ANONYMOUS GP v GLAXOSMITHKLINE

Relvar advertisements

An anonymous, contactable general practitioner complained about two bullet points in journal advertisements for Relvar Ellipta (fluticasone furoate and vilanterol inhalation powder) placed by GlaxoSmithKline UK Ltd. One of the advertisements was about the use of Relvar in asthma and the other was about its use in chronic obstructive pulmonary disease (COPD). The two claims at issue appeared in both advertisements.

With regard to the claim 'Delivered in a straightforward device' the complainant did not see why undue emphasis was put on an inhaler feature that worked in exactly the same way as existing inhalers that could be prescribed; it really seemed no different to the Symbicort Tubohaler. The complainant also referred to the claim 'That offers value to the NHS' and noted that the advertisements did not explain why or how Relvar offered value.

The detailed response from GlaxoSmithKline is given below.

The Panel noted GlaxoSmithKline's submission that the claim 'Delivered in a straightforward device' was a stand-alone claim which did not refer to any other inhalation device in asthma or COPD and thus did not invite any comparisons with them. The claim was referenced to Riley *et al* in the COPD advertisement. The study showed that following initial instruction, 98% (n=618/632) of COPD patients used Ellipta correctly at day 1. At 6 weeks without further verbal instruction or demonstration, 99% of subjects still used their Ellipta inhaler correctly and rated it either very easy or easy to use.

The claim in the asthma advertisement was referenced to Svedsater *et al* (2013a). The results of that study found that 95% of patients used the Ellipta device correctly at the baseline visit (as adjudicated by an investigator) after a single demonstration of correct usage (n=1,049). At week 2 and 4, >99% of patients used the inhaler correctly and 94% found the Ellipta device was easy or very easy to use.

The Panel noted that the steps for Relvar Ellipta on the product website, as derived from the package information leaflet (PIL), showed that sliding the cover open until a click was heard primed the device for inhalation. The Panel noted GlaxoSmithKline's submission that unlike Symbicort Turbohaler, no additional loading step was required. In addition the dose counter of the Ellipta device counted down by one for each dose administered unlike the dose counter on the Turbohaler which was only marked in intervals of 10.

The Panel considered that, given the details regarding the steps on how to use the Relvar device on the product website and in the PIL and the data from Riley *et al* and Svedsater *et al* (2013a), the claim 'Delivered in a straightforward device' was not misleading and unsubstantiable as alleged. No breach of the Code was ruled.

With regard to the claim 'That offers value to the NHS' and the complainant's concern that there was no explanation as to why or how Relvar offered value, the Panel noted that promotional material did not need to contain all of the relevant information to substantiate a claim. All claims had to be capable of substantiation and such substantiation had to be provided on request. The Panel noted that GlaxoSmithKline had provided information showing how Relvar Ellipta might offer value to the NHS including its effective once daily dosage regimen and ease of use of the device and the presumed effect this would have on compliance. The Panel further noted that, from information provided by GlaxoSmithKline, the two Relvar Ellipta preparations (92/22mcg) and (184/22mcg) were the least expensive options in the mid and high dose inhaled corticosteroid/long-acting beta2-agonist dosage bands for asthma. Only the 92/22mcg dose was licensed in COPD and was less expensive than Seretide 500/50mcg Accuhaler and Symbicort Turbohaler 400/12mcg or 200/6mcg.

The Panel noted that the claim 'That offers value to the NHS' was non-specific and did not make it clear exactly what value the device would offer the NHS. The Panel, however, noted the detailed information provided by GlaxoSmithKline and did not consider that, whether considered in monetary or non monetary terms, the claim was misleading or unsubstantiable. No breach of the Code was ruled.

The Panel noted its rulings above and consequently ruled no breach of the Code as it did not consider that GlaxoSmithKline had failed to maintain high standards.

An anonymous, contactable general practitioner complained about advertisements (refs UK/FFT/0096l/13 and UK/FFT/0056/13) for Relvar Ellipta (fluticasone furoate and vilanterol inhalation powder) placed in the 5 February issue of Prescriber and the 8 February issue of the BMJ by GlaxoSmithKline UK Ltd.

