CASE AUTH/3226/7/19

COMPLAINANT v TEVA

DuoResp Spiromax advertisement on BMJ hosted website

A complainant who described him/herself as a concerned UK health professional, complained about an advertisement for DuoResp Spiromax (budesonide/formoterol fumarate) placed on the BMJ website by Teva UK. DuoResp Spiromax, available in two strengths, 160/4.5mcg and 320/9mcg, was indicated for use in certain patients with asthma or chronic obstructive pulmonary disease (COPD).

The complainant stated that his/her initial impression was that DuoResp Spiromax was licensed for use in all asthma and COPD patients – then he/she noticed the footnotes that meant the product could only be used in those aged 18 years or more and that only one strength was licensed as maintenance and reliever therapy (MART) in asthma. The complainant noted from the summary of product characteristics (SPC) that the licensed indication in COPD was 'Symptomatic treatment of patients with COPD with forced expiratory volume in one second (FEV_1) <70% predicted normal (post-bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators'.

The complainant alleged that DuoResp Spiromax had been promoted beyond its licence. The complainant further noted that the prescribing information was over 2 years out-of-date – he/she did not think it had been updated since the SPC was last updated.

The detailed response from Teva is given below.

The Panel noted that the advertisement was headed 'DuoResp Spiromax (budesonide/formoterol) an award winning design containing the effective combinations of drugs you know'. Below the heading was a list of five, prominent bullet points beneath which were photographs of the two strengths of the inhaler available. The second bullet point read 'Licensed for asthma and COPD*'. The asterisk led the reader to a footnote in small font at the bottom of the list of bullet points, which stated 'DuoResp Spiromax is licensed for use in adults 18 years of age and older'. The fourth bullet point stated 'Maintenance and Reliever Therapy (MART) licence for asthma' which led the reader to a second footnote which read 'For 160mcg/4.5mcg strength only'.**

The Panel noted that the supplementary information to the Code stated that claims in promotional material must be capable of standing alone as regards accuracy etc and in general should not be qualified by the use of footnotes and the like.

The Panel considered that the second bullet point was misleading; read in isolation without the footnote, it implied that all patients with asthma or COPD were suitable for DuoResp Spiromax therapy which was not so; the medicine could not be used in those aged 17 years or less. The claim could not stand alone and so the Panel ruled a breach of the Code, which was upheld on appeal.

The Panel noted that the fourth bullet point was misleading if read in isolation as it implied that either strength of DuoResp Spiromax could be used. The advertisement promoted both strengths of DuoResp Spiromax but only one (160mcg/4.5mcg) was licensed for maintenance and reliever therapy in asthma. The claim could not stand alone and so the Panel ruled a further breach of the Code, which was upheld on appeal.

The Panel noted that the third bullet point stated that 'DuoResp Spiromax doses are therapeutically equivalent to Symbicort Turbohaler (budesonide/formoterol)'. In that regard the Panel noted that, depending on the strength and indication, Symbicort Turbohaler could be used in children as young as 6 years old. The Panel considered that it was misleading, without the benefit of further information, to directly compare DuoResp Spiromax, which could only be used in adults aged 18 years and older, with Symbicort Turbohaler which could potentially be used in children. In the Panel's view, given the reference to Symbicort and the lack of further detail about eligible patient groups, the advertisement would imply to those familiar with Symbicort, that DuoResp Spiromax could also be used in children which was not so. The Panel considered that the impression given by the advertisement was inconsistent with the particulars listed in the DuoResp Spiromax SPC. A breach of the Code was ruled, which was upheld on appeal.

The Panel further noted that the claim 'Licensed for asthma and COPD*' implied that DuoResp Spiromax was licensed for all COPD patients. The Panel noted, however, that according to the DuoResp Spiromax SPCs, both strengths were licensed only for the symptomatic treatment of COPD patients who met certain clinical criteria, ie those with forced expiratory volume in 1 second (FEV_1) < 70% predicted normal (post bronchodilator) and a history of repeated exacerbations, who had significant symptoms despite regular therapy with long-acting bronchodilators. The Panel considered that the impression given by the advertisement was inconsistent with the particulars listed in the DuoResp Spiromax SPC. A breach of the Code was ruled, which was upheld on appeal.

The Panel considered that Teva had failed to maintain high standards and a breach of the Code was ruled, which was upheld on appeal.

