CASE AUTH/2313/4/10

TEVA v CHIESI

Clenil journal advertisement

Teva complained about a journal advertisement for Clenil (CFC-free beclometasone dipropionate (BDP) inhaler for asthma) issued by Chiesi. The advertisement was headed 'Life's full of disruptions. Changing to Clenil needn't be one of them' and featured a photograph of a cow which had apparently fallen through a ceiling to land on a desk which was littered with ceiling debris. 'Make the change to CFC-free beclometasone metered-dose inhalers trouble-free' appeared in the bottom right hand corner of the advertisement next to a highlighted box which featured the product logo above the strapline 'CFC-free can be trouble-free'.

Teva alleged that the claims 'Make the change to CFC-free beclometasone metered-dose inhalers trouble-free' and 'CFC-free can be trouble free' were all-embracing, unqualified, misleading, not capable of substantiation and exaggerated the benefits of Clenil.

The claims failed to take into account patient groups for whom switching to CFC-free would not be trouble-free for themselves or the health professional. In particular, Teva drew attention to those groups of patients who, on changing to Clenil, would have to start using a Volumatic spacer which they had not needed before.

Further the Clenil SPC detailed a theoretical potential for interaction in sensitive patients taking disulfiram or metronidazole. It also detailed other undesirable effects such as paradoxical bronchospasm, hypersensitivity reaction including rashes, urticaria, pruritus, erythema and angiodema and these too were included in the prescribing information which accompanied the advertisement. It also detailed the need to rinse the mouth immediately after inhalation to avoid candidiasis of the mouth and throat. This further supported Teva's view that Clenil was not 'trouble-free'.

Teva noted that in inter-company correspondence Chiesi had stated that 'By trouble trouble-free, we mean the least disruption to patients' care and medication whilst also causing the least disruption to the healthcare professional'. This recognised that Clenil was not 'trouble-free' by referring to 'least disruption' and not 'no disruption' as one would expect if it were 'trouble-free'.

Teva noted that it had requested substantiation for the claims and this was not forthcoming.

The detailed response from Chiesi is given below.

The Panel considered that the overall message of the advertisement was that changing to Clenil would be trouble-free. The Panel did not accept Chiesi's submission that the advertisement was a reminder of the topical issue of the disruption that might be encountered if a proactive approach to the transition to CFC-free inhalers was not taken. Nor did the Panel accept Chiesi's submission that the advertisement urged readers to consider using any CFC-free alternative and that it thus applied equally to Qvar. The advertisement at issue clearly promoted changing to Clenil and readers would associate the claims within only with that product.

The Panel noted Teva's submission about the potential difficulties of the transition to CFC-free Clenil. The Clenil SPC, stated that the Volumatic spacer must be used with certain doses in adults and irrespective of dose when administered to children and adolescents ≤15 years. The SPC also stated that patients who had difficulty in co-ordinating actuation and inspiration of breath should be told to use a Volumatic spacer to ensure proper administration. Chiesi had not responded on these points. The Panel considered that the transition from CFC-containing inhalers to Clenil was not as straightforward as implied by the absolute claim 'trouble-free'. The use of the word 'can' in the strapline 'CFC-free can be trouble-free' did not negate the impression that changing to CFC-free was trouble-free for everyone. The claims at issue 'Make the change to CFC-free beclometasone metered-dose inhalers trouble-free' and 'CFC-free can be trouble free' were thus misleading, incapable of substantiation and all-embracing. Breaches of the Code were ruled. The Panel considered that given this ruling, the inference that a transition to Clenil from a CFC-containing inhaler was trouble-free for all patients was inconsistent with the terms of Clenil's marketing authorization; on changing to Clenil some patients would have to start using a Volumatic spacer which they had not had to do before on CFC-containing BDP. A breach of the Code was ruled.

The Panel noted that contrary to Chiesi's submission, Teva had clearly asked for substantiation of the two claims at issue. As substantiation had not been provided the Panel ruled a breach of the Code.

