CASE AUTH/3218/6/19

EX-EMPLOYEE v OTSUKA

Abilify Maintena detail aid

An anonymous, ex-employee of Otsuka UK complained about an Abilify Maintena (aripiprazole) electronic detail aid entitled 'Take the next step in the disease journey with Abilify Maintena'. Abilify Maintena was a long-acting intra-muscular injection indicated for maintenance treatment of schizophrenia in adults stabilised with oral aripiprazole.

One page of the electronic detail aid was headed 'Oral aripiprazole has a favourable tolerability profile vs other atypical antipsychotics – as described by Maudsley guidelines in the table below'. The table compared oral aripiprazole with three other atypical antipsychotics in terms of a number of possible side effects; a traffic light system of colours was used.

The complainant alleged that the table of data was misleading with regard to the safety of aripiprazole in that it implied that the incidence of sedation was 'very low' and the incidence of akathisia was 'low' whereas the SPC stated that both were 'common' and that the incidence of parkinsonism 'very low' although the SPC listed extrapyramidal disorders as 'common'. The complainant also alleged that the table disparaged other medicines eg the incidence of hypotension with oral risperidone was stated as 'moderate' whereas the SPC stated that it was 'uncommon' and the incidence of prolactin elevation with oral palperidone was stated as 'high' whereas the SPC stated that it was 'uncommon'.

One page of the detail aid featured a bar chart showing the potential millions of pounds saved over 10 years due to avoided diabetes or coronary heart disease (CHD) in patients treated with oral aripiprazole compared with oral standard of care (risperidone, olanzapine and quetiapine). The complainant alleged that the claim to the right of the bar chart 'Oral aripiprazole may be associated with long-term cost savings as a result of reduced incidence of treatment-related diabetes and CHD', was a hanging comparison.

The complainant submitted that the page at issue which was part of a sales aid for Abilify Maintena (not oral aripiprazole) used data from 1997 where costs were inflated to 2007 for a 2018 detail aid and stated that events of diabetes and CHD would be avoided if oral aripiprazole was used vs standard care. Diabetes was a common adverse effect for Abilify and Abilify Maintena and the complainant was concerned that the bar chart implied that there was only a low risk of diabetes with Abilify and Abilify Maintena whereas, even if it was lower than with other antipsychotics, it was still a common adverse effect.

Finally, the complainant stated that he/she expected Clauses 9.1 and 2 to be considered due to the severity of the above issues.

The detailed response from Otsuka is given below.

The Panel noted that the table at issue which was adapted from the Maudsley Guidelines was headed 'Tolerability comparison of oral aripiprazole with other atypical antipsychotics available as an LAI [long-acting injectable]' and compared the tolerability of oral aripiprazole with risperidone, paliperidone and olanzapine. The Panel noted Otsuka's submission that the table compared atypical long-acting injectables whereas it appeared that the complainant assumed it was a comparison of the oral formulations. In the Panel's view the table heading was ambiguous and therefore the subject matter of the table was not sufficiently clear in terms of the formulation of the three atypical antipsychotics being compared with oral aripiprazole.

The Panel noted Otsuka's submission about the status of the Maudsley Guidelines and the footnote to the table that referenced them stating that the data in the table was made up of estimates of relative incidence and/or severity, based on clinical experience, manufacturers' literature and published records. The footnote in small print also stated that other side effects, not mentioned in the table did occur. The reader was referred to the SPC for a full list of adverse events. The Panel noted that the Code required the promotion of a medicine to be in accordance with the terms of its marketing authorisation and not inconsistent with the particulars listed in its SPC. The Code did not prohibit the provision of information not included in an SPC if that information was not inconsistent with the particulars listed in that SPC.

The Panel noted that the colour coded table showed that for oral aripiprazole the incidence of sedation, weight gain, parkinsonism, anti-cholinergic, hypotension and prolactin elevation was very low and akathisia was low. This visual tolerability profile compared favourably with the incidence depicted for the three comparator antipsychotics, only one side effect for one comparator product was shown as very low (olanzapine, parkinsonism). Two side effects were shown as high incidence in red for three comparator products (prolactin elevation for risperidone and paliperidone, and weight gain for olanzapine).