The Panel noted that the prescribing information which appeared in the advertisement viewed by the complainant in July 2019 was prepared in May 2017. The Panel noted Teva's submission that the prescribing information was updated in November 2017 and again in September 2018. The Panel noted Teva's submission that the advertisement had been archived in July 2017 and withdrawn from use on 6 August 2018 and was not intended for subsequent use after that point. Teva did not know that the advertisement was still active until it was notified of the complaint in July 2019. The Panel noted Teva's submission that despite being notified to no longer use the advertisement at issue, human error, confirmed by the agency had resulted in the company's instructions not being followed. It was not clear to the Panel when or how Teva had instructed its agency to remove the advertisement and whether Teva had received confirmation from the agency that it had been withdrawn. The Panel further noted Teva's submission there had been two updates to the prescribing information since May 2017 (November 2017 and September 2018). It thus appeared that when Teva first requested the advertisement to be withdrawn in August 2018, it was already at fault for not having previously withdrawn the piece to update it with the November 2017 prescribing information. [As part of its appeal in this case Teva provided further clarification about the advertisement and its placement']

The Panel noted that whilst Teva submitted that it had been let down by its agency and the publisher, it was an established principle under the Code that pharmaceutical companies were responsible for third parties even if that third party failed to follow instructions from the pharmaceutical company. In that regard, however, it appeared to the Panel that, having given instructions for the removal of the advertisement (which already bore outdated prescribing information), Teva did not have a robust follow-up procedure to ensure that it had been withdrawn. The company had only recently required its media buyers to check with digital publishers that relevant material had been removed. The advertisement published on the BMJ website seen by the complainant in July 2019 contained out-of-date prescribing information which was not in line with the current SPC. The Panel considered that high standards had not been maintained and a breach of the Code was ruled, which was upheld on appeal. [As part of its appeal in this case Teva provided further clarification about the advertisement and its placement']

The Panel noted that it was crucial that health professionals and others could rely completely upon the industry for up-to-date and accurate information about their medicines. Prescribing information was an important component of patient safety. The Panel noted its comments and rulings above and considered that Teva had brought discredit upon and reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled, which was upheld on appeal.

A complainant who described him/herself as a concerned UK health professional, complained about an advertisement (ref UK/DUO/15/0053a(1)) for DuoResp Spiromax (budesonide/formoterol fumarate) placed on the BMJ website https://hosted.bmj.com by Teva UK Limited. DuoResp Spiromax, available in two strengths, 160/4.5mcg and 320/9mcg, was indicated for use in certain patients with asthma or chronic obstructive pulmonary disease (COPD).

COMPLAINT

The complainant stated that his/her initial impression was that DuoResp Spiromax was licensed for use in all asthma and COPD patients – then he/she noticed the footnotes that meant the product could only be used in those aged 18 years or more and that only one strength was licensed as maintenance and reliever therapy (MART) in asthma. The complainant then looked at the summary of product characteristics (SPC) and noted that the licensed indication in COPD was 'Symptomatic treatment of patients with COPD with forced expiratory volume in one second (FEV_1) <70% predicted normal (post-bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators'.

The complainant alleged that DuoResp Spiromax had been promoted beyond its licence. The complainant further noted that the prescribing information was over 2 years out-of-date – he/she did not think it had been updated since the SPC was last updated.

When writing to Teva, the Authority asked it to consider the requirements of Clauses 3.2, 7.2, 9.1 and 2 of the Code.

RESPONSE

Teva submitted that it had not claimed that DuoResp Spiromax was indicated for all asthma and COPD patients. The claim 'Licensed for asthma and COPD' highlighted the respiratory conditions

in which DuoResp Spiromax could be prescribed and was licensed; Teva noted that the inhaler market was full of various devices that were only licensed for either asthma or COPD or other respiratory diseases. The claim was clearly in line with the marketing authorization and the SPC and did not reflect promoting beyond the licence as alleged. The full indications listed in the prescribing information reflected those detailed in the SPC.

