CASE AUTH/2483/2/12

CONSULTANT IN SEXUAL HEALTH v PFIZER

Promotion of Prevenar 13

A consultant in sexual health and HIV medicine, complained about a Prevenar 13 (pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) leavepiece issued by Pfizer. Prevenar 13 was indicated, *inter alia*, for active immunisation for the prevention of invasive disease caused by *Streptococcus pneumoniae* in adults aged 50 years and older.

The one page leavepiece at issue was printed on both sides. One side was headed with the Prevenar 13 product logo in the top left hand corner. A white box of text, diagonally opposite the product logo, stood out prominently from the navy blue background and stated in large, navy blue capital letters 'HIV [human immunodeficiency virus] and invasive pneumococcal disease'. Below the boxed text, in smaller bright yellow type, was the statement 'New Indication' and then below this in white type against the navy blue background was the heading 'Adult indication' followed by, in much smaller white type, 'Prevenar 13 is indicated for active immunisation for the prevention of invasive pneumococcal disease caused by *Streptococcus pneumoniae* in adults aged 50 years and older'.

The complainant alleged that the leavepiece implied that Prevenar 13 was newly indicated in HIV infection which was not so and in the very small print prescribing information there were warnings about the lack of safety data for HIV infection. The indication referred to beneath the large banner about HIV was in fact regarding patients aged over 50 years of age.

The detailed response from Pfizer is given below.

The Panel noted that the Prevenar 13 Summary of product characteristics (SPC) stated that individuals with impaired immune responsiveness due to, *inter alia*, HIV infection might have a reduced antibody response to active immunisation and that safety and immunogenicity data for Prevenar 13 were not available for such patients and that vaccination should be considered on an individual basis. There was no reference in the leavepiece to this caution other than in the prescribing information.

The Panel considered that the leavepiece implied that use in HIV and invasive pneumococcal disease was a new indication for Prevenar 13. This was of particular concern given the statements in the SPC.

The Panel considered that the leavepiece did not promote Prevenar 13 in accordance with the terms of its marketing authorization, was inconsistent with the particulars in its SPC and misleading with regard to the licensed indication. High standards had not been maintained. Three breaches of the Code were ruled. The Panel noted that Pfizer had acknowledged all of these breaches and had already withdrawn the leavepiece.

The Panel considered that the legibility of the prescribing information was not unacceptable noting in particular the advice on legibility set out in the Code. The Panel ruled no breach of the Code.

A consultant in sexual health and HIV medicine complained about a Prevenar 13 (pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) leavepiece (ref VAC291) issued by Pfizer. Prevenar 13 was indicated, *inter alia*, for active immunisation for the prevention of invasive disease caused by *Streptococcus pneumoniae* in adults aged 50 years and older.

The material at issue was a one page leavepiece printed on both sides. One side was headed with the Prevenar 13 product logo in the top left hand corner. A white box of text, which was diagonally opposite the product logo, stood out prominently from the navy blue background and stated in large, navy blue capital letters 'HIV [human immunodeficiency virus] and invasive pneumococcal disease'. Below the boxed text, in smaller bright yellow type, was the statement 'New Indication' and then below this in white type against the navy blue background was the heading 'Adult indication' followed by, in much smaller white type, 'Prevenar 13 is indicated for active immunisation for the prevention of invasive pneumococcal disease caused by *Streptococcus pneumoniae* in adults aged 50 years and older'. The prescribing information appeared in black type on a white background on the lower half of the page.

The reverse side of the leavepiece referred to the increased risk of invasive pneumococcal infection in adults with HIV and the efficacy of pneumococcal conjugate vaccines in preventing such infections in that population. At the bottom of the page was the heading 'Prevenar 13 New Indication' below which was stated 'Prevenar 13 is now indicated for active immunisation for the prevention of invasive disease caused by *Streptococcus pneumoniae* in adults aged 50 years and older'.

COMPLAINT

The complainant alleged that the leavepiece implied that there was a new indication for Prevenar 13 in HIV infection, whereas in fact it was not so authorized and in the very small print prescribing information there were warnings about the lack of safety data for HIV infection. The indication referred to beneath the large banner about HIV was in fact regarding patients aged over 50 years of age.

The complainant further submitted that on the reverse side of the leavepiece the HIV theme continued, although studies cited related to previous versions of the vaccine and again appeared to imply that this particular PCV-13 (pneumococcal conjugate vaccine 13) vaccine might reduce invasive pneumococcal disease and this use was licensed in the UK.