Relvar Ellipta was indicated for the regular treatment of asthma in adults and adolescents aged 12 years and older not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta2-agonists and for the symptomatic treatment of adults with chronic obstructive pulmonary disease (COPD) with a FEV1 < 70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy.

The advertisements related either to the use of Relvar in COPD (ref UK/FFT/0096l/13) or in asthma (ref UK/FFT/0056/13). Each advertisement contained four bullet points the first three of which were common to both.

COMPLAINT

The complainant referred to two bullet points which appeared in both advertisements. With regard to the claim 'Delivered in a straightforward device' the complainant stated that in his/her view, having looked at the product website and the inhaler demonstration, the device steps were really no different to Symbicort Turbohaler where one primed the device and inhaled. The complainant did not see why undue emphasis was put on an inhaler feature that worked in exactly the same way as existing inhalers that could be prescribed. The complainant also referred to the claim 'That offers value to the NHS' and noted that the advertisements did not explain why or how Relvar offered value.

GlaxoSmithKline was asked to respond in relation to Clauses 7.2, 7.4 and 9.1 of the Code.

RESPONSE

GlaxoSmithKline stated that Relvar Ellipta was a new inhaled corticosteroid/long-acting beta2-agonist (ICS/LABA) combination product, which was licensed in the UK for both asthma and COPD as follows:

- The regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta2-agonist and inhaled corticosteroid) was appropriate ie in patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short-acting beta2-agonists.

- The symptomatic treatment of adults with COPD with a FEV1 < 70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy.

Two doses were licensed in asthma, 92/22mcg and 184/22mcg; only the 92/22mcg dose was licensed in COPD.

The advertisements informed health professionals about the availability of this new medicine and very briefly highlighted a few of its key attributes by means of four bullet points. Obviously, these four claims, as well as several others, which showed the total value that Relvar could offer the NHS were expanded upon in much greater depth in other materials specifically designed for health professionals and appropriate administrative staff for example the detail aid, formulary pack and budget impact model. Additionally, health professionals and appropriate administrative staff could also discuss, in detail, clinical data and the potential budgetary impact of using Relvar with GlaxoSmithKline employees such as representatives and health outcome consultants.

'Delivered in a straightforward device'

GlaxoSmithKline stated that this was a simple, stand-alone claim. It did not refer to any other inhalation device in asthma or COPD and as such did not invite any comparisons with them. The claim related to the Ellipta inhalation delivery device which was the only device via which patients could receive Relvar. Currently the Ellipta device was only available for Relvar.

The claim was substantiated in the COPD advertisement by the reference to Riley *et al* (2013). One of the objectives of this study was to determine whether COPD patients could easily use the Ellipta device. Following initial instruction 98% of patients (n=618/632) used Ellipta correctly at day one. Correct Ellipta inhaler use was re-assessed after 6 weeks, without further verbal instruction or demonstration to the patient; 99% (n=580/587) of subjects still used their Ellipta correctly. After 6 weeks of treatment; 99% (580/587) of patients rated the Ellipta inhaler as either very easy or easy to use.

The claim was substantiated in the asthma advertisement by the reference to Svedsater *et al* (2013a). The objective of this study was to assess participating patients' competence in the use of the Ellipta device, as judged by trial investigators. Participants were involved in one of three clinical studies which were part of the Relvar asthma development programme. Trial investigators assessed patients' competence using the Ellipta device at baseline, and again at weeks 2 and 4 of the treatment period. Patients were also asked to complete an ease of use questionnaire; one of the questions required rating the inhaler as very easy, easy, neutral, difficult, or very difficult to use.

The study results showed that 95% of patients used the Ellipta device correctly at the baseline visit (as adjudicated by the investigator) after a single demonstration of correct usage (n=1,049). Furthermore, when inhaler technique was reassessed at weeks 2 (n=1,024) and 4 (n=988) >99% of patients used the inhaler correctly. Additionally 94% (929/989) of patients reported the Ellipta device to be easy or very easy to use.

Although not referenced in the advertisements, Svedsater *et al* (2013b) conducted one-on-one interviews with asthma and COPD patients who had completed studies involving the Ellipta device, to find out what they thought of it. Several participants spontaneously reported that the device was straightforward and intuitive to use.

