Panel noted Novo Nordisk's submission that at no point were the representatives instructed to promote Saxenda as a treatment to improve fertility or the chances of becoming pregnant. According to Novo Nordisk both representatives had been trained on the Saxenda SPC which covered the contraindications and special warnings and precautions sections, including pregnancy, fertility and lactation and had been trained to promote Saxenda in accordance with the licensed indication. In addition, the representatives had been briefed verbally with regard to how to use the materials on the stand and their roles at the fertility conference. The Panel did not consider that the complainant had established, on the balance of probabilities, that the representatives had not been appropriately briefed as alleged and therefore the Panel ruled no breach of the Code. This ruling was appealed by the complainant.**

**The Panel noted that the patient brochure was re-certified in 2018 and therefore ruled no breach of the Code. This ruling was upheld by the Appeal Board following an appeal from the complainant.**

**The Panel noted Novo Nordisk's submission that the Saxenda injection device was available for the representatives to demonstrate its use if requested: it was not given away from the stand and Novo Nordisk did not have anything that matched the complainant's description of 'zapper from demo pens'. The Panel therefore ruled no**

**breaches of the Code in that regard. These rulings were upheld by the Appeal Board following an appeal from the complainant.**

**Turning to the complainant's concerns about the Saxenda women's health leavepiece, the Panel considered that it was not necessarily a breach of the Code for the leavepiece to only include information about women in general rather than very specific information about the outcome of clinical trials in relation to women who might be candidates for fertility treatment. The Panel did not consider that the complainant established, on the balance of probabilities, that the information was misleading as alleged and no breach of the Code was ruled. This ruling was appealed by the complainant.**

**With regard to the complainant's concerns regarding the patient brochure the Panel did not consider that making the patient brochure available at the fertility meeting was in itself unacceptable. The complainant had not established, on the balance of probabilities, that the patient brochure was misleading as alleged and no breach of the Code was ruled. This ruling was appealed by the complainant.**

**The Panel noted that the complainant listed a number of other clauses but provided few or no details of why, in his/her view, Novo Nordisk was in breach of those clauses. It was not for the Panel to make out a complainant's allegations. The Panel, therefore, ruled no breaches of the Code. All these rulings were appealed by the complainant.**

**The Panel noted that a ruling of a breach of Clause 2 of the Code was a sign of particular censure and reserved for such. In that regard, the Panel did not consider that the particular circumstances of this case warranted such a ruling and no breach of Clause 2 was ruled. This ruling was appealed by the complainant.**

**The complainant appealed all the Panel's rulings of no breaches of the Code.**

**The Appeal Board noted that this was the first fertility conference that Novo Nordisk had attended to promote Saxenda for weight loss. The Appeal Board noted the company's submission about the rationale for exhibiting at the conference, in particular the relevance of weight management prior to starting fertility management.**

**The Appeal Board noted that Section 4.6 of the Saxenda SPC Fertility, pregnancy and lactation stated, *inter alia*, that there were limited data from the use of liraglutide in pregnant women. Studies in animals had shown reproductive toxicity (see section 5.3). The potential risk for humans was unknown. It further stated that liraglutide should not be used during pregnancy. If a patient wished to become pregnant or pregnancy occurred, treatment with liraglutide should be discontinued. It also stated that apart from a slight decrease in the number of live implants, animal studies did not indicate harmful effects with respect to fertility. Section 5.3 referred to preclinical safety data. This section included a statement that animal studies did not indicate direct harmful effects with respect to fertility but slightly increased early embryonic deaths at the highest dose as well as information about the effects of dosing mid-gestation.**

**The Appeal Board was particularly concerned that, given Saxenda was being promoted at a fertility conference and the warnings in the Saxenda SPC for women trying to become pregnant, health professionals treating them should be fully informed of the position. Health professionals attending the conference might be managing woman with**

**sub-fertility prior to any referral for assisted fertility treatment. Some of these women would be advised to lose weight and it was possible that health professionals who did not work in assisted fertility might prescribe or the patient's general practitioner might be asked to prescribe, Saxenda. It was therefore important that all were made aware of the risks in pregnancy and the need to take precautions to not fall pregnant or to discontinue Saxenda if they fell pregnant.**

**The Appeal Board considered that women with fertility problems were potentially a vulnerable group and whilst being treated for fertility problems, there was a possibility that some might still be trying to conceive naturally.**

**The Appeal Board noted the Panel's consideration including its ruling that Novo Nordisk had failed to maintain high standards.**

**The Appeal Board considered that the intended audiences for the printed material, health professionals and patients, needed very clear and precise guidance about the use of Saxenda should a woman decide to try to conceive or fell pregnant due to the warnings in Sections 4.6 and 5.3 of the Saxenda SPC. This was particularly relevant when the company was promoting the medicine at a fertility conference.**

**The patient brochure contained no reference to such warnings. The Appeal Board considered that the failure to reflect the relevant warnings in the SPC was such that the patient brochure was misleading and it ruled a breach of the Code. The appeal on this point was successful.**

**The Appeal Board noted that information about prescription only medicines which was made available to the public either directly or indirectly must be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. The Appeal Board noted its ruling of a breach of the Code above with regard to the patient brochure and considered that the patient material was misleading with respect to the safety of the product in pregnancy, particularly given its availability at a fertility conference. The Appeal Board therefore also ruled a breach of the Code. The appeal on this point was successful.**

**The Appeal Board noted similarly that the women's health leavepiece contained no clear reference to the information and warnings regarding pregnancy in Sections 4.6 and 5.3 of the SPC. This was mentioned in the prescribing information. However, the Appeal Board considered that particularly given its use at a fertility conference the women's health leavepiece was misleading as it was unclear about these warnings and potential risks, and it therefore ruled a breach of the Code. The appeal on this point was successful.**

**The Appeal Board noted Novo Nordisk's submission that both representatives were experienced, each had had prior training on the Saxenda SPC; they had been verbally briefed on how to use the two pieces of material available on the stand and about their roles and responsibilities while at the conference. The Appeal Board noted that although Novo Nordisk was asked for copies of relevant briefing/training material none was provided. This was the first fertility conference Novo Nordisk had attended to promote Saxenda for weight loss. Given that this was a new area and the specific warnings in Sections 4.6 and 5.3 of the Saxenda SPC especially with regard to toxicity and safety, it was particularly important that certified briefing material for the representatives**

**(preferably written) was provided. Novo Nordisk had no written certified record of the verbal briefing given and in the Appeal Board's view the company had not been able to show that the representatives had been adequately trained to promote Saxenda within the fertility area. The Appeal Board therefore ruled a breach of the Code. The appeal on this point was successful.**