The Panel noted that contrary to the table at issue the Abilify SPC listed sedation, akathisia and extrapyramidal disorders (of which parkinsonism was an example) as common undesirable effects.

The Panel disagreed with Otsuka's submission that the preceding slides of the detail aid provided context.

The Panel noted that it appeared that the basis of the calculation of the adverse event data in the table at issue was different to that in the SPCs. The Panel noted that this matter was implied in a footnote in very small font at the bottom of the slide at issue. The Panel considered that with regard to the incidence of sedation, akathisia, and parkinsonism (an extrapyramidal disorder) the table did not fairly reflect, and appeared to be inconsistent with, the information in the Abilify SPC and was misleading in that regard. The Panel noted Otsuka's submission that readers were directed, via a footnote, to the relevant SPCs for a full list of adverse events. In the Panel's view, the footnote was wholly insufficient to qualify the misleading impression given by the table with regard to the incidence of adverse effects described above. In addition, it implied that

the data for those adverse events listed in the table in question was consistent with the SPC which was not so. A breach of the Code was ruled.

The Panel noted Otsuka's submission that the table reflected the available evidence about aripiprazole and could be substantiated by clinical experience; the purpose of the table was to reflect clinical experience in relation to the tolerability of certain antipsychotics, including aripiprazole, beyond that depicted in the relevant SPCs. The Panel noted its comments above about the inclusion of this detail in small font as a footnote which meant it was not sufficiently clear when looking at the table that it did not reflect the adverse reactions as set out in the products' SPCs. Noting its comments and ruling above the Panel considered that the table misleadingly implied that it reflected the incidence of adverse events as set out in the SPC and in this regard did not adequately reflect the adverse event information in the SPC as alleged and a breach of the Code was ruled.

The Panel noted that according to SPCs accessed on the electronic medicines compendium (eMC) website the incidence of hyperprolactinaemia with paliperidone was either uncommon or common (depending on the formulation). The table at issue, however, listed prolactin elevation as high incidence/severity. Similarly, the incidence of hypotension with risperidone was either uncommon or common (depending on the formulation) but was listed in the table at issue as moderate.

The Panel was unsure whether the categorisation of the incidence of adverse events in the table at issue (very low, low, moderate and high) was such that the incidence could be directly compared to the frequency of adverse reactions as set out in the products' SPCs (very common, common, uncommon, rare, very rare or not known). The Panel, however, noted its comments above about the visual impression given by the colour coded scheme of the table and about the footnote. In the Panel's view, given the frequency of adverse events listed in the products respective SPCs, the overall comparison of the incidence of adverse events experienced with oral aripiprazole compared with the other antipsychotics listed was misleading and disparaged other companies' medicines as alleged. Breaches of the Code were ruled.

The Panel noted that the complainant alleged that the claim 'Oral aripiprazole may be associated with long-term cost savings as a result of reduced incidence of treatment related diabetes and CHD' was a hanging comparison. The Panel noted that the claim appeared alongside a bar chart graph and below the prominent page heading 'Potential cost savings over 10 years due to avoided events in patients treated with oral aripiprazole compared to SOC [oral standard of care]'. The Panel noted that the final sentence to the footnote below the bar graph in small font stated 'SOC = Oral standard of care (risperidone, olanzapine or quetiapine)'. The Panel noted that whilst the lack of prominence given to the definition meant that it was not sufficiently clear what the standard of care was , the prominent page heading meant that it was clear that the comparator was oral standard of care. The Panel noted that whilst it would have been prudent to clearly detail what the standard of care was within the heading rather than in a footnote, the complainant had not alleged that the definition of the comparator was not clear and thus on balance the Panel ruled no breach of the Code based on the very narrow allegation.

The Panel noted that it was clear that the cost comparison related to oral aripiprazole despite the detail aid being about Abilify Maintena. The Panel noted Otsuka's submission that the information was highly relevant to the use of Abilify Maintena. The title of the detail aid was 'Take the next steps in the disease journey with Abilify Maintena'. The Abilify Maintena licence required that adult patients had to firstly be stabilised with oral aripiprazole before Abilify Maintena was started. The Panel did not consider that the complainant had established that including the cost comparison involving oral aripiprazole in an Abilify Maintena detail aid was misleading and based on the narrow allegation the Panel ruled no breach of the Code.

