CASE AUTH/3378/9/20

COMPLAINANT v FERRING

Alleged off-licence promotion of Cortiment

A complainant alleged that an advertisement for Cortiment (budesonide) placed by Ferring Pharmaceuticals Ltd in Guidelines in Practice, promoted the medicine beyond the terms of its licence.

Cortiment was indicated in adults for induction of remission in patients with mild to moderate active ulcerative colitis (UC) where 5-ASA treatment was not sufficient. The product logo included the strapline 'For flaring mild to moderate UC patients'.

The complainant provided an image of the advertisement and links to the Guidelines in Practice website and the Cortiment prescribing information and noted that in both it was stated that the medicine was indicated 'For flaring mild to moderate UC patients'. The licenced indication of Cortiment was for use in adults for 'induction of remission in patients with mild to moderate active ulcerative colitis (UC) where 5-ASA treatment was not sufficient' (emphasis added). The complainant alleged that the licenced patient group was smaller than that which was stated on the advertisement, therefore Ferring had promoted off-licence.

The detailed response from Ferring is given below.

The Panel noted that the claim in question 'For flaring mild to moderate UC patients' appeared as a strapline in the bottom right-hand corner beneath the brand and non-proprietary name on all five screens of the rotating banner advertisement. The Panel noted that, similarly, it appeared on the prescribing information and references page which was available via a click through from each of the five screens. The Panel noted that whilst Cortiment's full indication was included in the linked prescribing information, it was not included on any of the screens of the rotating banner advertisement including the second screen of the banner advertisement which read 'Cortiment The only oral budesonide licensed for active mild to moderate UC…'.

The Panel noted Ferring's submission that in a diagnosed patient, relapse was called active ulcerative colitis or alternatively a flare. The Panel noted that there did not appear to be a confirmed definition of an ulcerative colitis flare and in this regard it noted that the NICE UC Guidance referred to acute exacerbations of severely active UC and inflammatory exacerbations of extensive UC.

The Panel noted Ferring's submission that in the context of an established molecule, for an established and well documented medical condition, promoting a product 'for flaring mild to moderate UC patients' was completely consistent with a patient group for whom 5-ASAs were insufficient. The Panel noted, however, that according to the Asacol (mesalazine) 400mg MR SPC (accessed via the eMC on 9 February 2021), which was an

ASA, Asacol was indicated for the treatment of mild to moderate acute exacerbations. For the maintenance of remission. It therefore appeared that it was similarly indicated for treating relapse/active ulcerative colitis or 'flares'. The Panel further noted Ferring's submission that the BSG recommended that ulcerative colitis patients flaring on 5-ASA therapy should receive dose escalation to 4–4.8 g/day orally alongside 5-ASA enemas.

The Panel noted Cortiment's indication and considered that the strapline implied that Cortiment was suitable for treating all patients with mild to moderate flaring ulcerative colitis which was not consistent with the particulars listed in its SPC; it was only indicated in certain patients for whom 5-ASA treatment was not sufficient. The Panel therefore ruled a breach of the Code.

Whilst the Panel noted Ferring's submission that diagnosis of ulcerative colitis and initiation of treatment took place in specialist care, and as such, it would only be in rare circumstances such as where 5-ASAs were not tolerated or contraindicated that a specialist would prescribe anything else first line for mild to moderate ulcerative colitis. The Panel noted that the first screen of the advertisement stated 'Cortiment – Now supported by real-word evidence' and the second screen stated 'Cortiment the only oral budesonide licensed for active mild to moderate UC…'. In the Panel's view, the claims on the first and second screens in conjunction with its ruling above, meant that the strapline was misleading with regard to the licensed indication of Cortiment. A breach of the Code was ruled.

The Panel ruled a breach as high standards had not been maintained. No breach of Clause 2 was ruled.

A complainant, who described him/herself as a concerned UK health professional, alleged that an advertisement for Cortiment (budesonide) (ref UK-COR-2000004) placed by Ferring Pharmaceuticals Ltd in the online version of Guidelines in Practice, promoted the medicine beyond the terms of its licence.

Cortiment was indicated in adults for induction of remission in patients with mild to moderate active ulcerative colitis (UC) where 5-ASA treatment was not sufficient. The product logo included the strapline 'For flaring mild to moderate UC patients'.

COMPLAINT

The complainant provided an image of the advertisement and links to the Guidelines in Practice website and the Cortiment prescribing information and noted that in both it was stated that the medicine was indicated 'For flaring mild to moderate UC patients'. The licenced indication of Cortiment was for use in adults for 'induction of remission in patients with mild to moderate active ulcerative colitis (UC) *where 5-ASA treatment was not sufficient*' (emphasis added). The complainant alleged that the licensed patient group was smaller than that which was stated on the advertisement, ergo Ferring had promoted off-licence.

