**CASE AUTH/3399/10/20**

# VOLUNTARY ADMISSION BY NOVARTIS

## Conduct of a representative

**Novartis Pharmaceuticals UK Limited voluntarily admitted that one of its representatives had failed to maintain high standards with regard to discussions about Piqray (alpelisib) with two different clinicians.**

**As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Novartis.**

**Novartis explained that in June 2020, a representative held conversations with two separate customers regarding the wording of the Committee for Medicinal Products for Human Use's (CHMP's) published recommendation for Piqray which, at the time, had not been granted a licence from the European Medicines Agency (EMA). The intention was to gather insights as to the clinicians' interpretation of the CHMP's recommended wording.**

**An internal investigation identified that a marketing employee was also aware of the plans for the representative to hold these customer discussions.**

**The detailed response from Novartis is given below.**

**The Panel noted that the CHMP had adopted a positive opinion on 28 May 2020 and on 27 July 2020 the European Commission approved Piqray in combination with fulvestrant for use in certain patients with breast cancer.**

**The Panel noted Novartis' submission that a marketing employee, after discussion with his/her line-manager, had asked the representative in question to arrange meetings with certain breast cancer clinicians for the purpose of introducing the employee in marketing to these clinicians and to gather insights on the CHMP recommendation for Piqray. The Panel noted Novartis' submission that both the marketing employee and the representative had planned to attend these meetings.**

**The Panel noted Novartis' submission that the marketing employee, following a conversation with a medical adviser who informed him/her that this activity should not be undertaken due to the commercial nature of the marketing employee and representative's roles and that they must not discuss alpelisib with clinicians ahead of any licence being granted, sent two text messages to the representative to 'hold off' regarding the planned meetings. The Panel was concerned that despite this instruction from the marketing employee, the representative continued to have discussions with the marketing employee's line manager about the feasibility of repurposing the meetings. Four meetings were scheduled by the representative and the Panel noted that two of these meetings were held by the representative alone in June during the course of which**

**two clinicians were asked for their thoughts and insights as to the clinical implications of the CHMP recommendation for alpelisib.**

**In the Panel's view, the proactive discussion by any company employee about its unlicensed medicine would likely be seen as promotion although there were certain exemptions set out in the Code. An employee's role was an important consideration in determining whether an activity would be likely to be viewed as promotional. Perception was also important. Companies should be extremely careful to ensure that promotional activity was very clearly separated from non-promotional activity and that this distinction was clear to health professionals.**

**The Panel noted that the representative had proactively approached the two health professionals and in that regard the Panel considered that alpelisib had been promoted prior to the grant of its marketing authorisation and a breach of the Code was ruled.**

**The Panel noted that the first text message from the marketing employee to the representative stated '…we might not be able to collect feedback now..' and the second text message, stated 'We've been told by medical not to ask from the commercial side do [sic] we might need to hold off until we get insights on their side/we receive the EMA license….'. The Panel was very concerned that the representative, with the agreement of the marketing employee's line manager, went ahead with the meetings and insight gathering despite the marketing employee's messages but queried why clearer instructions were not given to the representative and in particular noted the use of the word 'might'. Furthermore, the Panel was extremely concerned about the lack of Code understanding demonstrated by senior marketing individuals. The Panel considered that high standards had not been maintained and a breach of the Code was ruled as acknowledged by Novartis.**

**The supplementary information to Clause 2 stated that ruling of a breach of Clause 2 was a sign of particular censure and activities that were likely to be in breach of Clause 2 included promotion prior to the grant of a marketing authorisation. The Panel also noted its comments above particularly in relation to its ruling of a breach of Clause 9.1 and considered that Novartis' activity in this regard brought discredit upon, and reduced confidence in, the industry. A breach of Clause 2 was ruled.**

Novartis Pharmaceuticals UK Limited voluntarily admitted that one of its representatives had failed to maintain high standards with regard to discussions about Piqray (alpelisib) with two different clinicians.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Novartis.

## VOLUNTARY ADMISSION

Novartis explained that in June 2020, a representative held two separate conversations with customers (2 clinicians in total) regarding the wording of the Committee for Medicinal Products for Human Use's (CHMP's) published recommendation for Piqray which, at the time, had not been granted a licence from the European Medicines Agency (EMA). The intention was to gather insights as to the clinicians' interpretation of the CHMP's recommended wording.