GlaxoSmithKline submitted that the above evidence, involving both asthma and COPD patients, strongly supported the claim that the Ellipta device was a straightforward device.

GlaxoSmithKline noted the complainant's allegation that undue emphasis was placed on the inhaler device by stating that it was a straightforward device. GlaxoSmithKline submitted that in asthma and COPD, consideration of the inhalation device was an important part of the prescribing decision for a new medicine. Inhalers, although commonly used in asthma and COPD, were often used suboptimally

which led to uncontrolled disease and increased costs, either as a result of uncontrolled disease or increased use of relief medication or preventative therapy (Price *et al*, 2013, Press *et al*, 2011). Price *et al* highlighted that one of the major compliance issues for asthma patients using inhalers was unintentional non-compliance ie when a patient made inadvertent mistakes using the device. They concluded that the more complex an instruction and the more handling steps needed to start the inhalation process, the greater the chance of an error occurring. In fact, they suggested that one way in which a device could be simplified was by combining the activation of the device with another step such as removing the cap. This was a feature of the Ellipta device.

For these reasons, GlaxoSmithKline submitted that it was important to tell clinicians that asthma and COPD patients found that the Ellipta device was straightforward; a claim substantiated by Riley *et al* and Svedsater *et al* (2013a).

Although this was a stand-alone claim, based on Ellipta device data only, the anonymous complainant compared information on the product website to his/her impression about the use of the Symbicort Turbohaler and stated that the device steps were really no different to Symbicort Turbohaler and an inhaler feature that worked in exactly the same way as existing inhalers. Given the nature of the stand-alone claim at issue, GlaxoSmithKline submitted that it was not appropriate to compare, in this response, how the Ellipta device worked with all the other available inhalers. However, given that the Symbicort Turbohaler was specifically mentioned, GlaxoSmithKline noted that the steps required to use the two inhalers were different.

The package information leaflet (PIL) for Symbicort Turbohaler involved a 5 stage approach for first 'Preparing your new Symbicort Turbohaler' followed by 9 steps for 'How to take an inhalation'. GlaxoSmithKline noted that in addition to removing the cover, the Turbohaler had to be loaded each time before use by turning the red grip at the base of the inhaler in two separate directions. The steps for Relvar Ellipta shown on the product website (which were derived from the Relvar Ellipta PIL) showed that with the Ellipta inhaler, opening the cover was all that was required to prepare the device for inhalation. Unlike the Turbohaler, no additional loading step was required. GlaxoSmithKline also noted that there were only four steps within the instructions for the Ellipta device in the PIL. Also, the dose counter on the Turbohaler was only marked in intervals of 10, therefore it did not show every dose. In particular, patients needed to know how many doses remained once the counter reached 10, so as to ensure they did not reach 0 without having a replacement inhaler. With the Ellipta device the dose counter counted down by 1 for each dose administered.

In summary, GlaxoSmithKline submitted that in both asthma and COPD the claim 'Delivered in a straightforward device' was accurate, fair, balanced and objective and capable of substantiation. The claim was therefore not in breach of Clauses 7.2 and 7.4 of the Code.

'That offers value to the NHS'

This claim was not referenced in the advertisements. However, in keeping with Clauses 7.4 and 7.5, GlaxoSmithKline could provide substantiation for the claim to any health professional or appropriate administrative staff who requested it.

GlaxoSmithKline submitted that the introduction of a new medicine and the value it could bring to the NHS might be considered both in monetary and non monetary terms. When clinicians, commissioning bodies and health appraisal organisations such as the National Institute for Health and Care Excellence (NICE) reviewed the value of a new medicine, they not only looked at the cost of the medicine but also assessed clinical efficacy, safety and other factors such as the route of administration, dosing regimen and service charges. Henshall *et al* (2013) reported that the Health Technology Assessment International Policy Forum concluded that in addition to elements related to cost, value also incorporated measures related to patient benefits such as clinical outcomes.

1 Non monetary value

GlaxoSmithKline noted that Relvar Ellipta was a new ICS/LABA treatment option for COPD and asthma and the first once daily ICS/LABA for COPD and asthma, which produced clinically significant outcomes. Despite the availability of a number of different treatments there still remained a large burden of illness with COPD and asthma in the UK.