Teva UK Limited complained about a journal advertisement (ref CHCLE20100035) for Clenil (CFC-free beclometasone dipropionate (BDP) inhaler for asthma) issued by Chiesi Limited. Teva supplied Qvar (also a CFC-free BDP inhaler). Inter-company dialogue had failed to resolve the issues.

The advertisement was headed 'Life's full of

disruptions. Changing to Clenil needn't be one of them' and featured a photograph of a cow which had apparently fallen through a ceiling to land on a desk which was littered with ceiling debris. 'Make the change to CFC-free beclometasone metered-dose inhalers trouble-free' appeared in the bottom right hand corner of the advertisement next to a highlighted box which featured the product logo above the strapline 'CFC-free can be trouble-free'.

COMPLAINT

Teva was concerned that the placement of the claims 'Make the change to CFC-free beclometasone metered-dose inhalers trouble-free' and 'CFC-free can be trouble free' was such that both were associated with Clenil. Teva alleged that the claims were all-embracing, unqualified, misleading, not capable of substantiation and exaggerated the benefits of Clenil.

Importantly the advertisement did not refer to different patient types, such as those on high dose or under the age of 16 who would need to use a Volumatic spacer as stated in the Clenil summary of product characteristics (SPC).

The claims were not consistent with the SPC. They failed to take into account groups for whom switching to a CFC-free would cause more trouble to themselves and the health professional. These patient groups included those who might be on a breath-actuated inhaler or might need to use of a Volumatic (as stated in the Clenil SPC) that was not previously required with their CFC BDP.

The claim 'Make the change to CFC-free beclometasone metered-dose inhalers trouble-free' was next to the Clenil logo and thus clearly associated with Clenil. There were major limitations to the use of Clenil as listed in its SPC. These would certainly not make the switch to Clenil 'trouble-free', would result in major inconvenience to the patient who would require additional training which would also inconvenience their health professionals.

Patients stabilised on CFC-containing BDP inhalers might receive and have been trained on different types of inhalers requiring different techniques. None of the CFC-containing BDP products required the use of spacers in patient groups identified in the Clenil SPC. The Clenil SPC stated that the following patients would need to use a Volumatic spacing device:

a) Patients who had difficulty synchronising actuation with inspiration with their inhaler.
b) Adults and adolescents ≥16 years of age taking total daily doses of ≥1000mcg BDP.
c) Children and adolescents ≤15 years of age, whatever the dose of BDP.

As above statements would have associated issues for patients and health professionals, Teva could not see how the use of Clenil could be deemed 'trouble-free'.

Further the Clenil SPC detailed a theoretical potential for interaction in sensitive patients taking disulfiram or metronidazole. It also detailed other undesirable effects such as paradoxical bronchospasm, hypersensitivity reaction including rashes, urticaria, pruritus, erythema and angiodema and these too were included in the prescribing information which accompanied the advertisement. It also detailed the need to rinse the mouth immediately after inhalation to avoid candidiasis of the mouth and throat. This further supported Teva's view that Clenil was not 'trouble-free'.

The claim 'Make the change to CFC-free beclometasone metered-dose inhalers trouble-free' was purported to be substantiated by Chiesi in a letter by stating that 'By trouble trouble-free, we mean the least disruption to patients' care and medication whilst also causing the least disruption to the healthcare professional'.

Chiesi's own attempt to substantiate the claim in this letter recognised that Clenil was not 'trouble-free' by referring to 'least disruption' and not 'no disruption' as one would expect if it were 'trouble-free'. By stating least disruption, this recognised that there was a degree of disruption with Clenil which could not be associated with being trouble-free.

Teva alleged breaches of Clauses 7.2, 7.4, 7.10 and 3.2 of the Code.

Teva noted that it had requested substantiation for the claims and this was not forthcoming within the 10 day period allotted. In its response Chiesi made no attempt to provide substantiation. A breach of Clause 7.5 was alleged.

Teva requested a voluntary submission of this breach but this was not referred to in Chiesi's response despite a repeated request to answer all points during the teleconference and subsequent telephone call with Chiesi afterwards. Teva therefore requested that it was ruled that a subsequent breach of Clause 7.5 had been made in this instance in failing to substantiate as requested.