The matter was brought to Novartis' attention by one of its medical advisors who reported that, during an advisory board organised by the medical department for the purpose of gaining clinician insight on the proposed licence wording, one of the clinicians in attendance mentioned that he/she had discussed this with a representative before the advisory board. Separately, a Novartis medical science liaison (MSL) reported that during a one-to-one meeting with a customer, the customer had mentioned that he/she had spoken to a representative about the licence wording.

An internal investigation had been conducted, with corrective and preventative action measures ongoing. The investigation identified that a marketing employee was also aware of the plans for the representative to hold these customer discussions. Novartis stated that it took its obligations with regards to compliance with the Code very seriously. The matter was being managed with utmost importance.

Novartis stated that it was, therefore, self-reporting a potential breach of Clause 9.1 – a failure to maintain high standards.

When writing to confirm that the matter would be taken up under the Code, The Authority asked Novartis to provide any further comments it might have in relation to Clause 9.1 and also to consider the requirements of Clauses 3.1 and 2 of the Code.

**RESPONSE**

**Summary of Authorisation timelines**

Novartis explained that on 28 May 2020, the CHMP of the EMA adopted a positive opinion recommending the approval of Piqray in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) locally advanced or metastatic breast cancer with a PIK3CA mutation after disease progression following endocrine therapy as monotherapy. The CHMP's recommendation was published on the EMA's website on 29 May 2020. For the avoidance of doubt, Piqray had not at that stage been granted a licence by the European Commission.

On 27 July 2020 the European Commission approved Piqray in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) locally advanced or metastatic breast cancer with a PIK3CA mutation after disease progression following endocrine therapy as monotherapy.

**Overview of the matter**

At a cross-functional, launch readiness team meeting on 17 June 2020, the Novartis Piqray team discussed the need to gather insights from clinicians as to the CHMP recommendation and what it might mean in relation to the treatment of advanced breast cancer patients. The meeting minutes did not mention any discussion relating to insight gathering nor stipulate that any actions had been agreed as to the collection of said insights, or by whom. However, subsequent integrated disease team meeting minutes detailed the plans for the Novartis oncology medical team to hold an advisory board with some breast cancer clinicians in order to gain these insights.

The planned advisory board was held on 8 July and conducted by employees of the Novartis oncology medical department. The advisory board objectives were to:

- Discuss the clinical community's initial impressions of the BYLieve Cohort A efficacy and safety data, and the Real World Evidence comparator
- Understand where clinicians believe PI3K inhibitors might fit within the treatment pathway for advanced breast cancer, considering the current evidence
- Discuss clinicians' interpretations of the recent CHMP opinion and summary of product characteristics (SPC) indication wording for Piqray plus fulvestrant, in the context of the CHMP Assessment Report and divergent opinion letter
- Establish which patient populations could benefit from Piqray plus fulvestrant according to the recent licence wording and based on the current UK treatment pathways
- Discuss the implications of the data and the licence on future PIK3CA testing for patients within the new Genomics Medicines Service
- Discuss data generation needs and potential studies that would support Piqray plus fulvestrant use and access in a broader group of patients that might benefit from that treatment.

Ten clinicians attended the advisory board as well as three Novartis employees - a medical advisor, a member of the health economics and outcomes research (HEOR) team and an employee from marketing. The presence of the HEOR team member and the marketing employee were documented in the approved meeting arrangements form.

> During the advisory board, one of the attending clinicians referred to the fact that a Novartis oncology customer relationship employee (with a commercially-facing role responsible for the management of a number of sales representatives) had shown him the wording a couple of weeks before the advisory board. The meeting was recorded and details were provided.

On realising that an employee in a commercially-facing role had undertaken a discussion about Piqray in the pre-licence phase, the medical advisor responsible for running the advisory board contacted the representative in question to understand the situation and subsequently reported the situation to medical.

In parallel, an MSL also reported that during a meeting with another clinician, that clinician told him/her that he/she had discussed the CHMP recommendation for Piqray with the same representative previously. The MSL reported this to his/her manager who then informed medical.