Teva stated that it was surprised and concerned that a health professional would interpret the claim as meaning that DuoResp Spiromax was licensed for all asthma and COPD patients. A health professional qualified to prescribe or recommend treatments in these therapy areas would know that patients with asthma and COPD were not a homogenous group, and that within each condition a number of clinical characteristics determined which particular medicines were most appropriate for an individual patient. These included severity of disease, lung function, response to prior therapies, exacerbation history and level of symptoms. Accordingly, the different classes of medicines available for these conditions, including inhalers, had such clinical criteria built into their licences, such that different medicines were suitable and licensed for different subgroups of asthma and COPD patients. The specific licensed indication criteria highlighted by the complainant from the SPC ('Symptomatic treatment of patients with COPD with forced expiratory volume in 1 second (FEV_1) <70% predicted normal and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators') was detailed within the prescribing information included in the BMJ advertisement which clearly highlighted the specific asthma and COPD patient populations for whom DuoResp Spiromax was indicated.

Teva submitted that the information contained within the advertisement was complete and not misleading and was addressed during the development of the advertisement. As noted by the complainant, clear and obvious caveats had been provided to aid health professionals in an attempt to avoid any potential misinformation. Firstly, it was clarified that DuoResp Spiromax was only licensed in those 18 years of age and older and secondly that the MART licence in asthma was only appropriate with the 160/4.5mcg strength inhaler (the 320/9mcg version of the inhaler was not licensed for MART therapy).

Teva noted that the Code did not require the full licensed indication to be stated in advertisements and, as highlighted above, it had provided only the disease therapy areas as reported in the SPC and the full licenced information was clearly provided to the reader in the prescribing information, with a recommendation to consult the SPC if further information was required as was standard practice. Teva submitted that the information in the advertisement was fair and balanced and would enable a health professional to form a balanced opinion of the therapeutic benefit of DuoResp Spiromax.

The complainant had alleged that the prescribing information (ref UK/MED/17/0034) was not within its two-year review period, having been prepared in May 2017 and the advertisement was viewed in July 2019. The prescribing information was updated in November 2017 and again in September 2018, but due to human error, as confirmed by the agency, despite being notified to no longer use the advertisement at issue, the advertisement continued to be used. Teva stated that, until notified of the complaint, it did not know that the advertisement was still active; the advertisement had subsequently been removed via the agency and the publisher at Teva's instruction. Teva noted that the job had been archived on 20 July 2017 and withdrawn from use on 6 August 2018 so it was not intended for subsequent use and viewing by health professionals after that point. Teva submitted that it had maintained high standards during the development of the DuoResp Spiromax material in question, and it was confident in its internal certification process for all promotional materials. In this rare instance, as highlighted in the email from the third party agency, human

error had resulted in the company's instructions not being followed and hence for the appearance of the outdated advertisement with outdated prescribing information. Teva noted that under the Code, it was responsible for the actions of third parties engaged, so it accepted that due to the publication of the outdated advertisement including outdated prescribing information, there had been an inadvertent breach of Clause 7.2 due to the actions of its agency and the publisher in this matter. Teva stated that in the spirit of continuous improvement, and maintaining the highest standards possible, it had now put in place additional steps when working with third party agencies to mitigate the risk of this happening again, whereby its media buyers would check with all digital publishers that the company's advertisements had been removed following their agreed paid for time/number of clicks.

Teva denied breaches of Clauses 3.2 and 9.1; it had maintained high standards in its actions, and as it had not brought discredit upon, or reduced confidence in the pharmaceutical industry, it had not breached Clause 2. However, the company accepted a breach of Clause 7.2 in the use of an outdated advertisement including outdated prescribing information through the actions of its agency in human error.

PANEL RULING

The Panel noted that the advertisement was headed 'DuoResp Spiromax (budesonide/formoterol) an award-winning design containing the effective combinations of drugs you know'. Below the heading was a list of five, prominent bullet points beneath which were photographs of the two strengths of the inhaler available. The second bullet point read 'Licensed for asthma and COPD*'. The asterisk led the reader to a footnote in small font at the bottom of the list of bullet points, which stated 'DuoResp Spiromax is licensed for use in adults 18 years of age and older'. The fourth bullet point stated 'Maintenance and Reliever Therapy (MART) licence for asthma**' which led the reader to a second footnote which read 'For 160mcg/4.5mcg strength only'.

The Panel noted that the supplementary information to Clause 7.2 stated that claims in promotional material must be capable of standing alone as regards accuracy etc and in general should not be qualified by the use of footnotes and the like.