The Panel further noted the complainant's concern that the bar chart implied that there was only a low risk of diabetes with Abilify and Abilify Maintena whereas, even if it was lower than with other antipsychotics, it was still a common adverse effect with Abilify and Abilify Maintena. The Panel noted Otsuka's submission that there was no claim that aripiprazole *per se* was associated with a low risk of diabetes. The Panel noted that, below the bar graph, in very small font, there was a statement which set out how many fewer cases of diabetes and CHD events would occur per 1,000 patients treated with Abilify vs standard care and the estimated savings over 10 years. The Panel noted the immediate impression given by the bar chart in relation to the avoided cost savings as a result of the reduced incidence of treatment-related diabetes. In the Panel's view, it was not unreasonable to assume that the implication to some readers was that the incidence of diabetes in patients taking Abilify was low which was not so - according to the Abilify SPC, diabetes was a common adverse reaction. It was not clear from the page in question that diabetes was a common adverse event of Abilify and this omission compounded the misleading impression given. The Panel considered that the page was misleading as alleged and a breach of the Code was ruled.

The Panel noted that it was important that health professionals could rely upon the industry for accurate, complete information about its medicines particularly with regard to the incidence of adverse events. The Panel noted its comments and rulings above and did not consider that high standards had been maintained and a breach of the Code was ruled.

The Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure and ruled accordingly.

An anonymous, contactable ex-employee of Otsuka UK complained about an Abilify Maintena (aripiprazole) electronic detail aid (ref UK/AM/0118/0014, date of preparation January 2018) entitled 'Take the next step in the disease journey with Abilify Maintena'. Abilify Maintena was a long-acting intra-muscular injection indicated for maintenance treatment of schizophrenia in adults stabilised with oral aripiprazole.

1 Tolerability

One page of the electronic detail aid was headed 'Oral aripiprazole has a favourable tolerability profile vs other atypical antipsychotics – as described by Maudsley guidelines in the table below'. The table compared oral aripiprazole with three other atypical antipsychotics in terms of sedation, weight gain, akathisia, parkinsonism, anti-cholinergic, hypotension and prolactin elevation; a traffic light system of colours was used. There was a minus sign on a dark green

background (very low) against all of the potential side effects with aripiprazole except for akathisia which had a plus sign on a light green background (low). The tolerability profile scores shown for the other three medicines were mostly low (green), but there were also some moderate (two plus signs on an orange background) and one high (three plus signs on a red background) incidence/severity score for each.

COMPLAINT

The complainant alleged that the information shown for aripiprazole presented it very favourably compared to some other antipsychotics and was contrary to that in its summary of product characteristics (SPC). Specifically, the table of data implied that the incidence of sedation was 'very low' and the incidence of akathisia (a significant and serious extrapyramidal side effect of antipsychotics) was 'low' although both were stated to be 'common' in the SPC. Similarly the table implied that the incidence of parkinsonism was 'very low' but, although parkinsonism was not spelt out in the SPC, the incidence of extrapyramidal disorders (of which parkinsonism was one so could reasonably be expected to be included under that heading) was also 'common'.

The complainant alleged that there were also misrepresentations about other medicines. Specifically, that the table of data implied that the incidence of hypotension with oral risperidone was 'moderate' however, according to the SPC, the incidence of hypotension with oral risperidone was 'uncommon'. Also the incidence of prolactin elevation with oral paliperidone was stated in the table as 'high incidence/severity'. However, according to the SPC, the incidence of hyperprolactinaemia with oral paliperidone was 'uncommon'.

The complainant alleged that the table of data was thus misleading with respect to the safety of aripiprazole (in breach of Clauses 7.2, 7.3 and 7.9) and that it disparaged the medicines of other pharmaceutical companies (in breach of Clause 8.1).

