CASE AUTH/2433/8/11

ANONYMOUS v JANSSEN

Promotion of Prezista

An anonymous, non-contactable prescriber alleged a Prezista (darunavir) advertisement placed by Janssen in a 'First Announcement' booklet for the British HIV Association (BHIVA) Autumn 2011 conference was misleading and did not include prescribing information. The complainant was concerned that the claim 'Simple once daily dosing in both naïve patients and those switching for tolerability and convenience' had an asterix to a small print footnote which described the individuals that this applied to. Furthermore, it was misleading that there was no reference to the fact that for all other patients Prezista was a twice daily regimen. The advertisement did not make the twice daily regimen clear. The complainant noted that none of the claims were substantiated since there was no list of references.

The detailed response from Janssen is given below.

The Panel noted that the advertisement did not contain prescribing information. Janssen's explanation that this was due to a series of process failures and the absence of several head office and agency staff involved was inadequate. In the Panel's view, the company's procedures should have been sufficiently robust such that even in the absence of key staff, compliance standards were maintained. A breach of the Code was ruled.

With regard to the claim 'Simple once daily dosing in both naïve patients and those switching for tolerability and convenience', the Panel noted from the Prezista summary of product characteristics (SPC) that a once-daily dose was only indicated for antiretroviral treatment (ART)-naïve patients or a certain population of ART-experienced patients. Other ART-experienced patients would need a twice daily dose. The Panel noted that the relevant population of ART-experienced patients was described in the footnote. However, the Code required claims in promotional material to be capable of standing alone as regards accuracy etc. In general, claims should not be qualified by the use of footnotes and the like. The Panel considered that the claim was misleading about the patient population for whom the once daily dosing was indicated; it was not clear that for some patients twice daily dosing was necessary. A breach of the Code was ruled.

The Panel did not accept that the failure to include references in itself meant that none of the claims were substantiated as alleged and ruled no breach of the Code in that regard.

An anonymous, non-contactable prescriber complained about a Prezista (darunavir) advertisement (ref UK/HIV/2011/0056) placed by Janssen in a 'First Announcement' booklet for the British HIV Association (BHIVA) Autumn 2011 conference.

COMPLAINT

The complainant stated that the Prezista advertisements came to his attention because he was interested in the content of the claims but could not find any reference which could substantiate them. The complainant also alleged that the advertisement was a little misleading and he could not find any Prezista prescribing information throughout the 20 page flyer, which was a serious omission.

The complainant was concerned that the claim 'Simple once daily dosing in both naïve patients and those switching for tolerability and convenience' had an asterix which pointed to a footnote, in very small print, which described the very individuals that this applied to. Furthermore, there was no reference to the fact that the Prezista licence stated that for all other patients, it was a twice daily regimen which the complainant considered was very important to point out to a prescriber. The complainant referred to the dosing instructions in the summary of product characteristics (SPC). The complainant considered that this was misleading, since the advertisement did not make the twice daily regimen clear. Furthermore, as the prescribing information was missing, the complainant could not check if this was the case or not; he had to check with the electronic Medicines Compendium website to check this claim.

The complainant noted that none of the claims in the advertisement were substantiated since there was no list of references.

When writing to Janssen, the Authority asked it to respond in relation to Clauses 4.1, 7.2 and 7.4.

RESPONSE

Janssen acknowledged the serious omission of the references and prescribing information. The omission was unintentional, as a result of an administrative error which led to an incomplete version of the advertisement being included in the BHIVA First Announcement.

Unfortunately, due to the absence of several of the usual head office and agency staff involved, the

advertisement was submitted for publication without going through the copy approval process which would have picked up the obvious defects in the material. Janssen accepted that a breach of Clause 4.1 had occurred. The company had identified the series of process failures that led to this unfortunate omission, and had instituted additional training for the staff involved. Janssen described steps it had take to prevent the error happening again and noted that it intended to print an acknowledgment of its error in the final BHIVA Autumn Conference Programme which would be available to conference attendees on 17 November 2011, as well as a placement of a corrected version. This would ensure that the majority of those who saw the previous advertisement would also see the corrected version.

Janssen did not agree that the claim 'Simple once daily dosing in both naïve patients and those switching for tolerability and convenience*' was misleading. The Prezista SPC recommended once daily dosing in naïve patients as well as in treatment experienced patients with no darunavir (DRV) resistant associated mutations (RAMs), HIV-1 RNA <100,000 copies/ml and CD4+ counts ≥100 cells $x10^6$/l.

The footnote to the claim was of appropriate font size, with characters being at least 1mm in height, and Janssen thus considered it was 'clear and legible'. In Janssen's view the footnote added clarity and precision to the claim, rather than altering its meaning. Had the prescribing information not been omitted, this information and references would have been available to the reader.

Janssen submitted that it could demonstrate that in treatment experienced patients, DRV-RAMs, CD4 counts <100 cells $x10^6$/l and viral loads (VL) >100,000 copies/ml were uncommon, and therefore, patients requiring twice daily dosing represented a small population subgroup, and that the claim applied to the vast majority of patients. Available data from routine clinical practice/clinical studies suggested that most patients did not harbour DRV-RAMs:

- A retrospective analysis from 1998 to 2006 showed that 83.4% of 207,910 isolates sent from routine clinical resistance testing did not harbour DRV-RAMs (Rinehart *et al* 2007).