**The Appeal Board queried whether a verbal briefing was appropriate in the circumstances and as there was no certified record of the verbal briefing the Appeal Board ruled a breach of the Code. The appeal on this point was successful.**

**The Appeal Board noted that the complainant had listed a number of other clauses of the Code to be considered. The Panel had dealt with these very briefly on the basis that the complainant had provided few or no details as to why Novo Nordisk was in breach of those clauses. All were appealed by the complainant and the Appeal Board agreed that little evidence had been provided by the complainant. Some of the matters were dealt with above by the Appeal Board and the remainder were ruled not to be in breach of various clauses of the Code.**

**The Appeal Board noted that a ruling of a breach of Clause 2 was a sign of particular censure and was reserved for such circumstances. The Appeal Board considered that the failure to provide highly relevant and vital information about the use of the product in pregnancy and those wishing to become pregnant meant that there was a potential patient safety issue. The Appeal Board considered that the circumstances amounted to a breach of Clause 2 and ruled accordingly. The appeal on this point was successful.**

A named individual complained about the promotion of Saxenda (liraglutide) by Novo Nordisk at the annual British Fertility Conference, 8-11 January 2020.

Saxenda was indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adults who were either obese or were overweight with at least one weight-related comorbidity. Saxenda was a glucagon-like peptide-1 (GLP-1) analogue. The Saxenda summary of product characteristics (SPC) stated in Section 4.6, Fertility, pregnancy and lactation, that the medicine should not be used during pregnancy or breastfeeding and that if a patient wished to become pregnant or pregnancy occurred, treatment with liraglutide should be discontinued. It was also stated that apart from a slight decrease in the number of live implants, animal studies did not indicate harmful effects with respect to fertility.

**COMPLAINT**

The complainant explained that the objective of the British Fertility Conference was to discuss fertility and reproduction. Every product (medicine, device, education etc) at the lecture and exhibition area was solely about fertility and reproduction. No product was there with a warning that it was clearly contraindicated in fertility and pregnancy. Saxenda had a clear warning, even in bold on its prescribing information regarding such a contraindication. The complainant alleged that the representative quite confidently promoted Saxenda to help with weight loss in order to help women get pregnant. Although it was clear that Saxenda could help to lose weight and help get the women pregnant, the representative never stated that Saxenda was contraindicated in pregnancy or fertility. Everyone at the conference worked in fertility clinics/centres with the objective to assist reproduction; therefore, it was well known that pregnant women at these fertility clinics/centres would be on a host of medicines to help with

reproduction such as clomifene and progesterone. Fertility clinicians were not familiar with GLP-1 analogues or the associated warnings and a few believed that it could be used for their patients already on clomifene and progesterone. The representative did not warn against this or tell health professionals about the warnings/contraindications associated with Saxenda. The complainant alleged that this was terrible off-label promotion and very dangerous prescription of use by the representative to fertility delegates.

The complainant stated that it was clear that the representative had not been trained specifically for promotion in fertility and he/she did not refer to safety in this area which was very worrying.

The complainant stated that the representative gave out two items from the stand (zapper from demo pens) and these were also left for delegates to take when the stand was not manned. The complainant was very concerned about a promotional piece approved in January 2020 which deliberately targeted women (at a fertility conference) with no regard for safety issues, specifically the warning not to use in the patients that conference delegates would be treating! The complainant stated that page 3 of the leavepiece, which referred to clinical trials, did not state that pregnancy, desire for pregnancy and lactation were exclusion criteria – a major omission especially at the biggest annual fertility congress. The point that the average patient starting weight of 106.3kg (also in illegible font size) was way above that of the fertility population thus gave a false impression of the amount of weight loss achievable in that population. There was also no mention that once Saxenda was stopped, weight increased therefore not addressing the cause of fertility issues in these women. The complainant alleged that the representative failed to talk about all of these points.

The 'benefits beyond weight loss' section did not mention anything about a woman's ability to get pregnant. The complainant queried the relevance of what was promoted at the conference.

The complainant stated that the leaflet and the representative iterated that the 'safety' of Saxenda was well investigated but queried how this was so given that pregnant women were excluded; but Novo Nordisk had the nerve to promote it at a major fertility conference.

The complainant queried whether Novo Nordisk had the data to substantiate the claim that the safety of Saxenda was well investigated in the fertility space and queried why the suspected unexpected serious adverse reactions with regard to pregnancy, fertility and lactation from the trials were not shared in the leavepiece. Surely this was critical information for health professionals treating women seeking fertility, even if the data was for liraglutide 1.2/1.8mg – it was vital to share safety data/yellow card data. [Liraglutide as Victoza was another Novo Nordisk medicine indicated for the treatment of certain patients with diabetes]. The complainant noted that the Medicines and Healthcare products Regulatory Agency (MHRA) had asked for a post-authorisation safety study to be undertaken on liraglutide. It was very clear from the SPC that if a patient wished to become pregnant that liraglutide should be stopped (or clearly not initiated). The promotion of Saxenda at a fertility conference could not be more controversial. Such promotion was so harmful to fertility patients.

The complainant drew attention to Sections 4.6 and 5.3 of the SPC:

Section 4.6 stated:

> 'Studies in animals have shown reproductive toxicity. Liraglutide should not be used during pregnancy. If a patient wishes to become pregnant or pregnancy occurs, treatment with liraglutide should be discontinued.'

Section 5.3 stated:

> 'Animal studies indicated slightly increased early embryonic deaths. Dosing with liraglutide during mid-gestation caused a reduction in maternal weight and foetal growth with equivocal effects on ribs in rats and skeletal variation in the rabbit. Neonatal growth was reduced in rats while exposed to liraglutide and persisted in the post-weaning period in the high dose group. It is unknown whether the reduced pup growth is caused by reduced pup milk intake due to a direct GLP-1 effect or reduced maternal milk production due to decreased caloric intake.'

The complainant also noted that patient material was given out from the exhibition stand to delegates along with the promotional leavepiece. The patient brochure was also left out for delegates to take when no representative was there. The 'eating healthy' section on page 13 of the brochure was not appropriate for a pregnant woman or one trying to become pregnant. Cutting down calories was not advised in pregnancy. Similarly, the 'increased activity' described was too generic and not appropriate for pregnant women who could not undertake vigorous/intensive exercise. The complainant alleged that the patient brochure, approved in 2016, was too old.

The complainant alleged that the Novo Nordisk stand was unmanned from about 3pm on 9 January 2020 and for most of 10 January 2020. Again, for the above reasons with no safety warning of Saxenda being explained, this was detrimental when delegates took the material from the stand with a view to treating women seeking assisted fertility.

The complainant stated that as an emergency measure, Novo Nordisk should apologise to all conference attendees and in fertility manuscripts as well as the BMJ, nursing and embryology journals. This was really worrying for the women seeking fertility treatment and a very real problem for the women who needed to lose weight to aid their fertility.