RESPONSE

Otsuka stated that, in its view, the table at issue was not misleading in relation to the safety of aripiprazole. The set up of the electronic detail aid, the context and the slide preceding the page referred to by the complainant had the full tolerability profile of Abilify Maintena compared with oral aripiprazole.

The electronic detail aid had been designed with a number of core slides, including supporting pop-up slides. These slides detailed the efficacy and tolerability profile of aripiprazole, specifically oral aripiprazole and Abilify Maintena. Abilify Maintena was licensed for the maintenance treatment of schizophrenia for patients stabilised on oral aripiprazole. Therefore, it was important to provide sufficient information on both oral aripiprazole and Abilify Maintena within sales materials.

Specifically, within the tolerability profile section of the electronic detail aid, two slides were provided. The first highlighted the full tolerability profile of Abilify Maintena compared with oral aripiprazole. The second provided context of oral aripiprazole tolerability profile vs other atypical antipsychotics, published within the Maudsley Prescribing Guidelines.

The Maudsley Prescribing Guidelines in Psychiatry ('the Guidelines') provided up-to-date information, expert guidance on prescribing practice in mental health, including medicine choice, treatment of adverse effects and how to augment or switch medicines. It was widely used in

responses prepared by UK medicines information pharmacists for NHS health professionals that were listed within the National Institute for Health and Care Excellence (NICE) evidence section.

The world-renowned Guidelines had been written in concise terms by an expert team of psychiatrists and specialist pharmacists; they helped with complex prescribing problems and included information on prescribing psychotropic medications as well as potential interactions with other medicines and substances such as alcohol, tobacco and caffeine. Furthermore, each of the book's 165 sections featured a full reference list so that the evidence upon which the Guidelines were based could be readily accessed.

The table at issue was adapted from the Guidelines (relevant extract provided) and had been reduced in size to show the atypical (second generation) antipsychotics that were available as long-acting injectables used in clinical practice and the legend had been colour coded. The accompanying table had a clear heading so that the reader knew that the information in the table was from the Guidelines and the reference was cited underneath. The heading was also clear that the table represented a comparison of atypical long-acting injectables. Within the page readers were guided to where they could access the full table. It also provided the exact extract on how the table had been created eg 'the table is made up of approximate estimates of relative incidence and/or severity, based on clinical experience, manufacturers' literature and published research. Other side effects not mentioned in this table do occur'. In addition to this statement, Otsuka noted that it had directed readers to refer to the relevant SPCs for a full list of adverse events.

The briefing document for the field force (copy provided) reiterated the above information and made it clear that representatives must point out to a prescriber that the table had been compiled by drawing from clinical experience and published research, as well as the SPCs.

The information within the table clearly identified that it was a comparison of atypical long-acting injectables and was based on clinical experience, manufacturers' literature and published research. Otsuka noted that it had not added any claims to the table and had simply presented an extract of the table published.

Given the above, Otsuka refuted that the table was misleading and that it made misleading comparisons, and it therefore denied a breach of Clauses 7.2 or 7.3. The table reflected the available evidence about aripiprazole and could be substantiated by clinical experience. Indeed, the purpose of the table was to reflect clinical experience in relation to the tolerability of certain antipsychotics, including aripiprazole, beyond that depicted in the relevant SPCs. Otsuka denied a breach of Clause 7.9. The information presented was factual and based on a highly reputable source; thus Otsuka did not consider that it disparaged any of the medicines referred to and it denied a breach of Clause 8.1.

PANEL RULING

The Panel noted that the table at issue which was adapted from the Maudsley Guidelines was headed 'Tolerability comparison of oral aripiprazole with other atypical antipsychotics available as an LAI [long-acting injectable]' and compared the tolerability of oral aripiprazole with risperidone, paliperidone and olanzapine. The Panel noted Otsuka's submission that the heading was clear that the table represented a comparison of atypical long-acting injectables whereas it appeared that the complainant assumed it was a comparison of the oral formulations. In the Panel's view the table heading was ambiguous and therefore the subject matter of the

table was not sufficiently clear in terms of the formulation of the three atypical antipsychotics being compared with oral aripiprazole.