It was estimated that three million people in England had COPD, with only just under a million diagnosed as such. COPD was the second most common cause of emergency admission to hospital; around a third of those admitted to hospital were readmitted within a month of discharge. COPD caused around 23,000 deaths in England each year. The total annual cost of COPD to the NHS was over £800 million (NHS Medical Directorate COPD Commissioning Toolkit, 2012).

The prevalence of asthma in England was among the highest in the world. In the UK, 5.4 million people currently received treatment for asthma. There were around 1,000 deaths from asthma a year in the UK, the majority of which were preventable. Most admissions were emergencies and 70% might have been prevented with appropriate early interventions; asthma cost the NHS an estimated £1 billion a year. Many people with asthma did not achieve freedom from symptoms and a recent large scale survey reported that around 35% of adult asthmatics had had an asthma attack in the previous 12 months (NICE Quality standard for asthma, 2013; An outcomes strategy for COPD and Asthma, Department of Health Best Practice Guidance, 2012).

The place of ICS/LABAs was well recognised within treatment guidelines such as the British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) guideline on the management of asthma

(revised 2011) and the NICE clinical guideline: Management of COPD in adults in primary and secondary care, June 2010. Although a number of ICS/LABAs were already licensed in COPD and asthma, Relvar was the first ICS/LABA combination that was licensed for once daily use only, due to its ability to provide continuous 24 hour efficacy from a once daily dose. GlaxoSmithKline submitted that due to the features highlighted below, the introduction of Relvar was of value to the NHS.

2 Once daily vs twice daily

COPD

GlaxoSmithKline submitted that the availability of a once daily ICS/LABA maintenance treatment in COPD was a valuable addition to the NHS. Patient adherence to COPD treatment was generally low and suboptimal (Charles *et al*, 2010). The importance of improved compliance was highlighted by the finding that <80% adherence to twice daily Seretide 500/50mcg was linked to increased hospital admissions and death (Vestbo *et al*, 2009). There was some evidence that a once daily COPD inhaler therapy might improve compliance (in the long-acting muscarinic antagonist (LAMA) class). In a retrospective analysis of 50,076 patients in the US looking specifically at adherence (Toy *et al*, 2011), COPD patients initiated on once daily tiotropium (n=3,678) had significantly higher adherence over 12 months than patients initiated twice a day Seretide 500/50mcg and Symbicort 400/12mcg (n=25,011) (43.3% vs 37% respectively, p<0.0001).

Currently there was no direct evidence that Relvar 92/22mcg improved patient compliance vs ICS/LABA combinations dosed twice daily. As might be expected in the controlled environment of a randomised control trial, in the head-to-head study between Relvar 92/22mcg and Seretide 500/50mcg (Agusti *et al*, 2013) compliance rates were very high in both treatment arms (97.5%). It was not unreasonable to postulate that in the real world setting, compliance rates might be less and that a once daily regime might result in improved compliance rates vs a twice daily regime.

Finally, with an increasing number of COPD patients taking 'triple therapy' (concomitant ICS/LABA and LAMA preparations), a once daily ICS/LABA would complement the once daily dosing schedule of the most widely prescribed LAMAs (Spiriva and Seebri).

Asthma

GlaxoSmithKline submitted that the availability of a once daily ICS/LABA maintenance treatment in asthma was a valuable addition to the NHS, as non-adherence to maintenance therapies was common and might contribute to poor asthma control (Haughney *et al*, 2008). As stated above, there was no direct evidence that Relvar improved patient compliance vs ICS/LABA combinations dosed twice daily. As might be expected in the controlled environment of a randomised control trial, in the head-to-head study between Relvar 92/22mcg and Seretide 250/50mcg (Woodcock *et al*, 2013) compliance rates were very high in both treatment arms (>94%). However, once again it was not unreasonable to postulate that in the real world setting, compliance rates might be less and that a once daily regimen might result in improved compliance rates vs a twice daily regimen. Indeed, it had been demonstrated that compliance with a once daily regimen was greater than with a twice daily regimen; in a 12-week study (Price *et al*, 2010) designed to mimic an actual clinical setting in subjects with mild to moderate persistent asthma, compliance with once daily mometasone was significantly better than with twice daily mometasone.