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

RESPONSE

Ferring explained that the licensed indication for Cortiment was: in adults for induction of remission in patients with mild to moderate active ulcerative colitis (UC) where 5-ASA treatment was not sufficient. Ferring provided a copy of the summary of product characteristics (SPC).

Ferring noted that according to the British Society of Gastroenterology (BSG) ulcerative colitis guidelines (copy provided), ulcerative colitis was a chronic inflammatory disease characterised by mucosal inflammation starting distally in the rectum, with continuous extension proximally for a variable distance, often with an abrupt demarcation between inflamed and non-inflamed mucosa. Typically, patients with ulcerative colitis experienced periods of relapse and remission. In a diagnosed patient, relapse was called active ulcerative colitis or alternatively a flare.

The mainstay of ulcerative colitis treatment were 5-ASAs. Diagnosis of ulcerative colitis and initiation of treatment took place in specialist care and as such it would only be in rare circumstances such as where 5-ASAs were not tolerated or contraindicated that a specialist would prescribe anything else first line for mild to moderate ulcerative colitis.

Ferring stated that the BSG recommended that ulcerative colitis patients flaring on 5-ASA therapy should receive dose escalation to 4–4.8 g/day orally alongside 5-ASA enemas.

These recommendations were also supported by ulcerative colitis guidelines issued by the National Institute for Health and Care Excellence (NICE) (copy provided).

If this was insufficient to bring the patient back into remission, then use of corticosteroids (including budesonide) was recommended.

Ferring stated that this pathway was widely known and adopted in the management of ulcerative colitis, and specialists or GPs would not initiate corticosteroids as a first-line treatment option unless as stated above. In such cases the guidelines recommended the use of prednisolone first line.

Cortiment was a prolonged release version of budesonide. Budesonide had been used to treat ulcerative colitis for over a decade and was available from a number of manufacturers. Clinicians were fully aware of the appropriate placement of budesonide in the treatment pathway of ulcerative colitis and so knew that it was only suitable after 5-ASAs had failed. The promotional focus for Cortiment, 'For flaring mild to moderate UC patients' should thus be seen in that context. Cortiment would be unlikely to be used first-line and therefore flaring patients would already be on a 5-ASA.

Ferring explained that the banner advertisement at issue was hosted on an independent medical journal website targeted at health professionals (Guidelines in Practice). The associated references/prescribing information were accessed via a direct click-through and was hosted on a Ferring platform. The image provided by the complainant was one element of a rotating banner. Copies of the banner advertisement and of the prescribing information were provided. Ferring stated that the claim in question appeared as a strapline on both the banner and the references/prescribing information page.

The banner advertisement was certified on 21 May 2020 and the reference/prescribing information piece was certified on 30 April 2020. Copies of the certificates were provided.

Ferring denied breaching Clauses 3.2, 7.2, 9.1 and 2 of the Code.

In relation to Clause 3.2 Ferring considered that the strapline 'For flaring mild to moderate UC patients' was not inconsistent with the particulars listed within the Cortiment SPC. In the context of an established molecule, for an established and well documented medical condition, promoting a product 'for flaring mild to moderate UC patients' was completely consistent with a patient group for whom 5-ASAs were insufficient.

In relation to Clause 7.2 Ferring stated that in the context of an established molecule, for an established and well documented medical condition, promoting a product for 'flaring mild to moderate UC patients' was completely consistent with a patient group for whom 5-ASAs were insufficient.
Given the established treatment Guidelines and established clinical use of budesonide, it was extremely unlikely that health professionals would misunderstand the meaning of 'flaring UC' and the appropriate use of Cortiment in treating this patient population ie after 5-ASAs had failed.

In relation to Clause 9.1 Ferring stated that the advertisement and associated obligatory information were reviewed and certified as per the requirements of the Code and the Ferring internal standard operating procedure for Approval of Certifiable Materials.

Ferring considered the claim appropriate in context and of the standards expected for promotional material.

Ferring categorically denied any breach of Clause 2.

Ferring stated that in the context of an established molecule, for an established and well documented medical condition, promoting a product for 'flaring mild to moderate UC patients' was completely consistent with a patient group for whom 5-ASAs were insufficient. The claims and material were certified according to documented procedures.

In relation to the allegation, Ferring submitted that it had done nothing that would bring the industry into disrepute.

Ferring stated that on investigation, whilst the final art-worked banner was certified, it appeared that the final, art-worked, version of the references/prescribing information piece was not certified, although the text of the piece was checked for accuracy and certified.

This was related to a combination of human error and a technical limitation in the electronic approval system.