The Panel noted Otsuka's submission about the status of the Guidelines and the footnote to the table that referenced the Maudsley Prescribing Guidelines stating that the data in the table was made up of estimates of relative incidence and/or severity, based on clinical experience, manufacturers' literature and published records. The footnote in small print also stated that other side effects, not mentioned in the table did occur. The reader was referred to the SPC for a full list of adverse events. The Panel noted that Clause 3.2 of the Code stated, *inter alia*, that the promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its SPC. This clause did not prohibit companies from providing information not included in an SPC if that information was not inconsistent with the particulars listed in that SPC.

The Panel noted that the colour coded table showed that for oral aripiprazole the incidence of sedation, weight gain, parkinsonism, anti-cholinergic, hypotension and prolactin elevation was very low and akathisia was low. This visual tolerability profile compared favourably with the incidence depicted for the three comparator antipsychotics, only one side effect for one comparator product was shown as very low (olanzapine, parkinsonism). Two side effects were shown as high incidence in red for three comparator products (prolactin elevation for risperidone and paliperidone, and weight gain for olanzapine).

The Panel noted that contrary to the table at issue the Abilify SPC listed sedation, akathisia and extrapyramidal disorders (of which parkinsonism was an example) as common undesirable effects.

The Panel disagreed with Otsuka's submission that the preceding slides of the detail aid provided context. The Panel noted that the slide preceding the one at issue was titled 'Tolerability of Abilify Maintena is comparable to that of oral aripiprazole' and detailed the adverse events reported for Abilify Maintena and oral aripiprazole in a randomised, double-blind, active-controlled study. In very small font at the bottom of the slide it stated 'Please refer to the SmPC for the full adverse event profile'. The Panel noted that the take home message of this slide was that the tolerability profiles of Abilify and Abilify Maintena were similar; it provided no information with regard to the incidence of the adverse events as stated in the SPC.

The Panel noted that it appeared that the basis of the calculation of the adverse event data in the table at issue was different to that in the SPCs. The Panel noted that this matter was implied in a footnote in very small font at the bottom of the slide at issue. The Panel considered that with regard to the incidence of sedation, akathisia, and parkinsonism (an extrapyramidal disorder) the table did not fairly reflect, and appeared to be inconsistent with, the information in the Abilify SPC and was misleading in that regard. The Panel noted Otsuka's submission that it had directed readers to refer to the relevant SPCs for a full list of adverse events. The Panel noted its comments above about the footnote in very small font at the bottom of the slide at issue: 'Other side effects, not mentioned in this table, do occur. Please refer to the product SmPCs for a full list of adverse events'. In the Panel's view, the footnote was wholly insufficient to qualify the misleading impression given by the table with regard to the incidence of adverse effects described above. In addition, it implied that the data for those adverse events listed in the table in question was consistent with the SPC which was not so. A breach of Clause 7.2 was ruled.

The Panel noted Otsuka's submission that the table reflected the available evidence about aripiprazole and could be substantiated by clinical experience; the purpose of the table was to reflect clinical experience in relation to the tolerability of certain antipsychotics, including aripiprazole, beyond that depicted in the relevant SPCs. The Panel noted its comments above about the inclusion of this detail in small font as a footnote to the table which meant it was not sufficiently clear when looking at the table that it did not reflect the adverse reactions as set out in the products' SPCs. Noting its comments and ruling above the Panel considered that the table misleadingly implied that it reflected the incidence of adverse events as set out in the SPC and in this regard did not adequately reflect the adverse event information in the SPC as alleged and a breach of Clause 7.9 was ruled.

The Panel noted that the table had four categories of incidence: very low, low, moderate and high incidence/severity. Adverse reactions were listed in SPCs by frequency: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1 000 to <1/100), rare (≥1/10 000 to <1/100), very rare (<1/10 000) or not known (cannot be estimated from the available data).

The Panel noted its comments above with regard to the subject matter of the table not being sufficiently clear in terms of the formulation of the three atypical antipsychotics being compared with oral aripiprazole and that it was not clear looking at the table that it did not reflect the adverse reactions as set out in the products' SPCs.