The complainant included a reference to thalidomide. The complainant alleged breaches of Clauses 2, 3.2, 4.2 (succinct statement of common adverse reactions likely to be encountered in clinical practice = clearly adverse events relevant to fertility practice were omitted), 7.2, 7.3, 7.4, 7.9, 9.1, 14.1, 14.3, 14.5, 15.1, 15.2, 15.9, 15.10, 16, 18.2 and 29 (as Clause 2 was issued in 2010 for liraglutide) and any other clauses that the Authority considered relevant.

When writing to Novo Nordisk, the Authority asked it to consider the requirements of Clauses 4.1 rather than 4.2, 16.1 rather than 16, 18.1 and 26.2 of the Code in addition to those clauses cited by the complainant save Clause 15.10 which was a statement of principle and could not be breached.

**RESPONSE**

Novo Nordisk explained that Fertility 2020 was an annual joint fertility conference hosted by the Association of Clinical Embryologists, the British Fertility Society and the Society for Reproduction and Fertility. Fertility 2020 took place 9-11 January 2020 in Edinburgh and focussed on fertility and reproductive medicine. A copy of the agenda was provided.

Novo Nordisk stated that it purchased stand space at the conference in order to exhibit Saxenda. A sponsorship agreement between the company and the conference organiser was in place.

Novo Nordisk noted that Saxenda was 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:
    - ≥30 kg/$m^2$ (obese), or
    - ≥27 kg/$m^2$ to <30 kg/$m^2$ (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.

Saxenda was promoted at the conference because obesity was a common and multi-system disease that had important clinical consequences on multiple disease areas. Many patients and health professionals understood the importance of weight management as an adjuvant therapy in addition to disease-specific treatment. In addition, obesity was strongly associated with the failure of assisted reproduction techniques. This was well documented and described in guidelines from the National Institute for Health and Care Excellence (NICE) CG156, from 2004, 2013 and 2017 (copy dated February 2013 provided). Section 1.2.6 of the guideline dealt solely with the effect of obesity on fertility detailing that women with a BMI of over 30 would likely take longer to conceive and that men with a BMI of over 30 might have reduced fertility. Section 1.10.4.1 stated: 'Women should be informed that female BMI should ideally be in the range 19–30 before commencing assisted reproduction, and that a female BMI outside this range is likely to reduce the success of assisted reproduction procedures. [2004]'.

Novo Nordisk noted that many clinical commissioning groups had a maximum BMI threshold when deciding who should be funded for assisted reproduction. The awareness of Saxenda as a treatment option for obesity was important to a medical community well versed with the above NICE guidelines. It was not uncommon for clinicians to advise patients about the importance of weight management before starting a cycle of treatment in order to maximise success. It was therefore highly relevant that health professionals working in fertility knew that Saxenda was a treatment option for obesity prior to starting fertility therapy, hence the reason for exhibiting at the conference.

The exhibition stand consisted of a table displaying Saxenda materials; no stand panels were used. The stand was manned by two representatives. Representative A set up and manned the stand on 9 January from 8am - 2:30pm; he/she took a break between noon and 12.30pm for which representative B covered the slot. Representative B manned the stand from 2.30pm for the remainder of the day on 9 January and on 10 January when the exhibition stand was taken down; it was not used on the final day of the conference. Both representatives had sat and passed the ABPI Medical Representatives' Examination.

Only two pieces of material were available on the stand:

1 A patient brochure (ref UK/SA/0616/0068) for health professionals to provide to patients prescribed Saxenda for the treatment of obesity;

2 A Saxenda women's health leavepiece (ref UK19SX00080) created to raise the awareness of comorbidities and complications of obesity in women and to provide information on the efficacy and safety of Saxenda.

Copies of each item and the accompanying certificates were provided. Novo Nordisk noted that the women's health leavepiece was certified on 7 January 2020, the final form check was performed on 8 January 2020 as confirmed in an email. The job bag certificate confirming the final form check was completed and signed in the copy approval system on 9 January 2020.

Novo Nordisk noted that the Saxenda injection device was also available on the stand so that the representatives could demonstrate how it was used if requested. Only one such device was used on the stand at any one time. The device was not given away from the stand. Novo Nordisk stated that it did not have anything that matched the complainant's description of 'zapper from demo pens'.

Novo Nordisk noted that both representatives were experienced and each had been trained on the Saxenda SPC which covered the contraindications and special warnings and precautions sections, including pregnancy, fertility and lactation; they had been verbally briefed on how to use the two pieces of material available on the stand and about their roles and responsibilities while at the conference.

Due to the positioning of the stand, minimal interactions occurred and included a delegate based overseas who enquired whether Saxenda was available in his country of residence and a separate enquiry regarding whether a sample of Saxenda could be provided which was refused.

The two representatives were trained to promote Saxenda in accordance with the licensed indication. At no point were they instructed to promote Saxenda as a treatment to improve fertility or the chances of becoming pregnant. In addition, none of the material on the stand referred to Saxenda as a treatment to improve fertility or to increase the chances of becoming pregnant.

Given the stand's poor positioning, and thus the limited number of interactions, it was unclear how the complainant had concluded that the representative had confidently promoted Saxenda to help with weight loss in order to help women get pregnant and never stated that Saxenda was contraindicated in pregnancy or fertility.

Novo Nordisk noted that pregnancy, fertility and lactation were not listed in Section 4.3 Contraindications, of the Saxenda SPC (as stated by the complainant). Section 4.6, Special Warnings and Precautions, stated:

> 'Pregnancy
> There are limited data from the use of liraglutide in pregnant women. Studies in animals have shown reproductive toxicity (see Section 5.3). The potential risk for humans is unknown.
>
> Liraglutide should not be used during pregnancy. If a patient wishes to become pregnant or pregnancy occurs, treatment with liraglutide should be discontinued.
>
> Breast-feeding

It is not known whether liraglutide is excreted in human milk. Animal studies have shown that the transfer of liraglutide and metabolites of close structural relationship into milk is low. Non-clinical studies have shown a treatment related reduction of neonatal growth in suckling rat pups (see Section 5.3). Because of lack of experience, Saxenda should not be used during breast-feeding.

Fertility
Apart from a slight decrease in the number of live implants, animal studies did not indicate harmful effects with respect to fertility (see Section 5.3).'

Section 5.3 Pharmacological Properties, stated:

'Animal studies did not indicate direct harmful effects with respect to fertility but slightly increased early embryonic deaths at the highest dose. Dosing with liraglutide during mid-gestation caused a reduction in maternal weight and foetal growth with equivocal effects on ribs in rats and skeletal variation in the rabbit. Neonatal growth was reduced in rats while exposed to liraglutide and persisted in the post-weaning period in the high dose group. It is unknown whether the reduced pup growth is caused by reduced pup milk intake due to a direct GLP-1 effect or reduced maternal milk production due to decreased caloric intake.'