A black and white version of the references/prescribing information was certified as it was believed by the signatories that this was the final form, having been labelled as such by the agency uploader.

However, the colour artwork version had been uploaded using the category 'Production Proof' and the black and white version was the one which was viewed by the signatories. Regrettably it now transpired that items in this category were not sent to the signatories as the final certification version.

Ferring stated that in addition to this, it seemed that there was a technical issue within the system; following the review phase of a job, the owner/administrator of the job should click

'complete' to initiate the certification phase and allow upload of the final form for certification by the signatories. However, if this was not done immediately, the system removed the job from the owner/administrator 'Tasks' inbox and placed it back into the main library. Unfortunately, this meant that owners/administrators were not provided with a safety net informing them that they had a task to complete.
Ferring stated that because of these two incidents, the colour version was not formally certified prior to release. However, the black and white version, the content of which had been checked for accuracy and compliance, had been certified. On certification of the black and white piece, the agency had assumed the art worked form had been certified and was ready for distribution.

Ferring outlined the process for certifying material and provided a copy of the relevant certificates.

PANEL RULING

The Panel noted Ferring's submission that the image provided by the complainant was one element of a rotating banner advertisement which consisted of five rotating screens. The banner provided by the complainant featured a picture of a stomach with a map imprinted on it and the claim 'Cortiment 9mg once daily for 8 weeks can help navigate your UC patients back into remission'. The Panel noted that the claim in question 'For flaring mild to moderate UC patients' appeared as a strapline in the bottom right-hand corner beneath the brand and non-proprietary name on all five screens of the rotating banner advertisement. The Panel noted that, similarly, it appeared on the prescribing information and references page which was available via a click through from each of the five screens. The Panel noted that whilst Cortiment's full indication was included in the linked prescribing information, it was not included on any of the screens of the rotating banner advertisement including the second screen of the banner advertisement which read 'Cortiment The only oral budesonide licensed for active mild to moderate UC…'.

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The Panel noted Ferring's submission that in the context of an established molecule, for an established and well documented medical condition, promoting a product 'for flaring mild to moderate UC patients' was completely consistent with a patient group for whom 5-ASAs were insufficient. The Panel noted, however, that according to the Asacol (mesalazine) 400mg MR SPC (accessed via the eMC on 9 February 2021), which was an ASA, Asacol was indicated for the treatment of mild to moderate acute exacerbations. For the maintenance of remission. It therefore appeared that it was similarly indicated for treating relapse/active ulcerative colitis or 'flares'. The Panel further noted Ferring's submission that the BSG recommended that ulcerative colitis patients flaring on 5-ASA therapy should receive dose escalation to 4–4.8 g/day orally alongside 5-ASA enemas.

The Panel noted Cortiment's indication and considered that the strapline implied that Cortiment was suitable for treating all patients with mild to moderate flaring ulcerative colitis which was not consistent with the particulars listed in its SPC; it was only indicated in certain patients where 5-ASA treatment was not sufficient. The Panel therefore ruled a breach of Clause 3.2.

The Panel noted that Clause 7.2 stated, *inter alia*, that claims must be accurate, balanced, fair, objective and unambiguous and must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. They must not mislead either directly or by implication, by distortion, exaggeration or undue emphasis and material must be sufficiently complete to enable the recipient to form their own opinion of the therapeutic value of the medicine.

Whilst the Panel noted Ferring's submission that diagnosis of ulcerative colitis and initiation of treatment took place in specialist care, and as such, it would only be in rare circumstances such as where 5-ASAs were not tolerated or contraindicated that a specialist would prescribe anything else first line for mild to moderate ulcerative colitis. The Panel noted that the first screen of the advertisement stated 'Cortiment – Now supported by real-word evidence' and the second screen stated 'Cortiment the only oral budesonide licensed for active mild to moderate UC…'. In the Panel's view, the claims on the first and second screens in conjunction with its ruling above, meant that the strapline was misleading with regard to the licensed indication of Cortiment. A breach of Clause 7.2 was ruled.

High standards had not been maintained. A breach of Clause 9.1 was ruled.

The Panel noted that a ruling of a breach of Clause 2 was a sign of particular censure and reserved for such. The Panel noted its rulings and comments above but considered that the matters were not such as to bring discredit upon, or reduce confidence in, the industry. No breach of Clause 2 was ruled.

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During its consideration of this case, the Panel was concerned to note Ferring's submission about its failure to certify the final colour art-worked version of the references/prescribing information piece prior to its release. The Panel noted that a robust certification procedure underpinned self-regulation. The Panel noted that this matter had not been raised as an allegation and therefore it could make no ruling in this regard but it requested that Ferring be advised of its concerns.

Complaint received **10 September 2020**

Case completed **3 March 2021**