Both medical employees sought to understand the situation and found that the meetings between the representative and the two clinicians had been instigated at the request of a marketing employee and his/her line manager. Medical escalated the matter to the ethics, risk and compliance group and a full investigation was undertaken. Details of the investigation were provided including that this involved interviews with staff including the two marketing employees and the representative, a report to the internal Novartis business practices office (Speak-Up Office) and to local (country) management for handling. The investigation resulted in corrective and preventative measures being recommended (details provided below).

**Investigation Summary**

The investigation involved interviews with the two staff in marketing and the representative which confirmed the marketing employee and his/her line manager had decided, following a cross-functional launch-readiness meeting, to arrange some introductory meetings for the marketing employee, with some breast cancer clinicians. The launch-readiness meeting minutes did not specify that any actions were to be taken by the two staff in marketing with regards to insight gathering. They made this decision alone, without consulting any other team members. Their idea was to ask the representative in question to arrange some virtual introductory meetings for the marketing employee with some clinicians he/she knew and at which the representative would also be present.

The marketing employee approached the representative to arrange these meetings with the intention of introducing him/herself and gathering insights on the CHMP recommendation. The representative then organized Introductory meetings with four clinicians.

A few days later, during the course of ongoing cross-functional discussions on pre-launch activities, the marketing employee shared the details of the plan with the medical advisor. The medical advisor informed the marketing employee that he/she should not undertake this activity due to the commercial nature of his/her own role as well as that of the representative, and that he/she must not discuss Piqray with clinicians ahead of any licence being granted. At this point, the marketing employee sent two text messages (copies provided) to the representative to advise him/her of that and to instruct him/her to 'hold off' regarding the meetings. From that point, there was no further involvement of the marketing employee.

Further discussions between the representative and marketing employee's line manager subsequently took place in which the feasibility of repurposing the meetings was discussed. However, the meetings were not repurposed or cancelled and the representative conducted two of the four planned meetings alone (ie without the marketing employee as originally planned). The representative asked the two clinicians concerned for their thoughts and insights as to the clinical implications of the CHMP recommendation. Following completion of the second of these meetings, the representative contacted the marketing employee's line manager to state that he/she felt uncomfortable in holding the discussions and was not going to conduct any further meetings. The marketing employee's line manger supported that position and no further meetings were conducted.

The business practice investigation interviews confirmed the sequence of events and individuals' roles in the matter per the preliminary interviews.

**Corrective and Preventative Remediation**

Novartis stated that it took potential breaches of the Code very seriously and sought to improve business practices in response. The recommendations from the investigation were provided and these including retraining on the Code and Novartis policies, communications with the clinicians, possible disciplinary action and good documentation practice for agreeing actions from meetings.

**Addressing the highlighted Clauses**

Novartis recognised and acknowledged that the actions of the representative and of the marketing employees line manager (through not definitively stopping the meetings from taking

place) had led to a commercial employee discussing a product, pre-licence, with two health professionals. In that regard, the company acknowledged a breach of Clause 9.1.

Both employees had been subject to a formal internal business practice investigation.

Novartis did not consider that there had been a breach of Clause 3.1 in these circumstances due to nature of and intent behind the interactions concerned.

Having interviewed all parties involved in the situation and those peripheral to the event itself, the investigation had confirmed that the intention of the meetings had originally been for the marketing employee to be introduced to a limited number of breast cancer clinicians and to gather insights on the clinical implications of the CHMP recommendation for Piqray. When the marketing employee withdrew his/her involvement, the representative kept the appointments and sought to gather insights on the publicly available CHMP recommendation. Despite failing to maintain high standards through conducting these meetings, and the potential perception of the activities as being promotional due to the commercial nature of his/her role, there was no intention by the representative to promote Piqray. The representative confirmed that no documentation (promotional or otherwise) was shared with either clinician. Although the recording transcript suggested that the representative showed the CHMP recommendation wording to the clinician, the representative stated that the clinician had searched for the wording on the internet during the discussion. Finally, the representative further confirmed that no promotional claims were made regarding Piqray during the meetings.

In light of these factors, there was no intention by the representative to promote the product. Rather, the interaction was to gain clinical insights as to the impact of the CHMP recommendation in clinical practice. The activity undertaken was, by its nature, non-promotional as demonstrated by it being an objective of the advisory board, organized and run by the medical department.