The prescribing information on the Saxenda women's health leavepiece included information on fertility, pregnancy and lactation and clearly stated 'Saxenda should not be used during pregnancy. If a patient wishes to become pregnant, or pregnancy occurs, treatment with Saxenda should be discontinued. It should not be used during breast-feeding'.

As mentioned previously, the focus of the Saxenda women's health leavepiece was to provide information on the comorbidities and complications associated with obesity and the efficacy and safety of Saxenda. The leavepiece did not promote Saxenda as a treatment to aid infertility or pregnancy. Any alleged discussions that took place on the stand around the safety of Saxenda would have occurred in the context of the licensed indication and in accordance with the adverse events listed in the SPC.

With regard to the complainant's comment that the 'patient start weight was way above that of the fertile population', Novo Nordisk reiterated that Saxenda was a treatment for obesity and should be used only in those with a BMI as stated in the SPC. Novo Nordisk was unclear about the complainant's reference to the 'fertile population'; as mentioned previously, NICE guidelines stated that female BMI should ideally be in the range 19–30 before commencing assisted reproduction. This suggested that some women who presented for assisted reproduction might have a BMI above 30 and were therefore within the indication to be treated for obesity with Saxenda should they and their clinician consider that this was suitable before commencing fertility treatment.

Novo Nordisk disagreed that the font size of the starting weight listed in the leavepiece was illegible.

Regarding the complainant's comment that the Saxenda women's health leavepiece 'does not mention that once Saxenda is stopped, the weight increases, therefore not addressing the cause of fertility issues in these women', Novo Nordisk stated that it was clear on page 2 of the leavepiece that obesity was associated with a number of diseases, and there was no claim that

Saxenda treated the underlying cause or pathology. Additionally, when patients stopped taking Saxenda as part of the follow-up period in the SCALE Obesity and Prediabetes study (le Roux *et al*, 2017), weight was still significantly lower at end of follow-up than at baseline and compared with the comparator arm.

The patient brochure provided Saxenda patients with information about weight loss, how Saxenda worked, the side-effects associated with the medicine and how to use the injection device. The brochure was clear as to the licensed indication for Saxenda and did not suggest that treatment would lead to improved fertility or pregnancy. Novo Nordisk noted that although the complainant had alleged that the 'eating healthy' section on page 13 was not appropriate for a pregnant woman or one trying to become pregnant, the booklet was not intended for a patient who might be pregnant or trying to conceive, given Saxenda would not be prescribed in that situation. The booklet was for patients who had been prescribed the medicine to lose weight, taking into account any contraindications or precautions listed in the SPC.

In reference to the complainant's comment stating the patient brochure was 'too old', Novo Nordisk confirmed that it was first certified in 2016 and re-certified in 2018; the job bag certificate demonstrated this.

With regard to the allegation that the stand was unmanned, Novo Nordisk's clear understanding was that it was manned at the times detailed above. The materials provided on the stand could stand alone and did not need the representative to provide additional supporting information if a delegate took one while the representative was helping another delegate or on a comfort break.

In reference to the specific clauses cited by the complainant:

- 3.2 – the promotion of Saxenda at the conference was in accordance with the licensed indication and was not inconsistent with the SPC;

- 4.1 – prescribing information for Saxenda was on the leavepiece and included all elements listed in Clause 4.2;

- 7.2, 7.3, 7.4, and 7.9 – the information provided in the two pieces of material was accurate, balanced and fair, was not misleading with regard to any comparisons made and was capable of substantiation. In addition, safety information was included on both items. The same could be said for any verbal conversations that took place on the stand;

- 14.1, 14.3, 14.5 – the two pieces of material were certified;

- 15.1, 15.2 and 15.9 – both representatives had been adequately trained and briefed and had maintained high standards at the conference;

- 16.1 – both representatives were conversant with the requirements of the Code. Neither were involved in the preparation or approval of the materials available on the stand: and;

- 18.2 – no items or any form of inducement were provided by Novo Nordisk to the delegates at the conference. There was no item that matched the description of the 'zapper pens'.

Novo Nordisk stated that it was unable to respond to the allegation regarding Clause 29 as no information had been provided regarding the case in question in relation to the clause.

In reference to the additional clauses cited by the PMPCA:

- 18.1 – no items or any form of inducement were provided by Novo Nordisk to the delegates at the conference.

- 26.2 – The patient brochure was to be provided by a health professional to those patients who had been prescribed Saxenda. The information included in the brochure did not raise unfounded hopes of successful treatment nor was it misleading with respect to the safety of the medicine.

In light of the above, Novo Nordisk strongly refuted that it had brought the industry into disrepute or failed to maintain high standards (Clauses 2 and 9.1).

Novo Nordisk noted that the complainant had provided no evidence to substantiate his/her concerns and the company denied any allegations that it had breached Clauses 2, 3.2, 4.1, 7.2, 7.3, 7.4, 7.9, 9.1, 14.1, 14.3, 14.5, 15.1, 15.2, 15.9, 16.1, 18.1, 18.2, 26.2 and 29.

**PANEL RULING**

The Panel noted the that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. The Panel noted however that the complainant bore the burden of proving their complaint on the balance of probabilities.

The Panel noted Novo Nordisk's submission that obesity was strongly associated with the failure of assisted reproduction techniques and it was not uncommon for clinicians to advise patients about the importance of weight management before starting a cycle of treatment in order to maximise success; many clinical commissioning groups had a maximum BMI threshold when deciding who should be funded for assisted reproduction.

Section 1.2.6 of the National Institute for Health and Care Excellence (NICE) CG156 guideline 'Fertility problems: assessment and treatment' dated February 2013 dealt solely with the effect of obesity on fertility detailing that women with a BMI of over 30 would likely take longer to conceive, and women with a BMI of over 30 who were not ovulating should be informed that losing weight was likely to increase their chance of conception. It further stated that men with a BMI of over 30 might have reduced fertility. Section 1.10.4.1 stated: 'Women should be informed that female BMI should ideally be in the range 19–30 before commencing assisted reproduction, and that a female BMI outside this range is likely to reduce the success of assisted reproduction procedures. [2004]'.

The Panel considered that the use of medicines in pregnancy and in those trying to become pregnant was an important area and health professionals prescribing medicines to such patients needed to take particular care in this regard. Similarly, companies promoting medicines needed to ensure that health professionals were given relevant information and material should be tailored to the audience.