For a number of reasons (eg forgetfulness, busy lifestyle, reliance on a carer), some COPD and asthma patients might find taking a medicine only once a day a better treatment option and Relvar offered these patients the opportunity to manage their condition with only a single daily dose, something not offered by other currently available ICS/LABAs.

3 Efficacy

GlaxoSmithKline stated that the clinical development programme for Relvar in COPD and asthma looked at a number of endpoints which were clinically important for patients and health professionals. Two important endpoints should be considered.

a) COPD

Lung function: Forced Expiratory Volume in 1 second (FEV1)

GlaxoSmithKline submitted that FEV1 was the most extensively used and one of the most repeatable lung function parameters to measure the obstructive element of COPD and to determine treatment strategies (EMA, 2012). In a 12 week head-to-head study, once daily Relvar 92/22mcg demonstrated an improvement from baseline trough of 0-24hr weighted mean FEV1 of 130mL compared with Seretide 500/50mcg twice daily which increased weighted mean FEV1 by 108mL (Agusti *et al*). The difference between the treatment groups of 22mL was not statistically significant (p=0.282); this study was a superiority study and as such the primary endpoint was not met. However, a clinically meaningful increase of FEV1 was accepted to be 100mL (NICE 2010 COPD clinical guidelines) and as such both Relvar and Seretide achieved this clinically meaningful increase from baseline.

This data demonstrated how clinically meaningful improvements in lung function were now possible with a once daily ICS/LABA.

COPD exacerbations

Exacerbations were possibly the most impactful consequence of COPD for both the patient and the local health economy. NICE described exacerbations as 'important events for patients and the NHS. Patients experiencing frequent exacerbations have a worse prognosis and much of the cost of caring

for COPD results from managing exacerbations. Strategies to reduce the frequency and impact of exacerbations are essential'.

In two one year studies (Dransfield *et al*, 2013), the annual rate of moderate/severe exacerbations was compared between Relvar 92/22mcg once daily and the LABA component alone, vilanterol 22mcg once daily. In the pooled analysis of these two studies, Relvar patients had a yearly rate of moderate and severe exacerbations of 0.81, compared with a rate of 1.11 for patients on vilanterol 22mcg alone. This represented a relative reduction in the yearly rate of moderate and severe exacerbations of 27%. Although direct comparisons of exacerbation reduction rates between studies was difficult due to different definitions of exacerbation and different baseline patient characteristics, the reduction seen in these studies were consistent with those seen for other licensed ICS/LABAs (Dransfield *et al*). This data demonstrated how clinically meaningful reductions in COPD exacerbations were now possible with a once daily ICS/LABA.

b) Asthma

Lung function: Forced Expiratory Volume in 1 second (FEV1)

GlaxoSmithKline submitted that FEV1 reflected asthma severity and correlated with symptoms and healthcare utilisation. It was well validated, reproducible, and an important element which defined asthma control. Relvar 92/22mcg given once daily was compared with Seretide 250/50mcg given twice daily in a 24 week head-to-head study (Woodcock *et al*). Clinically meaningful improvements from baseline in 0-24h weighted mean FEV1 were seen with both Relvar (341mL) and Seretide (377mL); although it should be noted that the primary endpoint of superiority was not met as the difference between the two treatment arms was not statistically significant (-37mL; p= 0.162).

This data demonstrated how clinically meaningful improvements in lung function were now possible with a once daily ICS/LABA.

Asthma exacerbations

GlaxoSmithKline submitted that prevention of asthma exacerbations was widely recognised as an important component of establishing ideal asthma control. It could be argued that exacerbations constituted the greatest risk to patients, caused anxiety to patients and their families, resulted in the greatest stress on healthcare providers, and generated the greatest cost to the healthcare system. The time to first severe exacerbation and annualised rate of severe exacerbations was compared for Relvar 92/22mcg vs fluticasone furoate 92mcg alone (Bateman *et al*, 2013). Relvar significantly delayed the time to first severe asthma exacerbation relative to fluticasone furoate. The adjusted probability of experiencing a severe asthma exacerbation by 52 weeks was 15.9% in the fluticasone group and 12.8% in the Relvar group. The hazard ratio for Relvar 92/22mcg vs fluticasone furoate 92mcg was 0.795 representing a 20% risk reduction. The rate of severe asthma exacerbations per patient per year was significantly lower in the Relvar 92/22mcg group than in the fluticasone furoate 92mcg group (0.14 vs 0.19), a reduction in rate of 25%. These results were consistent with the results of other studies which demonstrated the benefit of adding a LABA to an ICS in reducing the risk of severe asthma exacerbations (Bateman *et al*).