The Panel noted that according to SPCs accessed by the Panel on the electronic medicines compendium (eMC) website the paliperidone prolonged release tablets (Invega) SPC stated that hyperprolactinaemia was uncommon and according to the paliperidone prolonged release suspension for injection (Trevicta and Xeplion) SPCs it was common. The table at issue listed prolactin elevation in red as high incidence/severity.

The Panel further noted that according to the SPCs accessed by the Panel on the eMC website, the incidence of hypotension for oral risperidone was uncommon and it was common for risperidone prolonged release suspension for injection. The table at issue listed hypotension in orange as moderate.

The Panel was unsure whether the categorisation of the incidence of adverse events in the table at issue was such that the incidence could be directly compared to the frequency of adverse reactions as set out in the products' SPCs. The Panel, however, noted its comments above about the visual impression given by the colour coded scheme of the table and its comments about the footnote. In the Panel's view, given the frequency of adverse events listed in the products' respective SPCs, the overall comparison of the incidence of adverse events experienced with oral aripiprazole compared with the other antipsychotics listed was misleading and disparaged other companies' medicines as alleged. A breach of Clauses 7.3 and 8.1 were ruled.

2 Cost savings and reduced incidence of diabetes

One page of the detail aid featured a bar chart showing the potential cost savings over 10 years due to avoided diabetes (£37.3 million) or coronary heart disease (CHD) (£7.5 million) in patients treated with oral aripiprazole compared with oral standard of care (risperidone, olanzapine and quetiapine).

COMPLAINT

The complainant alleged that the claim to the right of the bar chart 'Oral aripiprazole may be associated with long-term cost savings as a result of reduced incidence of treatment-related diabetes and CHD[coronary heart disease]', was a hanging comparison.

The complainant submitted that the page at issue, part of a sales aid for Abilify Maintena (not oral aripiprazole) using data from 1997 where costs were inflated to 2007 (for a 2018 detail aid), stated that events of diabetes and CHD would be avoided if oral aripiprazole was used vs standard care. Diabetes was a common adverse effect for Abilify and Abilify Maintena and the complainant was concerned that the bar chart might lead readers to understand that there was only a low risk of diabetes (a serious condition with long-term consequences) with Abilify and Abilify Maintena whereas, even if it was lower than with other antipsychotics, it was still a common adverse effect with Abilify and Abilify Maintena. The complainant alleged a breach of Clause 7.2.

RESPONSE

Otsuka did not consider that the claim 'Oral aripiprazole may be associated with long-term cost savings as a result of reduced incidence of treatment-related diabetes and CHD' was a hanging comparison because above the claim was the prominent title 'Potential cost savings over 10 years due to avoided events in patients treated with oral aripiprazole compared to [oral standard of care]'. Oral standard of care was expanded below the graph as being risperidone, olanzapine and quetiapine. Otsuka further noted that below the claim at issue there was an explanation of the study design which reiterated that the comparison was of oral aripiprazole with the standard of care as defined above. And finally, information at the bottom of the page also stated clearly that the study was with oral aripiprazole compared with standard of care.

Given the above, Otsuka submitted that the complainant had taken the claim at issue out of context and it refuted a breach of Clause 7.2.

Otsuka noted that the complainant appeared to be concerned that data on the potential cost savings with oral aripiprazole should not be included in a detail aid about Abilify Maintena. Otsuka considered, however, that that information was highly relevant to the use of Abilify Maintena. The title of the detail aid was 'Take the next steps in the disease journey with Abilify Maintena'. The Abilify Maintena licence required that adult patients had to firstly be stabilised with oral aripiprazole before Abilify Maintena was started.

Otsuka refuted that complainant's allegation that the graph and text might imply that the risk of diabetes with aripiprazole or Abilify Maintena was low; the graph and accompanying text clearly related to a comparison of aripiprazole with oral standard of care and there was no claim that aripiprazole *per se* was associated with a low risk of diabetes. Otsuka denied a breach of Clause 7.2.

