CASE AUTH/3125/11/18

TAKEDA v MERCK SHARP & DOHME

Inter-company dialogue

Takeda UK Ltd complained about the failure of Merck Sharp & Dohme Ltd to comply with an undertaking provided during inter-company dialogue between the two parties. Takeda marketed Vipidia (alogliptin) and Merck Sharp & Dohme marketed Januvia (sitagliptin). Both medicines were used in adults with type 2 diabetes mellitus.

Takeda explained that it became aware of a Januvia promotional item displayed on a Merck Sharp & Dohme promotional stand in October 2018 at a diabetes conference which contained a mention of alogliptin and incorrectly associated the product with the inverted black triangle symbol, contrary to the undertaking provided by Merck Sharp & Dohme that no materials incorrectly associating alogliptin with the black triangle would be in use after the end of August 2018. Takeda was disappointed that Merck Sharp & Dohme failed to honour its undertaking and alleged that in doing so it had not maintained high standards

The detailed response from Merck Sharp & Dohme is given below.

The Panel noted that although undertakings given by companies during the course of inter-company dialogue were not covered by the Code and were thus not subject to the requirements of the Code, it was important that companies complied with such undertakings. Failing to implement an inter-company undertaking might indicate that previous inter-company dialogue had ultimately been unsuccessful.

The Panel noted that whilst Merck Sharp & Dohme had endeavoured to withdraw all the relevant material, the company had been let down by one of its representatives who confirmed that he/she had destroyed all of the relevant material in his/her possession but had not done so. The employee still possessed and had used a Januvia leavepiece in October in which five inhibitors of dipeptidyl peptidase 4 (DPP-4 inhibitors) were compared in a table and alogliptin was incorrectly associated with a black triangle when the black triangle had been removed from the product on 18 June 2018. The material was not up-to-date and the Panel considered therefore that high standards had not been maintained and a breach of the Code was ruled.

Takeda UK Ltd complained about the failure of Merck Sharp & Dohme Ltd to comply with an undertaking provided during inter-company dialogue between the two parties. Takeda marketed Vipidia (alogliptin) and Merck Sharp & Dohme marketed Januvia (sitagliptin). Both medicines were used in adults with type 2 diabetes mellitus.

COMPLAINT

Takeda explained that it initiated inter-company dialogue with Merck Sharp & Dohme on 29 June 2018 over concerns regarding a promotional item entitled 'Sitagliptin Information Pack', which Takeda alleged to be in breach of the Code.

Takeda received a response from Merck Sharp & Dohme on 13 July 2018 and a subsequent teleconference was held in August 2018 to clarify the detail relating to Merck Sharp & Dohme's commitments and to further discuss an outstanding issue. The teleconference minutes were agreed between both parties.

The sitagliptin information pack contained a number of mentions of Vipidia (alogliptin). On every page mentioning alogliptin the black triangle was also prominently displayed. Takeda's initial complaint letter (29 June 2018) stated that alogliptin no longer had a black triangle and requested that Merck Sharp & Dohme update all impacted materials accordingly without delay.

Merck Sharp & Dohme acknowledged that the black triangle for alogliptin had indeed been removed and that it had initiated the process for updating all materials on 19 June 2018.

As Merck Sharp & Dohme had not specified a date by which point all impacted material would be withdrawn from use, Takeda asked for a timeline in the subsequent teleconference. The agreed minutes showed that Merck Sharp & Dohme had provided a clear undertaking to withdraw all materials in which alogliptin was associated with the black triangle by the end of August 2018.

Following the apparent successful resolution of the black triangle issue by inter-company dialogue, Takeda became aware of a Januvia promotional item displayed on a Merck Sharp & Dohme promotional stand in October 2018 at a diabetes conference.

This promotional item contained a mention of alogliptin and incorrectly associated the product with the black triangle, contrary to the undertaking provided by Merck Sharp & Dohme to Takeda on 2 August 2018. Takeda did not have the item code or date of preparation but considered that a photograph was sufficient to enable Merck Sharp & Dohme to identify the item.

An assurance had been given by Merck Sharp & Dohme that no materials associating alogliptin with the black triangle would be in use after the end of August 2018 and this was not so. Takeda considered the inter-company-dialogue had failed on this point.

Takeda was disappointed that Merck Sharp & Dohme failed to honour its undertaking and in doing so had not maintained high standards. Accordingly, Takeda alleged that Merck Sharp & Dohme had breached Clause 9.1 of the Code.

RESPONSE

Merck Sharp & Dohme submitted that it took self-regulation very seriously and was committed to complying to both the spirit and letter of the Code. These fundamental behaviours were embedded within the organisation to ensure that it acted with the highest level of integrity.

Merck Sharp & Dohme noted that Takeda contacted it regarding the sitagliptin information pack (ref DIAB-1107051-0014, date of preparation August 2017) on 29 June. Takeda's concerns were centred around the inclusion of the black triangle for Vipidia within Merck Sharp & Dohme promotional material. The black triangle for Vipidia had been removed from the summary of

product characteristics (SPC) on 18 June 2018 and Merck Sharp & Dohme had identified this via its internal processes on 19 June and proceeded to initiate identification of the impacted promotional materials.