This data demonstrated how clinically meaningful reductions in asthma exacerbations were now possible with a once daily ICS/LABA.

Safety

GlaxoSmithKline submitted that in its separate clinical development programmes, 6,237 COPD patients and 7,034 asthmatics were included in integrated assessments of adverse reactions. Relvar was generally well tolerated; the range and frequency of adverse events seen was consistent with twice daily ICS/LABAs available for the treatment of asthma and COPD. GlaxoSmithKline noted that the risk of pneumonia in COPD patients was similar to that reported within the summaries of product characteristics (SPCs) of other ICS/LABAs licensed for COPD.

Device

GlaxoSmithKline reiterated that data showed that the Ellipta device was straightforward to use. This was important as clinicians needed to be confident that patients would find their inhaler easy to use and thus be able to benefit fully from the treatment. In addition to the introduction of a new medicine for COPD and asthma, GlaxoSmithKline submitted that the introduction of a new straightforward to use device also meant that Relvar Ellipta offered value to the NHS.

In summary GlaxoSmithKline submitted that the efficacy and safety profile seen with Relvar, coupled with the straightforward Ellipta device, meant that Relvar brought clinically meaningful benefits to COPD and asthma patients within the NHS. Moreover, such benefits, which were comparable to those seen with other ICS/LABAs, could be achieved for the first time with once daily dosing.

4 Monetary value

GlaxoSmithKline submitted that NHS clinicians and payors might expect that as the first ICS/LABA with only once daily dosing, Relvar would be priced at a premium. However, the two preparations of Relvar Ellipta were £27.80 (92/22mcg) and £38.87 (184/22mcg) for 30 days. These prices meant that the two Relvar preparations were the cheapest in 2 of the 3 steroid based dosage strengths for ICS/LABAs in asthma, ie mid dose and high dose (MIMS Feb 2014). Prescription data (Cegedim Patient Data Report, 2013) showed that over 50% of new ICS/LABA patients stepped up from an ICS alone, fell within the mid and high dose categories. Therefore,

if a clinician wished to prescribe Relvar to such patients instead of other available ICS/LABAs, this would result in cost savings in a significant number of asthma patients treated within the NHS. Only the 92/22mcg dose of Relvar Ellipta (£27.80) was licensed in COPD. This was the cheapest ICS/LABA licensed for COPD (30 day cost: Seretide 500/50mcg Accuhaler, £40.92; Symbicort Turbohaler 400/12mcg or 200/6mcg, £38.00) and again highlighted the monetary value afforded to health professionals who prescribed Relvar Ellipta instead of other ICS/LABAs (MIMS Feb 2014). In conclusion, for the first time Relvar Ellipta provided clinicians and patients with an ICS/LABA (a major class of medicine in the treatment of COPD and asthma) which delivered continuous 24 hour efficacy from a once daily dose. Furthermore, the device had been shown to be straightforward for patients to use. Relvar Ellipta was also priced such that it was the cheapest treatment option for patients who required a mid or high dose of ICS within an ICS/LABA combination in asthma, and was also the cheapest ICS/LABA for COPD. Thus the statement that 'Relvar offers value to the NHS' was accurate, fair, balanced and objective and capable of substantiation in COPD and asthma. GlaxoSmithKline refuted any breach of Clauses 7.2 and 7.4.

Finally, in the absence of the above breaches, GlaxoSmithKline refuted any breach of Clause 9.1 as it maintained that high standards had been maintained in the two advertisements. GlaxoSmithKline's internal processes required that all promotional claims were capable of substantiation prior to certification; this was achieved through the requirement for commercial and medical signatories to discuss such claims in a formal review meeting, and for material to be reviewed with references before final certification.