In relation to the complainant's query regarding the relevance of what was promoted at the conference, the Panel noted the indication for Saxenda and Novo Nordisk's submission that it was relevant that health professionals working in fertility knew that Saxenda was a treatment option for obesity prior to starting fertility therapy. In the Panel's view, it was not necessarily unacceptable for Novo Nordisk to promote Saxenda at the fertility conference providing the way in which it was done complied with the Code.

The Panel noted Novo Nordisk's submission that pregnancy, fertility and lactation were not listed in Section 4.3 Contraindications, of the Saxenda SPC as stated by the complainant and that the relevant details were included in the prescribing information at the end of the leavepiece about women's health (ref UK19SX00080).

The Panel noted that Section 4.6 of the Saxenda SPC Fertility, pregnancy and lactation stated, *inter alia*, that there were limited data from the use of liraglutide in pregnant women. Studies in animals had shown reproductive toxicity (see section 5.3). The potential risk for humans was unknown. It further stated that liraglutide should not be used during pregnancy. If a patient wished to become pregnant or pregnancy occurred, treatment with liraglutide should be discontinued. It also stated that apart from a slight decrease in the number of live implants, animal studies did not indicate harmful effects with respect to fertility.

The Panel noted that the materials on the stand were general and had not been tailored to the audience at the fertility meeting. Although the health professionals attending the meeting would be aware of the need for care when prescribing medicines in women hoping to become pregnant, in the Panel's view, on balance, it was not sufficient to rely on the prescribing information to provide the highly relevant information about the use of Saxenda in patients hoping to become pregnant or who became pregnant. In the Panel's view it would have been prudent to include a more prominent, clear reference to the relevant information within the Saxenda SPC considering the product was being promoted at a fertility conference. Delegates should be in no doubt about the use of Saxenda prior to fertility treatment. The Panel considered that failure to do so meant that Novo Nordisk had not maintained high standards and a breach of Clause 9.1 was ruled.

The Panel noted the complainant's allegation that the representative on the stand confidently promoted Saxenda for weight loss in order to help women get pregnant but did not state the warnings/contraindications associated with Saxenda with regard to pregnancy or fertility. The Panel noted Novo Nordisk's submission that the promotion of Saxenda at the conference was in accordance with the licensed indication and was not inconsistent with the SPC. According to Novo Nordisk at no point were the representatives instructed to promote Saxenda as a treatment to improve fertility or the chances of becoming pregnant. In addition, none of the material on the stand referred to Saxenda as a treatment to improve fertility or to increase the chances of becoming pregnant. The Panel noted the that the parties' accounts differed. The Panel noted that according to Novo Nordisk the two representatives had been verbally briefed in relation to how to use the two pieces of material available on the stand and about their roles and responsibilities while at the conference. The Panel did not consider that the complainant had established, on the balance of probabilities, that the promotion of Saxenda by the Novo Nordisk representatives at the fertility conference or the materials available on the stand were such that they were inconsistent with the particulars listed in the Saxenda SPC and therefore no breach of Clause 3.2 was ruled.

The Panel noted that the complainant referred to the fact that pregnant women at fertility clinics/centres would be on a host of medicines to help with reproduction such as clomifene and progesterone and fertility clinicians were not familiar with GLP-1 analogues or the associated warnings and a few believed that it could be used for their patients already on clomifene and progesterone. The Panel noted that the complainant provided few or no details of why, in his/her view, this was in breach of the Code. According to the SPC there did not appear to be any interactions with the medicines referred to by the complainant. It was not for the Panel to make out a complainant's allegations and the Panel therefore made no ruling in this regard.

There was no evidence before the Panel that either of the representatives had failed to maintain a high standard of ethical conduct or had not complied with all of the relevant requirements of the Code when manning the stand at the fertility conference and no breach of Clause 15.2 was ruled.

The Panel noted that Clause 15.1 stated that representatives must be given adequate training and have sufficient scientific knowledge to enable them to provide full and accurate information about the medicines which they promote. The complainant alleged that the representative had not been trained specifically for promotion in fertility and did not refer to safety in this area which was very worrying. Novo Nordisk noted that both representatives were experienced and each had been trained on the Saxenda SPC which covered the contraindications and special warnings and precautions sections, including pregnancy, fertility and lactation; they had been verbally briefed on how to use the two pieces of material available on the stand and about their roles and responsibilities while at the conference. The Panel considered that the complainant had not established, on the balance of probabilities, that the representatives had not been given adequate training in relation to Saxenda as alleged and no breach of Clause 15.1 was ruled.

Clause 15.9 stated that companies must prepare detailed briefing material for medical representatives on the technical aspects of each medicine which they will promote. The supplementary information stated that the detailed briefing material referred to in Clause 15.9 consisted of both the training material used to instruct medical representatives about a medicine and the instructions given to them as to how the product should be promoted.

The Panel noted Novo Nordisk's submission that at no point were the two representatives instructed to promote Saxenda as a treatment to improve fertility or the chances of becoming pregnant. According to Novo Nordisk both representatives had been trained on the Saxenda SPC which covered the contraindications and special warnings and precautions sections, including pregnancy, fertility and lactation and had been trained to promote Saxenda in accordance with the licensed indication.

In addition, the Panel noted that the two representatives had been briefed verbally with regard to how to use the materials on the stand and their roles at the fertility conference. The Panel did not consider that the complainant had established, on the balance of probabilities, that the representatives had not been appropriately briefed as alleged and therefore the Panel ruled no breach of Clause 15.9.

The Panel noted that whilst the patient brochure was first certified in 2016, it had been re-certified in 2018 as shown on the job bag certificate provided by Novo Nordisk. The Panel therefore ruled no breach of Clauses 14.3 and 14.5.

The Panel noted that delegates could take printed material from the stand. It also noted Novo Nordisk's submission that the Saxenda injection device was available on the stand for the representatives to demonstrate how it was used if requested. The device was not given away from the stand and Novo Nordisk did not have anything that matched the complainant's description of 'zapper from demo pens'. The Panel therefore ruled no breach of Clauses 18.1 and 18.2 in that regard.

The Panel noted that the complainant had a number of concerns about the Saxenda women's health leavepiece (ref UK19SX00080) including that: page 3 which referred to clinical trials, did not state that pregnancy, desire for pregnancy and lactation were exclusion criteria – a major omission especially at the biggest annual fertility congress; the fact that the average patient starting weight of 106.3kg (also in illegible font size) was way above that of the fertility population and thus gave a false impression of the amount of weight loss achievable in that population; there was no mention that once Saxenda was stopped, weight increased therefore not addressing the cause of fertility issues in these women; and that the leavepiece stated that the 'safety' of Saxenda was well investigated but queried how this was so given that pregnant women were excluded. The Panel noted that it did not have before it any of the studies referenced in relation to the information detailed above apart from le Roux *et al*. The Panel noted Novo Nordisk's submission that NICE guidelines stated that female BMI should ideally be in the range 19–30 before commencing assisted reproduction which suggested that some women who presented for assisted reproduction might have a BMI above 30 and were therefore within the indication to be treated for obesity with Saxenda should they and their clinician consider that this was suitable before commencing fertility treatment. The Panel considered that it was not necessarily a breach of the Code for the leavepiece to only include information about women in general rather than very specific information about the outcome of clinical trials in relation to women who might be candidates for fertility treatment. The Panel did not consider that the complainant established, on the balance of probabilities, that the information was misleading as alleged and no breach of Clause 7.2 was ruled.