- A more recent analysis carried out in 2009, showed that most routine clinical HIV isolates (93.9%) harboured no DRV-RAMs (De La Rosa *et al* 2010)

- In the TITAN trial 83% of 595 treatment-experienced patients harboured no DRV RAMs at baseline (DeMeyer *et al* 2007).

- The authors of the ODIN (Once-daily Darunavir In treatment-experieNced patients) study concluded: 'Therefore data from the ODIN study may be applicable to a large group of treatment experienced patients currently under treatment' (Cahn *et al* 2011)

Gupta *et al* (2008), a systematic review of patients failing first line therapies currently prescribed in clinical practice, found:

- Virological failure (VF) at 48 weeks occurred in 4.9% of non nucleoside reverse transcriptase inhibitor (NNRTI) recipients compared with 5.3% of boosted protease inhibitor (bPI)

- Of those VF patients, 53% developed resistance to NNRTIs and 0.9% developed resistance to bPI

The 2007/2008 UK Drug Resistance Database Annual Report showed that the incidence of PI resistance in HIV population was 16%. This supported the low occurrence of bPI RAMS, and indeed, even more so of DRV-RAMS.

With regard to CD4 counts/viral loads, recent (2010) data from Stethos, an international marketing and market research company that conducted an annual HIV market report based on physician-reported patient cases, found that:

- Regarding CD4 count: of 711 patients' records, of which 565 were treatment experienced, 10% had CD4+ counts less than 200 cells/mm^3

- Regarding the VL, of 705 patient records, of which 559 were treatment experienced, only 5% had VL > 100,000 copies x 10^6/l

2010 SOPHID (Survey Of Prevalent HIV Infections Diagnosed) data from the Health Protection Agency showed only 1,068 out of 56,071 HIV patients receiving care had CD4 counts 0-100.

In summary, Janssen did not believe that the claim as it appeared on the advertisement breached Clauses 7.2 and 7.4. However, as the complainant had considered otherwise and the company wished to avoid any potential ambiguity in its materials, it committed to not use this claim with the explanatory footnote in the same way in future promotional items.

PANEL RULING

The Panel noted that the single page advertisement at issue contained a number of claims for Prezista, but did not contain prescribing information. The Panel considered that Janssen's explanation that this was due to a series of process failures and the absence of several of the usual head office and external agency staff involved, was inadequate. In the Panel's view, the company's procedures should have been sufficiently robust such that even in the absence of key staff, compliance standards were maintained. The Panel was very concerned that the advertisement had not been through the Janssen copy approval process and was published without being certified. It noted Janssen's submission that it had instituted additional training for staff involved.

Nonetheless, the omission of the prescribing information was contrary to the requirements of Clause 4.1, and a breach of that clause was ruled.

With regard to the complainant's second allegation concerning the claim 'Simple once daily dosing in both naïve patients and those switching for tolerability and convenience', the Panel noted that Section 4.2 of the Prezista SPC, Posology and method of administration, stated:

- 'For ART-experienced adults with no darunavir resistance associated mutations (DRV-RAMs) and who have plasma HIV-1 RNA < 100,000 copies/ml and CD4+ cell count ≥100 cells x 10^6/l, a dose regimen of 800 mg once daily with ritonavir 100 mg once daily taken with food may be used.

- In all other ART-experienced adults or if HIV-1 genotype testing is not available, the recommended dose regimen is 600 mg twice daily taken with ritonavir 100 mg twice daily taken with food. PREZISTA 75 mg and 150 mg tablets can be used to construct the twice daily 600 mg regimen. The use of 75 mg or 150 mg tablets to achieve the recommended dose is appropriate when there is a possibility of hypersensitivity to specific colouring agents, or difficulty in swallowing the 300 mg or 600 mg tablets.'

For ART-naïve patients, the recommended dose regimen was 800mg once daily with ritonavir 100mg once daily taken with food.

The Panel noted that a once-daily dose was only indicated for ART-naïve patients or a certain population of ART-experienced patients. Other ART-experienced patients would need a twice daily dose. The Panel noted Janssen's submission that the relevant population of ART-experienced patients was described in the footnote at the bottom of the page. However, the supplementary information to Clause 7 required 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. For ART-experienced patients to receive once daily dosing of Prezista, they must have no DRV-RAMs, and a viral load and CD4 count within certain parameters. The Panel noted Janssen's submission that patients requiring twice daily dosing represented a small subgroup and the claim at issue applied to the vast majority of patients. The Panel considered that the claim at issue 'Simple once daily dosing in both naïve patients and those switching for tolerability and convenience*' was misleading about the patient population for whom the once daily dosing was indicated and did not make it clear that for some patients twice daily dosing was necessary. A breach of Clause 7.2 was ruled.

The Panel noted that the Code required references to be given in certain circumstances, such as when referring to published studies (Clause 7.6) or when using artwork etc from published studies (Clause 7.8). The Code required that material be capable of substantiation and that substantiation be provided on request (Clauses 7.4 and 7.5). The Panel did not accept that the failure to include references in itself meant that none of the claims were substantiated as alleged and ruled no breach of Clause 7.4 in that regard.

Complaint received **22 August 2011**

Case completed **4 October 2011**