CASE AUTH/2400/4/11

NOVO NORDISK v BAXTER

Promotion of FEIBA

Novo Nordisk complained about the promotion of FEIBA (Factor VIII Inhibitor Bypassing Activity) by Baxter. The materials at issue were a double-sided single page document 'Introducing the FEIBA Prophylaxis Algorithm' and a six page brochure 'FEIBA A systematic treatment approach' which featured the claim 'Up to 85% reduction in bleed frequency'.

Novo Nordisk queried whether the claim reflected the available evidence as some reports suggested that the response rate to FEIBA was highly variable (range 50-90%). Novo Nordisk considered that the 'Up to 85%...' claim demonstrated cherry picking of favourable data and was therefore misleading.

The detailed response from Baxter is given below.

The Panel noted that the claim was referenced to Perry *et al* (2010) which summarized paediatric and adult data on FEIBA prophylaxis. The results given for reduction in bleed frequency varied from 57-85% for children and 50-90% for adults. Perry *et al* summarized the position that in patients with severe haemophilia and inhibitors, FEIBA prophylaxis had been shown to reduce the frequency of bleeding by up to 85% and to improve patient quality of life.

The Panel considered that the selection of 85% for the claim up to 'Up to 85% reduction in bleed frequency' was misleading as it did not reflect all the evidence contemporaneous with when it was used. A breach of the Code was ruled.

Novo Nordisk Limited complained about the promotion of FEIBA (Factor VIII Inhibitor Bypassing Activity) by Baxter Healthcare Ltd. Inter-company dialogue had failed to resolve all of Novo Nordisk's concerns.

The materials at issue were a double-sided single page document, 'Introducing the FEIBA Prophylaxis Algorithm (ref ADV 09/2758B) and a six page brochure 'FEIBA A systematic treatment approach' (ref ADV 09/2815B).

The claim at issue 'Up to 85% reduction in bleed frequency' was referenced to Perry *et al* (2010). Novo Nordisk stated that on closer inspection of Table 2, the reference attributed to this claim (reference 31 within Perry *et al*) originated from an abstract by Valentino (2008) which was presented as a poster at the World Federation of Haemophilia congress in 2006.

COMPLAINT

Novo Nordisk queried whether the claim reflected all the available evidence clearly, as reports from other published evidence (as seen in Tables 2 and 3 of Perry *et al*) suggested that the response rate to FEIBA was highly variable (range 50-90%). Novo Nordisk believed that the use of this efficacy figure in a promotional context ('Up to 85% bleed reduction') demonstrated cherry picking of favourable data at one end of a highly variable results range. Novo Nordisk alleged that the claim was misleading as it did not reflect the evidence clearly in breach of Clause 7.2 of the Code.

Novo Nordisk noted that the abstract by Valentino reported on a single patient with haemophilia B and inhibitors. FEIBA was licensed for use in haemophilia A patients with an inhibitor and was not licensed for use in patients with haemophilia B. Furthermore, it was well documented that there was a potential and significant risk of anaphylaxis with the use of FEIBA in patients with haemophilia B and specific mutations.

In inter-company dialogue Baxter had stated that, in response to a request for advice from the Authority, about the use of a reference that included a haemophilia B inhibitor patient to support a claim around use in a haemophilia A inhibitor patient, the Authority had advised that 'it was acceptable to use such an article as substantiation for a promotional claim however such an article could not be used promotionally by the sales force'.

Novo Nordisk was not convinced that Baxter had followed the Authority's advice, as it was aware that a Baxter representative had handed over a copy of Perry *et al* within a reprint folder (ref ADV09/2711B) at the UK Haemophilia Centre Doctors' Organisation (UKHCDO) meeting in Newcastle in November 2010.

RESPONSE

Baxter stated that in its view Perry *et al* fully substantiated the claim, and it rejected the allegation that it was using a haemophilia B patient case as the source of the figure quoted.

This article was the result of a meeting of an expert panel of clinicians, all of whom had experience in this use of FEIBA from their clinical practice. The purpose of the meeting was to review all the published evidence in this area and then devise evidence-based guidance on how FEIBA should be used to best effect. The results of this review of the evidence was clearly stated in the publication abstract and summary; the authors concluded

'regular FEIBA prophylaxis has been shown to reduce the frequency of bleeding by up to 85%'. This was the source of the number Baxter quoted in its claim.

This publication included data relating to 86 children and 32 adults, all with haemophilia A and inhibitors, therefore all in the patient group where FEIBA was licensed.

It was coincidental that the single case reported by Valentino in this article referred to exactly the number quoted in the claim. Excluding possible double-counting of haemophilia B cases less than 2% of the total cohort fell into that category; as at least 95% of the cases reported were within the licence for FEIBA Baxter did not accept the allegation.

Baxter was not surprised that this case report was highlighted as it was the only one in Perry *et al* to refer to cost of treatment, and Baxter had been in dispute with Novo Nordisk for some time over cost-effectiveness claims it made for its product NovoSeven compared with FEIBA.

In addition, Baxter would only use a conference abstract to substantiate an efficacy claim where no other published evidence existed. This was clearly not the case; however it seemed that Novo Nordisk was not prepared to accept this, however Baxter made the point, or however often it stated it.

Baxter did not claim 'FEIBA prophylaxis reduces bleed frequency by 85%' – although this specific figure was stated in the reference, such an absolute statement would be factually inaccurate.

Baxter noted that the other publication by Valentino cited in Perry *et al*, a retrospective case series reporting experience with six patients, suggested that an 84% reduction in bleeding episodes was in fact the mean percentage reduction, and not the upper limit.

Baxter submitted that response to treatment in this patient group could indeed be variable, whichever product was used. That said, there was an equal variation in the dose and frequency of treatment between case series. Despite this, the authors stated that the results of case series 'consistently demonstrate the efficacy and safety of FEIBA prophylaxis'. The individual case studies presented by the authors to illustrate their individual experience reinforced this.

What was also clear from the Perry article was that in many situations the use of FEIBA to prevent bleeding achieved exactly that outcome – the incidence of bleeding in these patients had become comparable to that seen in haemophilia patients without inhibitors, and in some cases no bleeding episodes were seen while on treatment.

Baxter maintained that the claim at issue was accurate and substantiated by the reference; it fairly reflected the evidence available. Baxter rejected the allegation of a breach of Clause 7.2. In a subsequent letter Baxter stated that the claim at issue had been withdrawn due to recently published data that materially affected it.

PANEL RULING

The Panel noted that after it had submitted its response, Baxter withdrew the claim pending revision due to new evidence. The new evidence was not identified. The Panel decided that in the circumstances it would consider the complaint in relation to its use prior to withdrawal.

The Panel noted that the claim was referenced to Perry *et al* (2010) which summarised paediatric and adult data on FEIBA prophylaxis. The results given for reduction in bleed frequency varied from 57-85% for children (Table 2 of Perry *et al*) and 50-90% for adults (in two of the studies in Table 3 of Perry *et al* the mean reduction in bleed frequency was 53% with a range of 10-85%). Perry *et al* summarised the position that in patients with severe haemophilia and inhibitors, FEIBA prophylaxis had been shown to reduce the frequency of bleeding by up to 85% and to improve patient quality of life.

The Panel considered that the selection of 85% for the claim up to 'Up to 85% reduction in bleed frequency' was misleading as it did not reflect all the evidence contemporaneous with when it was used. A breach of Clause 7.2 was ruled.

Complaint received	**15 April 2011**
Case completed	**7 June 2011**