Given the intention behind the interaction and nature of the activity, Novartis disagreed that there was a breach of Clause 3.1.

Novartis stated that as the representative's intention was to gather insights and not to promote Piqray, as set out above in relation to the alleged breach of Clause 3.1, Novartis disagreed that there was a breach of Clause 2.

While Novartis accepted that this activity should not have happened, there was no intention by the representative to promote Piqray pre-licence. No promotional claims were made.

The representative recognised his/her error of judgment and accepted responsibility for undertaking an activity that he/she should not have conducted. Furthermore, he/she understood the risks that his/her actions had caused.

**PANEL RULING**

The Panel noted Novartis' admission that in June 2020, a representative held conversations with two separate clinicians regarding the wording of the Committee for Medicinal Products for Human Use's (CHMP's) recommendation for Piqray (alpelisib) which at that time had not been granted a licence from the European Medicines Agency (EMA). The CHMP had adopted a positive opinion on 28 May 2020 and on 27 July 2020 the European Commission approved

Piqray in combination with fulvestrant for use in certain patients with breast cancer. The Panel noted Novartis' submission that the intention of the representative's meetings on 24 June was to gather insights about the clinicians' interpretation of the CHMP's recommended wording.

The Panel noted Novartis' submission that a marketing employee, after discussion with his/her line-manager, had asked the representative in question to arrange meetings with certain breast cancer clinicians for the purpose of introducing the marketing employee to these clinicians and to gather insights on the CHMP recommendation for Piqray. The Panel noted Novartis' submission that both the marketing employee and representative had planned to attend these meetings.

The Panel noted Novartis' submission that the marketing employee, following a conversation with a medical adviser who informed him/her that this activity should not be undertaken due to the commercial nature of the marketing employee and representative's roles and that they must not discuss alpelisib with clinicians ahead of any licence being granted, sent two text messages to the representative to 'hold off' regarding the planned meetings. The Panel was concerned that despite this instruction from the marketing employee, the representative continued to have discussions with the marketing employee's line manager about the feasibility of repurposing the meetings. Four meetings were scheduled by the representative and the Panel noted that two of these meetings were held by the representative alone in June during the course of which two clinicians were asked for their thoughts and insights as to the clinical implications of the CHMP recommendation for alpelisib.

The Panel noted that Clause 3.1 prohibited the promotion of a medicine prior to the grant of its marketing authorization. Clause 1.2 defined 'promotion' as 'any activity undertaken by a pharmaceutical company or with its authority which promotes the administration, consumption, prescription, purchase, recommendation, sale, supply or use of its medicines'.

In the Panel's view, the proactive discussion by any company employee about its unlicensed medicine would likely be seen as promotion although there were certain exemptions set out in the Code. An employee's role was an important consideration in determining whether an activity would be likely to be viewed as promotional. Perception was also important. Companies should be extremely careful to ensure that promotional activity was very clearly separated from non-promotional activity and that this distinction was clear to health professionals.

The Panel noted that the representative had proactively approached the two health professionals and in that regard the Panel considered that alpelisib had been promoted prior to the grant of its marketing authorisation and a breach of Clause 3.1 was ruled.

The Panel noted that the first text message from the marketing employee to the representative stated '…we might not be able to collect feedback now..' and the second text message, stated 'We've been told by medical not to ask from the commercial side do [sic] we might need to hold off until we get insights on their side/we receive the EMA license….'. The Panel was very concerned that the representative, with the agreement of the marketing employee's line manger , went ahead with the meetings and insight gathering despite the marketing employee's messages but queried why the marketing employee did not give clearer instructions to the representative and in particular noted the use of the word 'might'. Furthermore, the Panel was extremely concerned about the lack of Code understanding demonstrated by senior marketing

individuals. The Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled as acknowledged by Novartis.

The supplementary information to Clause 2 stated that ruling of a breach of Clause 2 was a sign of particular censure and activities that were likely to be in breach of Clause 2 included promotion prior to the grant of a marketing authorisation. The Panel also noted its comments above particularly in relation to its ruling of a breach of Clause 9.1 and considered that Novartis' activity in this regard brought discredit upon, and reduced confidence in, the industry. A breach of Clause 2 was ruled.

**Complaint received** **7 October 2020**

**Case completed** **5 March 2021**