Merck Sharp & Dohme and Takeda completed inter-company dialogue on 2 August where Merck Sharp & Dohme provided reassurance that all the impacted materials would be withdrawn by the end of August 2018, which was agreed by Takeda. Merck Sharp & Dohme submitted that internal processes were followed to withdraw all impacted promotional materials by the end of August 2018, as per its commitment provided during inter-company dialogue. The aforementioned sitagliptin information pack containing the black triangle had already been withdrawn on 13 April 2018.

Following receipt of the complaint, Merck Sharp & Dohme conducted a thorough investigation of the withdrawal process to verify that all impacted promotional material had been withdrawn from circulation. The Merck Sharp & Dohme detailed the steps involved in its withdrawal process.

Merck Sharp & Dohme confirmed that all of its active field-based employees received an email on 29 August regarding the withdrawal of the printed promotional materials which contained the black triangle for alogliptin. Each employee was required to respond to confirm understanding of the instruction provided within a withdrawal website within three working days of receiving the email. Merck Sharp & Dohme stated that all of its field-based employees responded to confirm receipt of the email and to verify that all impacted material in their possession had been destroyed on 5 September. A few field-based employees were on long-term sick leave and their responses had not been documented.

Merck Sharp & Dohme submitted that, regrettably, it now understood that one of its promotional materials, a leavepiece for Januvia (DIAB-1248337-0000, date of preparation March 2018) which contained the black triangle for alogliptin was displayed on a promotional stand at the diabetes conference in October 2018. The material was withdrawn on 29 August with the explicit instruction to immediately cease using it and to destroy any stock.

Merck Sharp & Dohme was aware that one of its field-based employees attended the diabetes conference to set up a promotional stand. Unfortunately the single leavepiece (DIAB-1248337-0000) was within his/her collection of promotional materials and Merck Sharp & Dohme was considering action as per its local policy for failure to comply with the withdrawal process. In addition, Merck Sharp & Dohme submitted that it had briefed its entire diabetes field force on 12 December on the importance of adhering to instructions specifically around withdrawals and the correct use of current promotional materials.

Merck Sharp & Dohme considered this to be an isolated incident as it was assured that all of its field-based employees had confirmed destruction of the impacted promotional materials, for which they had received withdrawal notifications. Merck Sharp & Dohme took this matter with the utmost seriousness and, whilst clearly unfortunate, this incident had highlighted the requirement for the company to revisit its process to ensure that it did not happen again. Importantly, Merck Sharp & Dohme considered that it had a minimal impact on patient safety.

Merck Sharp & Dohme submitted that its current process was robust and it disagreed that it had failed to maintain high standards. Merck Sharp & Dohme submitted that the error resulted from the actions of an individual representative who failed to follow the required process for withdrawal of material and from its investigations was identified as an isolated case. Merck Sharp & Dohme submitted that this was supported by its proactive actions on 19 June following

the removal of the black triangle for alogliptin which was published on the electronic medicines compendium website on 18 June 2018 where it had identified the change and had began to identify all the impacted materials which required withdrawal. Merck Sharp & Dohme submitted that it was in full agreement with Takeda during inter-company dialogue regarding the update of its promotional materials which Merck Sharp & Dohme considered to be consistent with the Code and it had honoured its commitment of undertaking with the instruction and follow up to confirm its withdrawal by the agreed date. Merck Sharp & Dohme therefore denied a breach of Clause 9.1.

PANEL RULING

The Panel noted that although undertakings given by companies during the course of inter-company dialogue were not covered by the Code and were thus not subject to the requirements of the Code, it was important that companies complied with such undertakings. Failing to implement an inter-company undertaking might indicate that previous inter-company dialogue had ultimately been unsuccessful.

The Panel noted Merck Sharp & Dohme's submission that on 19 June, prior to being contacted by Takeda, it had identified that the black triangle for Vipidia had been removed from the SPC on 18 June 2018 and it proceeded to identify and withdraw affected materials.

The Panel noted that further to the provision of the undertaking given by Merck Sharp & Dohme to Takeda in August to withdraw all material in which alogliptin was associated with a black triangle by the end of August 2018, a Januvia leavepiece where alogliptin was associated with a black triangle was subsequently used at a diabetes conference in October.

The Panel noted that whilst Merck Sharp & Dohme had endeavoured to withdraw all the relevant material, the company had been let down by one of its representatives who confirmed that he/she had destroyed all of the relevant material in his/her possession but had not done so. The employee still possessed and had used a Januvia leavepiece in October in which five inhibitors of dipeptidyl peptidase 4 (DPP-4 inhibitors) were compared in a table in which alogliptin was the only product associated with a black triangle when the black triangle had been removed from the product on 18 June 2018. The material was not up-to-date.

The Panel considered therefore that high standards had not been maintained and a breach of Clause 9.1 was ruled.

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During the consideration of this case the Panel were concerned to note that it appeared that a number of representatives did not complete the withdrawal on time as indicated by the text 'completed late' on the spreadsheet provided. This appeared to be in addition to the employees referred to by Merck Sharp & Dohme as being on long-term sick leave. The Panel noted that it was important that employees complied with withdrawal notices and requested that Merck Sharpe & Dohme be advised of its concerns.

Complaint received **23 November 2018**

Case completed **9 January 2019**