RESPONSE

Chiesi explained that 25 years ago scientists first alerted the world to the damage that CFC gases caused to the Antarctic ozone layer in the atmosphere. The ozone layer was crucial to life on earth as it shielded all life forms from the harmful UV radiation of the sun. As a result of this knowledge, there was widespread international consensus to ban the use of CFC gases and the Montreal Protocol treaty was first signed in 1987 to phase out the use of these harmful gases. Consequently, the global industrial production and use of CFC gases was sharply curtailed in the next

few years. However, it was deemed essential to continue to use CFC gases as propellants in inhalers for medicinal purposes until such time as suitable alternatives could be developed and manufactured on a sufficient scale. Over time, several pharmaceutical companies were able to do this successfully.

Over the past decade or so the transition from CFC-containing to CFC-free inhalers had taken place slowly in the UK and in a patchy geographical manner. These transitions had been handled with varying degrees of success, depending on the numbers of patients to be transitioned and the resources available to health professionals. The problem of transitioning patients from CFC-containing to CFC-free inhalers had occurred mainly where there had been large numbers of patients and little time to plan for these changes. This was borne out in 2003, when CFC-containing salbutamol inhalers were discontinued. As health professionals were not well prepared for this discontinuation, large numbers of patients were given prescriptions which their pharmacists could not fulfil because some pharmacies did not hold adequate stocks of CFC-free salbutamol inhalers whilst the CFC-containing versions had already been discontinued. Needless to say, the disruptions to patients, GPs and pharmacists were not only of a logistical nature but could have clinical significance, as these inhalers were needed to relieve the symptoms of early asthmatic attacks. It was in a similar context that the Clenil advertisement was run.

The last product in the UK to contain CFC-propellant delivered by a metered-dose inhaler was BDP which accounted for over 9 million units per annum in the UK (IMS data). Two CFC-free alternatives had been made available over the last few years in the UK ie Qvar (Teva) and Clenil (Chiesi). Since their launches, health professionals had been urged by both companies to consider a planned therapeutic transition to one of these two alternatives, in order to avoid disruptions to their patients and also to the daily running of their practices. If a therapeutic transition was planned and implemented in a timely manner, patients could quite easily be transitioned to a CFC-free alternative with a minimum of disruption.

Chiesi noted that in June 2009, Teva, wrote to all health professionals notifying them that it was going to discontinue CFC-containing BDP delivered via the Easi-breathe device from 30 September 2009; this gave health professionals three months in which to plan the transition of those patients on the Easi-Breathe device. In the same letter, Teva also stated that it expected stocks of its more widely used Beclazone (a CFC-containing BDP) metered-dose inhaler to be depleted during the first quarter of 2010.

Chiesi further noted that in January 2010, Teva wrote to wholesalers informing them that it would not supply any Beclazone metered-dose inhaler from 31 March 2010. This information was only sent to wholesalers and other relevant stakeholders and not sent directly to health professionals. A statement to health professionals from Teva was posted on its website on 7 February 2010.

On being made aware of the above letter to wholesalers, Chiesi began to run advertisements to highlight the fact that unless health professionals took immediate action to plan for therapeutic reviews and transition all their patients who were still receiving a CFC-containing BDP metered-dose inhaler to a CFC-free alternative, they and their patients could face disruptions to their practices and treatments respectively.

It was therefore within the above context of the imminent withdrawal of CFC-containing BDP inhalers and the need for health professionals to plan well ahead for the transition to CFC-free alternatives, that the Clenil advertisement at issue was run. The two claims, 'Make the change to CFC-free beclometasone metered-dose inhalers trouble-free' and 'CFC-free can be trouble-free', were not directed to any one brand specifically but applied to all CFC-free BDP inhalers. As such, the claims simply urged health professionals to consider using any of the CFC-free alternatives which were currently available ie Qvar or Clenil.