PANEL RULING

The Panel noted the clauses cited by the case preparation manager, Clauses 7.2, 7.4 and 9.1 of the Code. The 2014 Code came into operation on 1 January 2014 with a transition period for newly introduced requirements. The clauses cited in this case were the same in the 2014 and 2012 Second Edition (amended) Codes, thus the Panel used the 2014 Code.

The Panel noted the complainant's concern regarding the claims 'Delivered in a straightforward device' and 'That offers value to the NHS' which appeared as bullet points in both Relvar advertisements. The Panel noted GlaxoSmithKline's submission that the purpose of the Relvar advertisements was to make health professionals aware of the availability of the new medicine and to very briefly highlight a few of its key attributes by means of four bullet points.

The complainant alleged that looking at the product website and the inhaler demonstration, the device steps were no different to Symbicort Turbohaler where one primed the device and inhaled. The Panel noted GlaxoSmithKline's submission that the statement was a stand-alone claim which did not refer to any other inhalation device in asthma or COPD and thus did not invite any comparisons with them.

The Panel noted that the claim 'Delivered in a straightforward device' was referenced to Riley *et al* in the Relvar COPD advertisement. The study showed following initial instruction, 98% (n=618/632) of COPD patients used Ellipta correctly at day 1. At a 6 week re-assessment without further verbal instruction or demonstration, 99% (n=580/587) of subjects still used their Ellipta inhaler correctly. After 6 weeks of treatment, 99% (580/587) of patients rated the Ellipta inhaler as either very easy or easy to use.

The claim in the Relvar asthma advertisement was referenced to Svedsater *et al* (2013a). The objective of this study was to assess participating patients' competence in the use of the Ellipta device, as judged by trial investigators. Participants were involved in one of three clinical studies which were part of the Relvar asthma development programme. The results of the study found that 95% of patients used the Ellipta device correctly at the baseline visit (as adjudicated by the investigator) after a single demonstration of correct usage (n=1,049). At weeks 2 (n=1,024) and 4 (n=988) >99% of patients were using the inhaler correctly and 94% (929/989) of patients reported the Ellipta device to be easy or very easy to use.

The Panel noted that the steps for Relvar Ellipta on the product website, as derived from the package information leaflet (PIL), showed that sliding the cover open until a click was heard primed the device for inhalation. The Panel noted GlaxoSmithKline's submission that unlike Symbicort Turbohaler, no additional loading step was required. In addition the dose counter of the Ellipta device counted down by one for each dose administered unlike the dose counter on the Turbohaler which was only marked in intervals of 10.

The Panel considered that, given the details regarding the steps on how to use the Relvar device on the product website and in the PIL and the data from Riley *et al* and Svedsater *et al* (2013a), the claim 'Delivered in a straightforward device' was not misleading and unsubstantiable as alleged. No breach of Clauses 7.2 and 7.4 was ruled.

The Panel noted with regard to the claim 'That offers value to the NHS', the complainant's concern that the advertisements did not explain why or how Relvar offered value.

The Panel noted promotional material did not need to contain all of the relevant information to substantiate a claim, however all claims had to be capable of substantiation and such substantiation had to be provided on request. The Panel noted that GlaxoSmithKline had provided information showing how Relvar Ellipta might offer value to the NHS including its effective once daily dosage regimen and ease of use of the device and the presumed

effect this would have on compliance. The Panel further noted that, from information provided by GlaxoSmithKline, the two Relvar Ellipta preparations (92/22mcg) and (184/22mcg) were the least expensive options in the mid and high dose ICS/LABA dosage bands for asthma. Only the 92/22mcg dose was licensed in COPD and was less expensive than Seretide 500/50mcg Accuhaler and Symbicort Turbohaler 400/12mcg or 200/6mcg.

The Panel noted that the claim 'That offers value to the NHS' was non-specific and did not make it clear exactly what value the device would offer the NHS. The Panel, however, noted the detailed information provided by GlaxoSmithKline and did not consider that, whether considered in monetary or non monetary terms, the claim was misleading or unsubstantiable. No breach of Clauses 7.2 and 7.4 was ruled.

The Panel noted its rulings above and consequently ruled no breach of Clause 9.1 as it did not consider that GlaxoSmithKline had failed to maintain high standards.

Complaint received **11 February 2014**

Case completed **25 April 2014**
