CASE AUTH/2185/11/08

PHARMACIST PRACTITIONER v SCHERING-PLOUGH

NeoClarityn journal advertisement

A pharmacist practitioner complained about an advertisement for NeoClarityn (desloratadine) placed in GP, 7 November, by Schering-Plough.

The advertisement was headed 'Triple stopping power for allergic rhinitis' beneath which was an illustration of three goal keepers in a goal mouth. On the front of the goal keepers' shirts were the words 'anti-histaminic', 'anti-allergic' and 'anti-inflammatory' respectively.

The complainant considered that the claim that desloratadine was anti-inflammatory might be accurate for *in vitro* studies but to claim that it had clinically relevant anti-inflammatory actions was contradicted by the summary of product characteristics (SPC). The complainant alleged that the advertisement was inaccurate and therefore misleading.

The detailed response from Schering-Plough is given below.

The Panel noted that NeoClarityn was indicated for the relief of symptoms associated with allergic rhinitis and urticaria. The SPC stated that desloratadine had demonstrated anti-allergic properties from *in vitro* studies including inhibition of the release of pro-inflammatory cytokines. The clinical relevance of these observations remained to be confirmed.

The Panel noted that there was some data (Bachert and Reinartz *et al*) to suggest that desloratadine might have an anti-inflammatory effect. However Bachert had reported only the preliminary results from a study conducted by others (Marshall *et al* 2002), and Reinartz *et al* was unable to show that airway mucosal inflammation was altered by one week's treatment.

The Panel considered that the impression from the advertisement was that NeoClarityn was authorized for use as an antihistamine, an anti-allergic or an anti-inflammatory and that clinical data supported each element. This was not so with regard to the anti-inflammatory action as acknowledged by Schering-Plough. The advertisement was inconsistent with the NeoClarityn SPC and was misleading as alleged. Breaches of the Code were ruled.

A pharmacist practitioner complained about an advertisement (ref NCL/08-579) for NeoClarityn (desloratadine) placed in GP, 7 November, by Schering-Plough Ltd.

The advertisement was headed 'Triple stopping power for allergic rhinitis' beneath which was an illustration of three goal keepers in a goal mouth. On the front of the goal keepers' shirts were the words 'anti-histaminic', 'anti-allergic' and 'anti-inflammatory' respectively.

NeoClarityn was indicated for the relief of symptoms associated with allergic rhinitis and urticaria.

COMPLAINT

The complainant noted that the advertisement cited three references; one was the current summary of product characteristics (SPC) which stated:

> 'Desloratadine has demonstrated antiallergic products from *in vitro* studies. These include inhibiting the release of proinflammatory cytokines such as IL-4, IL-6, IL-8, and IL-13 from human mast cells/basophils, as well as inhibition of the expression of the adhesion molecule P-selectin on endothelial cells. The clinical relevance of these observations remains to be confirmed.'

The complainant considered that the claim that desloratadine was anti-inflammatory might be accurate for *in vitro* studies but to claim that it had clinically relevant anti-inflammatory actions was contradicted by the SPC.

The complainant alleged that the advertisement was inaccurate and therefore misleading.

When writing to Schering-Plough the Authority asked it to respond in relation to Clauses 3.2 and 7.2 of the Code.

RESPONSE

Schering-Plough stated that the advertisement listed three pharmacodynamic properties of desloratadine that were referred to in the SPC ie anti-allergenic, anti-histaminic and anti-inflammatory. The advertisement referred readers to three sources of information; the SPC, Marshall (2000) and Molet *et al* (1997). The complainant unfortunately considered that the inclusion of the phrase 'anti-inflammatory' did not reflect the data contained in the SPC and was therefore inaccurate and misleading.

Schering-Plough submitted that the current available data supported the use of the phrase 'anti-inflammatory' in the advertisement. Desloratadine

was among the newest anti-allergy products, developed from second-generation anti-histamines. Its anti-inflammatory activity was well recognised in scientific literature, both *in vitro* and *in vivo*. For instance, Marshall commented 'the high therapeutic index for antiallergenic and anti-inflammatory effects of newer agents, such as desloratadine, offers promise for improved therapeutic and perhaps even prophylactic options'. Geha and Meltzer (2001) stated 'Desloratadine is a new, selective, H_1-receptor antagonist that also has anti-inflammatory activity'.

Schering-Plough noted the requirements of Clause 7.2, specifically that *in vitro* data might only be extrapolated to the clinical situation if there was data to show that it was of direct relevance and significance. Geha and Meltzer considered that observations from the *in vitro* studies were relevant to clinical use. 'Regardless, the mechanism by which desloratadine exerted these anti-inflammatory effects was independent of H_1-receptor antagonism, and it was reasonable to consider the observations from these studies to be relevant to clinical use'.

To further substantiate the clinical relevance of *in vitro* data, *in vivo* studies in subjects with allergic rhinitis confirmed the systemic anti-inflammatory effect of desloratadine. Bachert (2002) observed decreased expression of IL-4, IL-5 and IL-10 in patients treated with desloratadine compared with those treated with placebo. Also, Reinartz *et al* (2005) concluded that desloratadine reduced systemic allergic inflammation following nasal provocation in allergic rhinitis and asthma patients.

Direct evidence for clinical relevance was derived from clinical studies. Clinically, the late inflammatory response was associated with symptoms of nasal obstruction and increased mucus production. In two different clinical trials, patients with allergic rhinitis treated with desloratadine had greater reduction in nasal obstruction and nasal congestion compared with those treated with placebo, confirming the anti-inflammatory component.

Therefore, based on the specific *in vitro*, *in vivo* and clinical data for desloratadine discussed above, Schering-Plough believed that it could substantiate a claim that the product had anti-inflammatory properties. However, it noted the complainant's concerns that the advertisement did not include a clear explanation of these data. Therefore, working in the spirit of the Code, Schering-Plough had withdrawn the advertisement. Any future use of the claim would include clear explanation of the nature of the *in vitro* data and also the *in vivo* and clinical data to enable readers to make an informed opinion.

PANEL RULING

The Panel noted that NeoClarityn was indicated for the relief of symptoms associated with allergic rhinitis and urticaria. Section 5.1 of the SPC stated that desloratadine had demonstrated anti-allergic properties from *in vitro* studies including inhibition of the release of pro-inflammatory cytokines. The clinical relevance of these observations remained to be confirmed.

The Panel noted that there was some data (Bachert and Reinartz *et al*) to suggest that desloratadine might have an anti-inflammatory effect. However Bachert had reported only the preliminary results from a study conducted by others (Marshall *et al* 2002), and Reinartz *et al* was unable to show that airway mucosal inflammation was altered by one week's treatment.

The Panel considered that the impression from the advertisement was that NeoClarityn was authorized for use as an antihistamine, an anti-allergic or as an anti-inflammatory and that clinical data supported each element. This was not so with regard to the anti-inflammatory action as acknowledged by Schering-Plough. The Panel considered that in that regard the advertisement was inconsistent with the particulars listed in the NeoClarityn SPC. A breach of Clause 3.2 was ruled. The advertisement was misleading as alleged and thus the Panel ruled a breach of Clause 7.2.

Complaint received **17 November 2008**

Case completed **5 January 2009**