The Panel considered that the second bullet point was misleading; read in isolation without the footnote, it implied that all patients with asthma or COPD were suitable for DuoResp Spiromax therapy which was not so; the medicine could not be used in those aged 17 years or less. The claim could not stand alone and so the Panel ruled a breach of Clause 7.2.

The Panel noted that the fourth bullet point was misleading if read in isolation as it implied that either strength of DuoResp Spiromax could be used. The advertisement promoted both strengths of DuoResp Spiromax but only one (160mcg/4.5mcg) was licensed for maintenance and reliever therapy in asthma. The claim could not stand alone and so the Panel ruled a further breach of Clause 7.2.

The Panel noted that the third bullet point stated that 'DuoResp Spiromax doses are therapeutically equivalent to Symbicort Turbohaler (budesonide/formoterol)'. In that regard the Panel noted that, depending on the strength and indication, Symbicort Turbohaler could be used in children as young as 6 years old. The Panel considered that it was misleading, without the benefit of further information, to directly compare DuoResp Spiromax, which could only be used in adults aged 18 years and older, with Symbicort Turbohaler which could potentially be used in children. In the Panel's view, given the reference to Symbicort and the lack of further detail about eligible

patient groups, the advertisement would imply to those familiar with Symbicort, that DuoResp Spiromax could also be used in children which was not so. The Panel considered that the impression given by the advertisement was inconsistent with the particulars listed in the DuoResp Spiromax SPC. A breach of Clause 3.2 was ruled.

The Panel further noted that the claim 'Licensed for asthma and COPD*' implied that DuoResp Spiromax was licensed for all COPD patients. The Panel noted, however, that according to the DuoResp Spiromax SPCs, both strengths were licensed only for the symptomatic treatment of COPD patients who met certain clinical criteria, ie those with forced expiratory volume in 1 second (FEV_1) < 70% predicted normal (post bronchodilator) and a history of repeated exacerbations, who had significant symptoms despite regular therapy with long-acting bronchodilators. The Panel considered that the impression given by the advertisement was inconsistent with the particulars listed in the DuoResp Spiromax SPC. A breach of Clause 3.2 was ruled.

The Panel considered that Teva had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted that the prescribing information (ref UK/MED/17/0034) which appeared in the advertisement (ref UK/DUO/15/0053a(1)) viewed by the complainant in July 2019 was prepared in May 2017. The Panel noted Teva's submission that the prescribing information was updated in November 2017 and again in September 2018. The Panel noted Teva's submission that the advertisement had been archived on 20 July 2017 and withdrawn from use on 6 August 2018 and was not intended for subsequent use after that point. Teva did not know that the advertisement was still active until it was notified of the complaint in July 2019. The Panel noted Teva's submission that despite being notified to no longer use the advertisement at issue, human error, confirmed by the agency had resulted in the company's instructions not being followed. The Panel did not have before it any of the communication between Teva and its agency in this regard other than an email dated 12 September 2019 from the agency which stated that the publisher believed [the advertisement] was booked back in 2017 and should have been removed from the site but was overseen [sic] due to human error. It was not clear to the Panel when or how Teva had instructed its agency to remove the advertisement and whether Teva had received confirmation from the agency that it had been withdrawn. The Panel further noted Teva's submission there had been two updates to the prescribing information since May 2017 (November 2017 and September 2018). It thus appeared that when Teva first requested the advertisement to be withdrawn in August 2018, it was already at fault for not having previously withdrawn the piece to update it with the November 2017 prescribing information. [As part of its appeal in this case Teva provided further clarification about the advertisement and its placement']

The Panel noted that whilst Teva submitted that it had been let down by its agency and the publisher, it was an established principle under the Code that pharmaceutical companies were responsible for third parties even if that third party failed to follow instructions from the pharmaceutical company. In that regard, however, it appeared to the Panel that, having given instructions for the removal of the advertisement (which already bore outdated prescribing information), Teva did not have a robust follow-up procedure to ensure that it had been withdrawn. The company had only recently required its media buyers to check with digital publishers that relevant material had been removed. The advertisement published on the BMJ website seen by the complainant in July 2019 contained out-of-date prescribing information which was not in line with the current SPC. The Panel considered that high standards had not been maintained and a breach of Clause 9.1 was ruled. [As part of its appeal in this case Teva provided further clarification about the advertisement and its placement']

The Panel noted that it was crucial that health professionals and others could rely completely upon the industry for up-to-date and accurate information about their medicines. Prescribing information was an important component of patient safety. The Panel noted its comments and rulings above and considered that Teva had brought discredit upon and reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled.