The Panel noted the complainant's concerns regarding the patient brochure (ref UK/SA/0616/0068) including that: the 'benefits beyond weight loss' section did not mention anything about a woman's ability to get pregnant; the 'eating healthy' section was not appropriate for a pregnant woman or one trying to become pregnant as cutting down calories was not advised in pregnancy; and the 'increased activity' section described was too generic and not appropriate for pregnant women who could not undertake vigorous/intensive exercise. The Panel noted Novo Nordisk's submission that the brochure was not intended for a patient who might be pregnant or trying to conceive, given Saxenda would not be prescribed in that situation; it was for patients who had been prescribed the medicine to lose weight, taking into account any contraindications or precautions listed in the SPC. The Panel did not consider that making the patient brochure available at the fertility meeting was in itself unacceptable. The complainant had not established, on the balance of probabilities, that the patient brochure was misleading as alleged and no breach of Clause 7.2 was ruled.

The Panel noted that the complainant listed a number of other clauses but provided few or no details of why, in his/her view, Novo Nordisk was in breach of those clauses. It was not for the Panel to make out a complainant's allegations. The Panel, therefore, ruled no breach of Clauses 4.1, 7.3, 7.4, 7.9, 16.1, 14.1, 26.2 and 29 of the Code.

The Panel noted that a ruling of a breach of Clause 2 of the Code was a sign of particular censure and reserved for such. In that regard, the Panel did not consider that the particular circumstances of this case warranted such a ruling and no breach of Clause 2 was ruled.

**APPEAL BY THE COMPLAINANT**

The complainant appealed the Panel's rulings of no breach of Clauses 2, 3.2, 4.1, 7.2, 7.3, 7.4, 7.9, 9.1, 14.1, 14.3, 14.5, 15.1, 15.2, 15.9, 16.1, 18.1, 18.2, 26.2 and 29.

The complainant alleged that Novo Nordisk's entire defence was on weight and fertility/assisted reproductive technology so it was obvious that that was its focus ie to deceive and mislead the British Fertility Society audience.

The complainant referred to the photograph of the material provided with his/her complaint and alleged that Novo Nordisk had given out patient material from its stand which was against the Code,

Further, the complainant alleged that the Code stated that briefing needed to be certified so why wasn't there a sanction there? Verbal briefing was nonsense because it did not happen!

**COMMENTS FROM NOVO NORDISK**

Novo Nordisk noted that the complainant had provided no additional evidence to support his/her reasons for raising an appeal and it continued to refute any allegation that it had breached Clauses 2, 3.2, 4.1, 7.2, 7.3, 7.4, 7.9, 9.1, 14.1, 14.3, 14.5, 15.1, 15.2, 15.9, 16.1, 18.1, 18.2, 26.2 and 29.

Novo Nordisk disagreed with the complainant's comment about the distribution of the Saxenda patient booklet from the stand; and submitted that it was compliant with the Code to distribute certified materials in the form of patient information to health professionals visiting an exhibition stand who in turn passed on the material to patients prescribed the medicine. This point was not raised by the complainant in his/her original complaint, Novo Nordisk was unclear as to why it was being raised now.

Novo Nordisk noted that with regard to the complainant comment about briefings, it submitted that the two sale representatives staffing the stand were appropriately trained and briefed and as per the Panel ruling, the complainant had not established, on the balance of probabilities, that the representatives had not been appropriately briefed as alleged.

**FINAL COMMENTS FROM THE COMPLAINANT**

The complainant alleged that all the clauses raised were still valid and in question and he/she urged Novo Nordisk to read it! The complainant questioned how he/she ended up with the leaflet meant for patients as part of supper program if it was not given out at the stand? Could Novo Nordisk provide an undertaking from the male representative?

The complainant alleged that the Code stated that adverse events could not be relied upon solely on prescribing information. Why was relevant adverse events (see original complaint for details) appropriate to the fertility area not provided?

The complainant noted that the Code also very cleverly stated that briefing must be certified. So where was the evidence of the verified briefing, specifically for a new area, fertility, which clearly Novo Nordisk was ill equipped for.

The complainant alleged that if indeed it were true that a verbal briefing took place, which nevertheless was in breach of certification and representative training clauses anyway amongst others clauses, then could Novo Nordisk provide evidence of this eg email communications, calendar invitations, phone or video calls?

The complainant alleged that Novo Nordisk confirmed that its intention was indeed to show that losing weight helped to promote fertility as clearly its entire rebuttal was based on improving fertility - it quoted NICE. Whereas the two appropriate guidance were the following:

> '1 Weight management before, during and after pregnancy Public health guideline [PH27].'

The complainant alleged that this guideline did not include pharmaceutical medicine use for weight loss management as clearly these were risky for pregnant women 'Weight loss programmes are not recommended during pregnancy as they may harm the health of the unborn child'. Therefore, Novo Nordisk had cherry picked its evidence and had not been balanced and had mislead the fertility health professionals and therefore put patients at risk.

> '2 Fertility problems: assessment and treatment Clinical guideline [CG156] Published date: 20 February 2013 Last updated: 06 September 2017 [nb: after Saxenda launch].'
>
> '1.2.6 Obesity
>
> 1.2.6.1 Women who have a body mass index (BMI) of 30 or over should be informed that they are likely to take longer to conceive. **[2004, amended 2013]**
>
> 1.2.6.2 Women who have a BMI of 30 or over and who are not ovulating should be informed that losing weight is likely to increase their chance of conception. **[2004, amended 2013]**
>
> 1.2.6.3 Women should be informed that participating in a group programme involving exercise and dietary advice leads to more pregnancies than weight loss advice alone. **[2004]**
>
> 1.2.6.4 Men who have a BMI of 30 or over should be informed that they are likely to have reduced fertility. **[2004, amended 2013]**.'

The complainant alleged that there was no advice on using Saxenda or pharmaceutical weight loss because many of these were inappropriate and harmful for unborn babies. These warnings were on Saxenda label and Novo Nordisk had chosen to deliberately mislead the fertility specialists therefore putting patients at harm.