PANEL RULING

The Panel noted that the complainant alleged that the claim 'Oral aripiprazole may be associated with long-term cost savings as a result of reduced incidence of treatment-related diabetes and CHD' was a hanging comparison. The Panel noted that the claim appeared alongside a bar chart graph and below the prominent page heading 'Potential cost savings over 10 years due to avoided events in patients treated with oral aripiprazole compared to SOC [oral standard of care]'. Beneath the claim at issue details of the study design were provided in

smaller font size including that metabolic data from STAR (Schizophrenia Trial of Aripirazole), a 26-week prospective multicentre, randomised, open-label study, (n=555, 18-65 years) comparing oral aripiprazole with SOC (standard of care) (26-week treatment) were used in a follow-up study by Blonde *et al* to predict long-term risks of diabetes and CHD. The Panel noted that the final sentence to the footnote below the bar graph in small font stated 'SOC = Oral standard of care (risperidone, olanzapine or quetiapine)'. The Panel noted that whilst the lack of prominence given to the definition meant that it was not sufficiently clear what the standard of care was, the prominent page heading meant that it was clear that the potential cost saving as a result of reduced incidence of treatment-related diabetes and CHD for patients treated with oral aripiprazole was compared with patients treated with standard of care. The Panel noted that whilst it would have been prudent to clearly detail what the standard of care was within the heading rather than in a footnote, the complainant had not alleged that the definition of the comparator was not clear and thus on balance the Panel ruled no breach of Clause 7.2 based on the very narrow allegation.

The Panel noted that it was clear that the cost comparison related to oral aripiprazole despite the detail aid being about Abilify Maintena. The Panel noted Otsuka's submission that the information was highly relevant to the use of Abilify Maintena. The title of the detail aid was 'Take the next steps in the disease journey with Abilify Maintena'. The Abilify Maintena licence required that adult patients had to firstly be stabilised with oral aripiprazole before Abilify Maintena was started. The Panel did not consider that the complainant had established that including the cost comparison involving oral aripiprazole in an Abilify Maintena detail aid was misleading and based on the narrow allegation the Panel ruled no breach of Clause 7.2.

The Panel further noted the complainant's concern that the bar chart might lead readers to understand that there was only a low risk of diabetes with Abilify and Abilify Maintena whereas, even if it was lower than with other antipsychotics, it was still a common adverse effect with Abilify and Abilify Maintena. The Panel noted Otsuka's submission that there was no claim that aripiprazole *per se* was associated with a low risk of diabetes. The Panel noted that below the bar graph in very small font it stated 'Based on data from a study with oral aripiprazole and not Abilify Maintena. Compared to SOC treatment: 23.4 fewer new cases of diabetes per 1,000 patients treated were predicted over 7.5 years, saving an estimated £37,261.293 over 10 years. 3.7 fewer CHD events per 1,000 patients treated were predicted over 10 years, saving an estimated £7,506.770'. The Panel noted the immediate impression given by the bar chart in relation to the avoided cost savings as a result of the reduced incidence of treatment-related diabetes. In the Panel's view, it was not unreasonable to assume that the implication to some readers was that the incidence of diabetes in patients taking Abilify was low which was not so. According to the Abilify SPC, diabetes was a common adverse reaction. It was not clear from the page in question that diabetes was a common adverse event of Abilify and this omission compounded the misleading impression given. The Panel considered that the page was misleading as alleged and a breach of Clause 7.2 was ruled.

3 Clauses 9.1 and 2

COMPLAINT

The complainant stated that he/she expected Clauses 9.1 and 2 to be considered due to the severity of the above issues.

RESPONSE

Given all of the above, Otsuka did not consider that there had been any failure to maintain high standards and it denied a breach of Clause 9.1. The electronic detail aid did not reduce confidence in, or bring disrepute upon, the pharmaceutical industry and so the company denied a breach of Clause 2.

PANEL RULING

The Panel noted that it was important that health professionals could rely upon the industry for accurate, complete information about its medicines particularly with regards to the incidence of adverse events. The Panel noted its comments and rulings above and did not consider that high standards had been maintained and a breach of Clause 9.1 was ruled.

The Panel did not consider that the particular circumstances of this case warranted a ruling of a breach of Clause 2 which was reserved as a sign of particular censure and ruled accordingly.

Complaint received **21 June 2019**

Case completed **1 May 2020**