APPEAL BY TEVA

Teva stated that it took compliance with the Code extremely seriously.

Teva noted that Clause 2 stated:

> 'Activities or materials associated with promotion must never be such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry'.

Furthermore, the supplementary information to Clause 2 stated:

> 'Examples of activities that are likely to be in breach of Clause 2 include prejudicing patient safety and/or public health, excessive hospitality, inducements to prescribe, unacceptable payments, inadequate action leading to a breach of undertaking, promotion prior to the grant of a marketing authorization, conduct of company employees/ agents that falls short of competent care and multiple/ cumulative breaches of a similar and serious nature in the same therapeutic area within a short period of time.'

Teva submitted that it concurred with the Panel that prescribing information was an important part of patient safety in advising health professionals of the attributes of the medicine advertised and agreed that the prescribing information should be consistent with the SPC. The prescribing information in the advertisement was correct at the time the advertisement was placed. Further, the advertisement was placed for a fixed term period of 6 months commencing August 2017. The prescribing information was updated internally in Teva's Zinc system with a price change in November 2017 (due to a price drop made by the competitor product Symbicort Turbohaler). This new price was not implemented until January 2018, which coincided with the end of the advertisement period. Apart from the price change, the prescribing information implemented in January 2018 had no other content changes and the advertisement remained consistent with the SPC and prescribing information (which did not incorporate price changes).

Teva submitted that as the advertisement was due to have been taken down by the time the price change was implemented, there was no need to update the advertisement with the new prescribing information. Further, the price change had no bearing whatsoever to patient safety. As advised previously, the publisher made an error in leaving Teva's advertisement online for a period longer than its agreement. Teva had sought clarification from its media-buying agency and it had confirmed that the industry, as a whole, did not check that advertisements had been taken down following their agreed periods. Teva expected compliance with the agreed period to be the responsibility of the publisher (as it would be in publications in printed journals). Further, Teva would not routinely check the following month's journal to ensure its advertisements had not been placed in breach of its agreement. Indeed, as a pharmaceutical company, Teva did not have access to all web based or printed journals in order to perform such checking. As previously stated, there was another change to the prescribing information in September 2018 but this was a minor change with no bearing on patient safety. The change to the prescribing information was

the inclusion of the additional words 'post bronchodilator' so that the previous sentence in the prescribing information of 'Symptomatic treatment of patients with COPD with forced expiratory volume in 1 second (FEV1) < 70% predicted normal.' now read as: 'Symptomatic treatment of patients with COPD with forced expiratory volume in 1 second (FEV1) < 70% predicted normal (post bronchodilator).'

Teva submitted that despite the advertisement continuing to be published in error, the prescribing information remained consistent with the SPC. Teva had previously noted that the prescribing information had been updated and reviewed in the two-year period and therefore contended that the statement by the complainant 'I do not think it has been updated since the SPC has since been updated' was incorrect. In addition, the updating of the prescribing information as detailed here clearly demonstrated that Teva had robust processes in place. At no time had patient safety by virtue of Teva's processing and use of the prescribing information been compromised. Further, Teva had not brought discredit on, or reduced confidence in, the industry and therefore it appealed the ruling of a breach of Clause 2.

As slightly misstated in the response from the Panel – the supplementary information to Clause 7.2 stated that 'It should be borne in mind that claims in promotional material must be capable of standing alone as regards accuracy etc. In general claims should not be qualified by the use of footnotes and the like'.

Teva submitted that these were two separate sentences. They were not statements linked by an 'and'. This changed what was intended by the clause, which was that footnotes could be used in certain circumstances. It did not prohibit their use. Otherwise, the clause would have expressly stated that. Teva's view (and indeed the view of much of the pharmaceutical industry) of this clause was that footnotes could be used where appropriate to add clarity (not detract from it). Indeed, the Panel had ruled on numerous advertisements in the past and not ruled breaches where footnotes had been used. Indeed, advertisements published in journals and online journals by numerous members of the pharmaceutical industry (both in the past and as could be found in current publications) included such footnotes.