The complainant alleged that in the material given out at the stand, Novo Nordisk had yet again mislead health professionals as it had omitted these 3 vital pieces of evidence:

**1 'Body Mass Index and Short-Term Weight Change in Relation to Treatment Outcomes in Women Undergoing Assisted Reproduction' - Jorge E Chavarro *et al.* 2012**

The complainant alleged that this study showed that overweight and obesity were related to lower live birth rates in women undergoing ART. Short-term weight loss was related to higher MII yield, particularly among overweight and obese women, **but unrelated to clinical outcomes.**

'**1.1. Outcome of assisted reproductive technology in overweight and obese women – MacKenna *et al***

The complainant noted that this study concluded 'The prevalence of obesity among women seeking ART in Latin America is surprisingly high; **however, BMI does not influence the outcome of ART performed** in these women.'

**2 Endoscan meta-analysis review by** Wexler

The complainant provided the following information 'Of those studies that this examine the effect of weight loss on fertility in obese women, the majority focus on women with known PCOS or on women undergoing ART. In a prospective cohort study of 170 women undergoing assisted reproduction (233 ART cycles), short-term weight loss (average 3kg)—particularly in women with higher baseline BMI—was associated with better oocyte retrieval, **though not with a significant difference in clinical pregnancy or live birth'**

Therefore the complainant alleged that Novo Nordisk had cherry picked evidence, provided a biased slant and mislead by not including appropriate adverse events relevant to the audience enough for them to form their own independent conclusions and ultimately put desperate pregnant women (as they were seeking fertility assistance) and their unborn babies at risk, promoting off label with regard to improved fertility and outcomes with weight loss thereby bringing the whole industry into disrepute.

**APPEAL BOARD RULING**

The Appeal Board noted from the company representatives at the appeal that the British Fertility Conference, 8-11 January 2020 was the first fertility conference that Novo Nordisk had attended to promote Saxenda for weight loss. The Appeal Board noted the company's submission about the rationale for exhibiting at the conference, in particular the relevance of weight management prior to starting fertility management.

The Appeal Board noted that Section 4.6 of the Saxenda SPC Fertility, pregnancy and lactation stated, *inter alia*, that there were limited data from the use of liraglutide in pregnant women. Studies in animals had shown reproductive toxicity (see section 5.3). The potential risk for humans was unknown. It further stated that liraglutide should not be used during pregnancy. If a patient wished to become pregnant or pregnancy occurred, treatment with liraglutide should be discontinued. It also stated that apart from a slight decrease in the number of live implants, animal studies did not indicate harmful effects with respect to fertility. Section 5.3 referred to preclinical safety data. This section included a statement that animal studies did not indicate direct harmful effects with respect to fertility but slightly increased early embryonic deaths at the highest dose as well as information about the effects of dosing mid-gestation.

The Appeal Board was particularly concerned that, given Saxenda was being promoted at a fertility conference and the warnings in the Saxenda SPC for women trying to become pregnant, the health professionals treating them should be fully informed of the position regarding the use of Saxenda and its effects on fertility, pregnancy and lactation. In this regard the Appeal Board noted that health professionals attending the conference might be managing woman with sub-fertility prior to any referral for assisted fertility treatment. Some of these women would be advised to lose weight and it was possible that health professionals who did not work in assisted fertility might prescribe or the patient's general practitioner might be asked to prescribe, Saxenda. It was therefore important that all were made aware of the risks in pregnancy and the need to take precautions to not fall pregnant or to discontinue Saxenda if they fell pregnant.

The Appeal Board considered that women with fertility problems were potentially a vulnerable group, some would be desperate to become pregnant and that whilst being treated for fertility problems there was a possibility that some might still be trying to conceive naturally.

The women's health leavepiece included prescribing information. This stated under the heading Fertility pregnancy and lactation that Saxenda should not be used during pregnancy and included that if a patient wished to become pregnant or a pregnancy occurred, treatment with Saxenda should be discontinued. It should not be used during breast feeding.

The Appeal Board noted the Panel's consideration including that the materials on the stand were general and had not been tailored to the audience at the fertility meeting. Although the health professionals attending the meeting would be aware of the need for care when prescribing medicines in women hoping to become pregnant, in the Panel's view, on balance, it was not sufficient to rely on the prescribing information to provide the highly relevant information about the use of Saxenda in patients hoping to become pregnant or who became pregnant. In the Panel's view it would have been prudent to include a more prominent, clear reference to the relevant information within the Saxenda SPC considering the product was being promoted at a fertility conference. Delegates should be in no doubt about the use of Saxenda prior to fertility treatment. The Panel had considered that failure to do so meant that Novo Nordisk had not maintained high standards and a breach of Clause 9.1 was ruled which was accepted by the company. This ruling was not appealed.

The Appeal Board noted the complainant's allegation that the representative on the stand confidently promoted Saxenda for weight loss in order to help women get pregnant but did not state the warnings/contraindications associated with Saxenda with regard to pregnancy or fertility. The Appeal Board noted Novo Nordisk's submission that the promotion of Saxenda at the conference was in accordance with the licensed indication and was not inconsistent with the SPC. According to Novo Nordisk at no point were the representatives instructed to promote Saxenda as a treatment to improve fertility or the chances of becoming pregnant. In addition, none of the materials on the stand referred to Saxenda as a treatment to improve fertility or to increase the chances of becoming pregnant. The Appeal Board noted the that the parties' accounts differed. The Appeal Board noted that according to Novo Nordisk the two representatives had been verbally briefed in relation to how to use the two pieces of material available on the stand and about their roles and responsibilities while at the conference. The Appeal Board did not consider that the complainant had established, on the balance of probabilities, that the promotion of Saxenda by the Novo Nordisk representatives at the fertility conference or the materials available on the stand were such that they were inconsistent with

the particulars listed in the Saxenda SPC and therefore no breach of Clause 3.2 was ruled. The appeal on this point was unsuccessful.

The Appeal Board considered that there was no evidence before it that either of the representatives had failed to maintain a high standard of ethical conduct or had not complied with all of the relevant requirements of the Code when manning the stand at the fertility conference and it upheld the Panel's ruling of no breach of Clause 15.2. The appeal on this point was unsuccessful.

The Appeal Board considered that the intended audiences for the printed material, health professionals and patients, needed very clear and precise guidance about the use of Saxenda should a woman decide to try to conceive or fell pregnant due to the warnings in Sections 4.6 and 5.3 of the Saxenda SPC. This was particularly relevant when the company was promoting the medicine at a fertility conference.

The patient brochure contained no reference to such warnings. The Appeal Board noted the submission of the company representatives at the appeal that the patient brochure referred to the package leaflet which contained relevant information. The Appeal Board noted that the brochure should stand alone with regard to the requirements of the Code. The Appeal Board considered that the failure to reflect the relevant warnings in the SPC was such that the patient brochure was misleading and it ruled a breach of Clause 7.2. The appeal on this point was successful.