Through the advertisement, Chiesi aimed to remind the reader of the window of opportunity to make the change to CFC-free BDP inhalers trouble-free, before CFC-containing BDP inhalers ran out of stock at the wholesalers and pharmacies. This clearly meant deciding to change patients proactively to a CFC-free alternative. The strapline 'CFC-free can be trouble-free' was valid when transitions were undertaken in a proactive manner. Clenil was a CFC-free alternative for adults and children with asthma and was available in the same range of devices and at the same dose regimens when transferring from a CFC-containing inhaler. Hence, the advertisement was seen as a reminder of the very topical issue of disruption that might be encountered if a proactive approach to transition was not taken.

Chiesi submitted that, with regard to patient safety, if repeat prescriptions of CFC-containing BDP inhalers were not changed in the immediate future to a CFC-free alternative, patients might be at risk of presenting pharmacist with prescriptions that could not be fulfilled when the former became unavailable. This would lead to the pharmacists ringing the patients' GPs and requesting urgently that they authorise changes of prescriptions there and then. Not only would this take up an inordinate amount of time by the pharmacists and the GPs, it might also confuse patients as they would be issued with a new inhaler without their prior knowledge. At the time of the advertisement, approximately 155,000 prescriptions still required a change and there was approximately only 8 weeks of CFC-containing product in the supply chain (IMS data).

In summary, the Clenil advertisement alerted health professionals of the imminent need to transition patients who were still on CFC-containing BDP inhalers to a CFC-free alternative. It focused on the clinical and logistical needs to make this transition proactively. Both Qvar and Clenil were available in the UK as suitable CFC-free alternatives. As such, the two claims at issue were not all embracing and not misleading. They were also not directed to any brand in particular and therefore it could not be alleged to be inconsistent with the Clenil SPC. Hence, Chiesi contended that the claims did not breach Clauses 7.2, 7.4, 7.10 and 3.2. Lastly, Clause 7.5 was not breached, as Chiesi was asked to provide substantiation on claims which it simply did not make in the advertisement, namely that it had disparaged Qvar and Teva; this was not possible when neither was mentioned in the advertisement.

PANEL RULING

The Panel considered that the overall message of the advertisement was that changing to Clenil would be trouble-free. The Panel did not accept Chiesi's submission that the advertisement was a reminder of the topical issue of the disruption that might be encountered if a proactive approach to the transition to CFC-free inhalers was not taken. Nor did the Panel accept Chiesi's submission that the advertisement urged readers to consider using any CFC-free alternative and that it thus applied equally to Qvar. The advertisement at issue clearly promoted changing to Clenil and readers would associate the claims within only with that product.

The Panel noted Teva's submission about the potential difficulties of the transition to CFC-free Clenil. Section 4.2 of the Clenil SPC, Posology and method of administration, stated that the Volumatic spacer must be used when Clenil was administered to adults and adolescents ≥16 years and taking total daily doses of ≥ 1000mcg and irrespective of dose when administered to children and adolescents ≤15 years. The SPC also stated that patients who had difficulty in co-ordinating actuation and inspiration of breath should be told to use a Volumatic spacer to ensure proper administration of the product. Chiesi had not responded on these points. The Panel considered that the transition from CFC-containing inhalers to Clenil was not as straightforward as implied by the absolute claim 'trouble-free'. The use of the word 'can' in the strapline 'CFC-free can be trouble-free' did not negate the impression that changing to CFC-free was trouble-free for everyone. The claims at issue 'Make the change to CFC-free beclometasone metered-dose inhalers trouble-free' and 'CFC-free can be trouble free' were thus misleading, incapable of substantiation and all-embracing. A breach of Clauses 7.2, 7.4 and 7.10 was ruled. The Panel considered that given this ruling, the inference that a transition to Clenil from a CFC-containing inhaler was trouble-free for all patients was inconsistent with the terms of Clenil's marketing authorization; on changing to Clenil some patients would have to start using a Volumatic spacer which they had not had to do before on CFC-containing BDP. A breach of Clause 3.2 was ruled.

The Panel noted that contrary to Chiesi's submission, Teva had clearly asked for substantiation of the two claims at issue. As substantiation had not been provided the Panel ruled a breach of Clause 7.5.

Complaint received **30 April 2010**

Case completed **15 June 2010**