Teva submitted that a recent ruling (Case AUTH/3175/3/19) which concerned an advertisement with footnotes and was not ruled to be a breach by virtue of the use of footnotes. Similarly, in Case AUTH/2945/3/17, the Panel did not rule a breach with respect to the positioning and use of a footnote. These cases demonstrated that the Panel did not rule that use of footnotes in advertisements (in of themselves) constituted a breach. Indeed, the Panel in Case AUTH/2945/3/17 acknowledged a footnote was used to differentiate different inhalers but stated it would have been helpful if the relevant footnote had appeared at the outset rather than six pages later where it might be read as the heading to table 9 rather than the footnote to table 8. The Panel ruled the intended audience would know that not all medicines licensed for asthma were licensed for COPD and there had not been a breach of the Code. In addition, the complainant in the current case did not complain about the use of a footnote and so Teva appealed the Panel's ruling in this matter.

Teva submitted that the advertisement clearly stated the strengths of DuoResp Spiromax available and being promoted. It also clearly stated that these were licensed in adults 18 and above, which was further clarified by the prescribing information. In that regard the advertisement was not misleading in its comparison to Symbicort Turbohaler as the doses of DuoResp (both included in the advertisement) were therapeutically equivalent to the same doses of Symbicort Turbohaler in adults 18 years and older as stated. There could be no inference of the advertisement attempting

to promote DuoResp Spiromax in an age range other than as expressly stated in the advertisement and which was consistent with the SPC. Furthermore, the statements made in the advertisement were entirely in accordance with the DuoResp Spiromax marketing authorisation and were not inconsistent with the SPC.

Teva submitted that the statements in the advertisement did not mislead, nor intend to mislead, by stating that DuoResp Spiromax was licensed for asthma and COPD. The advertisement did not claim that this statement meant every single indication related to asthma and/or COPD. The detailed indications were in the prescribing information. The Code did not mandate the use of full indications in advertisements. Indeed, numerous advertisements included no indications or therapy area for the products advertised as well as footnotes (examples attached, eg Seretide advertisement had no therapy area and these advertisements used footnotes). The advertisement simply highlighted the products that were licensed in these therapeutic areas and distinguished the product from other products that might only be licensed in asthma or COPD, but not both. The advertisement did not claim or endeavour to comprehensively state this product was for all patients in these therapeutic areas. Teva therefore appealed the rulings of breaches of Clause 3.2.

Teva submitted that the based on its statements in relation to its grounds for appealing the rulings of breaches of Clauses 3.2 and 7.2 above, it also appealed the rulings of breaches of Clauses 9.1 and 2.

COMMENTS FROM THE COMPLAINANT

The complainant stated that he/she was sure that the Appeal Board was best placed to review the evidence.

APPEAL BOARD RULING

The Appeal Board noted that the digital advertisement at issue was headed 'DuoResp Spiromax (budesonide/formoterol) an award winning design containing the effective combinations of drugs you know'. Below the heading was a list of five, prominent bullet points beneath which were photographs of the two strengths of the inhaler available.

The Appeal Board considered that the second bullet point 'Licensed for asthma and COPD*' was misleading in isolation as it implied that all patients with asthma or COPD were suitable for DuoResp Spiromax therapy which was not so. The asterisk led to a footnote in smaller font that read 'DuoResp Spiromax is licensed for use in adults 18 years of age and older'. Thus, alone the claim was inaccurate and could not rely on qualification in either a footnote or the prescribing information. The Appeal Board upheld the Panel's ruling of a breach of Clause 7.2. The appeal on this point was unsuccessful.

The Appeal Board considered that the fourth bullet point 'Maintenance and Reliever Therapy (MART) licence for asthma**' which led the reader to a second footnote 'For 160mcg/4.5mcg strength only' was misleading if read in isolation as it implied that either strength of DuoResp Spiromax could be used and that was not so. The advertisement promoted both strengths of DuoResp Spiromax but only one (160mcg/4.5mcg) was licensed for maintenance and reliever therapy in asthma. This misleading impression was compounded by the prominent visual of both inhaler strengths. The Appeal Board upheld the Panel's ruling of a breach of Clause 7.2. The appeal on this point was unsuccessful.