The Appeal Board noted that Clause 26.2 included that information about prescription only medicines which is made available to the public either directly or indirectly must be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. The supplementary information referred to the need for the public, which would include patients, to comply with the requirements of Clause 7.2 of the Code.

The Appeal Board noted its ruling of a breach of Clause 7.2 above with regard to the patient brochure. It considered that the patient material was misleading with respect to the safety of the product in pregnancy, particularly given that its availability at a fertility conference. The Appeal Board therefore also ruled a breach of Clause 26.2. The appeal on this point was successful.

The Appeal Board noted similarly that the women's health leavepiece contained no clear reference to the information and warnings regarding pregnancy in Sections 4.6 and 5.3 of the SPC. This was mentioned in the prescribing information which included under the heading Fertility pregnancy and lactation that Saxenda should not be used during pregnancy. If a patient wished to become pregnant or a pregnancy occurred, treatment with Saxenda should be discontinued. It should not be used during breast feeding. However, the Appeal Board considered that particularly given its use at a fertility conference the women's health leavepiece was misleading as it was unclear about these warnings and potential risks, and it therefore ruled a breach of Clause 7.2. The appeal on this point was successful.

The Appeal Board noted that Clause 15.1 stated that representatives must be given adequate training and have sufficient scientific knowledge to enable them to provide full and accurate information about the medicines which they promote. The Appeal Board noted Novo Nordisk's submission that both representatives were experienced and each had had prior training on the Saxenda SPC which covered the contraindications and special warnings and precautions

sections, including pregnancy, fertility and lactation; they had been verbally briefed on how to use the two pieces of material available on the stand and about their roles and responsibilities while at the conference. The Appeal Board noted that the case preparation manager had asked for copies of relevant briefing/training material and none was provided by Novo Nordisk. This was the first fertility conference Novo Nordisk had attended to promote Saxenda for weight loss. Given that this was a new area and the specific warnings in Sections 4.6 and 5.3 of the Saxenda SPC especially with regard to toxicity and safety, it was particularly important that certified briefing material for the representatives (preferably written) was provided. Novo Nordisk had no written certified record of the verbal briefing given and in the Appeal Board's view the company had not been able to show that the representatives had been adequately trained to promote Saxenda within the fertility area. The Appeal Board therefore ruled a breach of Clause 15.1. The appeal on this point was successful.

Given the nature of the warning in the SPC and that it was the company's first time at a fertility conference and that the SPC warnings were not reflected in the materials on the stand the Appeal Board queried whether a verbal briefing was appropriate. As there was no certified record of the verbal briefing the Appeal Board also ruled a breach of Clause 15.9. The appeal on this point was successful.

The Appeal Board noted that whilst the patient brochure was first certified in 2016, it had been re-certified in 2018 as shown on the job bag certificate provided by Novo Nordisk. The Appeal Board therefore upheld the Panel's ruling of no breach of Clauses 14.3 and 14.5. The appeal on this point was unsuccessful.

The Appeal Board noted that the women's health leavepiece had been certified and therefore upheld the Panel's ruling of no breach of Clause 14.1. The appeal on this point was unsuccessful.

The Appeal Board noted that delegates could take printed material from the stand. It also noted Novo Nordisk's submission that the Saxenda injection device was available on the stand for the representatives to demonstrate how it was used if requested. The device was not given away from the stand and Novo Nordisk did not have anything that matched the complainant's description of 'zapper from demo pens'. The Appeal Board therefore upheld the Panel's ruling of no breach of Clauses 18.1 and 18.2 in that regard. The appeal on this point was unsuccessful.

The Appeal Board noted that the complainant had listed a number of other clauses of the Code to be considered. The Panel had dealt with these very briefly on the basis that the complainant had provided few or no details as to why Novo Nordisk was in breach of those clauses. All were appealed by the complainant and the Appeal Board agreed that little evidence had been provided by the complainant. Some of the matters were dealt with above by the Appeal Board and the remainder were considered as follows.

The Appeal Board noted that Clause 4.2 set out what should be included in prescribing information. The prescribing information in the women's health leavepiece included a reference that Saxenda should not be used during pregnancy or whilst breast feeding and if a patient wished to become pregnant or a pregnancy occurred, treatment with Saxenda should be discontinued. The Panel had ruled no breach of the Code in relation to the allegation that adverse events relevant to fertility treatment were omitted. The Appeal Board did not consider

that the prescribing information was illegible. It upheld the Panel's ruling of no breach of Clause 4.1. The appeal was unsuccessful.

The Appeal Board noted that the complainant had not provided information about what he/she alleged was a misleading comparison and therefore upheld the Panel's ruling of no breach of Clause 7.3. The appeal on this point was unsuccessful.

The Appeal Board noted that the complainant had not provided information about what he/she alleged was not capable of substantiation and therefore upheld the Panel's ruling of no breach of Clause 7.4. The appeal on this point was unsuccessful.

The Appeal Board noted that the complainant had not provided information about what he/she alleged were claims about adverse reactions that did not reflect the available evidence or were incapable of substation and therefore upheld the Panel's ruling of no breach of Clause 7.9. The appeal on this point was unsuccessful.

The Appeal Board noted that the representatives had passed the ABPI representative examination. There was no evidence that the representatives were not conversant with the Code. The Appeal Board therefore upheld the Panel's ruling of no breach of Clause 16.1. The appeal on this point was unsuccessful.

The Appeal Board noted that the complainant had not identified the original case in relation to the alleged breach of undertaking. A broad reference was made in relation to the promotion of liraglutide in 2010. There was no evidence of a breach of undertaking and therefore the Appeal Board upheld the Panel's ruling of no breach of Clause 29. The appeal on this point was unsuccessful.

The Appeal Board noted its comments and rulings above about the importance of ensuring that both health professionals and relevant patients being treated with Saxenda were aware of the risks in pregnancy and the need to take precautions to not fall pregnant. Delegates attending the conference should be in no doubt about the use of Saxenda prior to fertility treatment. The Appeal Board also noted the Panel's ruling of a breach of Clause 9.1.

The Appeal Board noted that a ruling of a breach of Clause 2 was a sign of particular censure and was reserved for such circumstances. The Appeal Board considered that the failure to provide highly relevant and vital information about the use of the product in pregnancy and those wishing to become pregnant meant that there was a potential patient safety issue. The Appeal Board considered that the circumstances amounted to a breach of Clause 2 and ruled accordingly. The appeal on this point was successful.

**Complaint received** **19 January 2020**

**Case completed** **15 July 2020**