The Appeal Board noted the third bullet point 'DuoResp Spiromax doses are therapeutically equivalent to Symbicort Turbohaler (budesonide/formoterol)' and that, depending on the strength and indication, Symbicort Turbohaler could be used in children as young as 6 years old. DuoResp Spiromax could only be used in adults aged 18 years and older. The Appeal Board considered that the advertisement might imply to those familiar with Symbicort, that DuoResp Spiromax could also be used in children which was not so. The Appeal Board considered that the impression given by the advertisement was inconsistent with the particulars listed in the DuoResp Spiromax SPC and it upheld the Panel's ruling of a breach of Clause 3.2. The appeal on this point was unsuccessful.

The Appeal Board considered that the second bullet point 'Licensed for asthma and COPD' implied that DuoResp Spiromax was licensed for all COPD patients. However, according to the DuoResp Spiromax SPCs, both strengths were licensed only for the symptomatic treatment of COPD patients who met certain clinical criteria, ie those with forced expiratory volume in 1 second (FEV1) < 70% predicted normal (post bronchodilator) and a history of repeated exacerbations, who had significant symptoms despite regular therapy with long-acting bronchodilators. The Appeal Board considered that the impression given by the advertisement was inconsistent with the particulars listed in the DuoResp Spiromax SPC and it upheld the Panel's ruling of a breach of Clause 3.2. The appeal on this point was unsuccessful.

The Appeal Board considered that Teva had failed to maintain high standards and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board noted that in its appeal Teva stated that the advertisement had been placed for a fixed six-month contract period commencing August 2017. The Appeal Board noted Teva's submission that the advertisement had been archived on 20 July 2017 and withdrawn from further use on 6 August 2018 and was not intended for further use. The complaint was received in July 2019 thus the advertisement had remained published on the BMJ website for a total of two years rather than for the six-month contract period. Teva confirmed that its third party agency had left the advertisement on the website due to human error. The Appeal Board noted that neither Teva nor its third party media agency had apparently taken any steps to ensure the advertisement was taken down after the contracted period.

The Appeal Board noted that the prescribing information (ref UK/MED/17/0034) which appeared in the advertisement (ref UK/DUO/15/0053a(1)) and was viewed by the complainant in July 2019 was prepared in May 2017. The Appeal Board noted Teva's submission that the prescribing information was updated in November 2017 and implemented in January 2018. This was due to a price change and as the change was only implemented after the contractual publication period for the advertisement had expired, the advertisement was not updated. The Appeal Board noted a further change to the prescribing information in September 2018 was the inclusion of the additional words 'post bronchodilator' in relation to the COPD indication at Section 4.1 so that the sentence in the prescribing information 'Symptomatic treatment of patients with COPD with forced expiratory volume in 1 second (FEV1) < 70% predicted normal and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators' now read : 'Symptomatic treatment of patients with COPD with forced expiratory volume in 1 second (FEV1) < 70% predicted normal (post bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators.' The Appeal Board disagreed with, and was concerned about, Teva's submission that this was a minor change with no bearing on patient safety. This change potentially meant that the patient population that could be prescribed DuoResp Spiromax might be reduced as after taking a bronchodilator, forced expiratory

volume in 1 second (FEV1) < 70% predicted normal, might be less likely. The advertisement as published without the update to the prescribing information meant that a group of patients could potentially be prescribed DuoResp Spiromax for whom it was not indicated. In the Appeal Board's view this was a patient safety issue.

The Appeal Board noted that there had been further changes to the SPC in 2019.

The Appeal Board noted that whilst Teva submitted that it had been let down by its agency and the publisher, it was an established principle under the Code that pharmaceutical companies were responsible for third parties even if that third party failed to follow instructions from the pharmaceutical company. The Appeal Board considered that Teva did not have a robust follow-up procedure to ensure that its advertisement had been withdrawn. The advertisement published on the BMJ website seen by the complainant in July 2019 contained out-of-date prescribing information which was not in line with the SPC at that time. The Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board noted that it was crucial that health professionals and others could rely completely upon the industry for up-to-date and accurate information about their medicines. Prescribing information was an important component of patient safety. The Appeal Board noted its comments and rulings above and considered that Teva had brought discredit upon and reduced confidence in the pharmaceutical industry and it upheld the Panel's ruling of a breach of Clause 2. The appeal on this point was unsuccessful.

Complaint received **16 July 2019**

Case completed **7 April 2020**