The complainant accepted that there might be theoretical benefits to using pneumococcal conjugate vaccines but he objected to marketing spin that implied that Prevenar 13 was safe, effective and had a marketing authorization for use in HIV infection and the matter was concluded. The HPA (Health Protection Agency) had complicated matters by recommending introduction of Prevenar 13 in a report on HIV infection in advance of formally considering this as part of the Green Book update later in 2012, so the complainant accepted that the situation was blurred. However, he considered that Pfizer had strayed over the boundary with its leavepiece.

When writing to Pfizer the Authority asked it to respond in relation to Clauses 3.2, 4.1, 7.2 and 9.1 of the Code.

RESPONSE

Pfizer submitted that whilst it had intended to raise awareness of an important treatment option for a vulnerable patient group, it recognised that the leavepiece had not adhered to the Code. The leavepiece was used from 19 January by representatives with health practitioners in HIV, sexual medicine and genitourinary medicine.

In consideration of Clause 3.2, Pfizer submitted that it had taken account of the two different elements which together made up the clause; firstly the promotion of a medicine must be in accordance with the terms of its marketing authorization and secondly must not be inconsistent with the particulars listed in its summary of product characteristics (SPC).

Pfizer submitted that Prevenar 13 was indicated in adults aged 50 years and over; some of these patients would have HIV and were at increased risk of pneumococcal disease. The licence for Prevenar 13 did not exclude use of the medicine in this group. The European Public Assessment Report (EPAR) for Prevenar 13 noted that 'clinical studies in human immunodeficiency virus (HIV)-infected adult populations have provided evidence that conjugated vaccines exhibit noted efficacy against invasive pneumococcal disease and possibly pneumonia, in circumstances where [the current standard of care pneumococcal vaccine] has not afforded such protection to these immune-compromised adults'. Pfizer therefore did not consider that it had breached the first element of Clause 3.2 (as set out above). However, Pfizer stated that it recognised that the leavepiece did not draw attention to the following wording in the Prevenar 13 SPC:

> 'Individuals with impaired immune responsiveness, whether due to the use of immuno-suppressive therapy, a genetic defect, human immunodeficiency virus (HIV) infection, or other causes, may have reduced antibody response to active immunization.
>
> Safety and immunogenicity data for Prevenar 13 are not available for individuals in specific immuno-compromised groups (e.g., congenital or acquired splenic dysfunction, HIV infected, malignancy, haematopoietic stem cell transplant, nephrotic syndrome) and vaccination should be considered on an individual basis.'

Pfizer submitted that this therefore made the leavepiece inconsistent with the SPC and breached the second element of Clause 3.2. As Clause 3.2 was made up of two elements and it agreed that the leavepiece did not meet the requirements of the second element, Pfizer acknowledged a breach of Clause 3.2.

Pfizer considered that the prescribing information that was an integral part of the leavepiece was in line with the requirements of the Code, but the company could understand that the quality of the scanned copy provided by the complainant made this difficult to ascertain. Pfizer submitted that the original piece did not breach Clause 4.1.

Pfizer stated that as the current material might be misinterpreted to suggest a specific indication in HIV regardless of age, and with evidence from the complainant of the confusion this might cause, it acknowledged a breach of Clause 7.2.

In view of the acknowledged breaches of Clauses 3.2 and 7.2, Pfizer considered it had not maintained high standards and acknowledged a breach of Clause 9.1.

Pfizer submitted that it took this matter extremely seriously and confirmed that it had already withdrawn the leavepiece and briefed its sales team accordingly.

PANEL RULING

The Panel noted the statement in Section 4.4, Special Warnings and Precautions for Use, of the Prevenar 13 SPC that individuals with impaired immune responsiveness whether due to a number of factors including HIV infection or other causes might have a reduced antibody response to active immunisation and that safety and immunogenicity data for Prevenar 13 were not available for individuals in specific immuno-compromised groups, including those with HIV and that vaccination should be considered on an individual basis. There was no reference in the leavepiece to this caution other than in the prescribing information.

The Panel examined the leavepiece and considered that overall it gave the impression that use in HIV and invasive pneumococcal disease was a new indication for Prevenar 13. This was of particular concern given the statements in the SPC.

The Panel considered that the leavepiece did not promote Prevenar 13 in accordance with the terms of

its marketing authorization and was inconsistent with the particulars in its SPC. A breach of Clause 3.2 was ruled. The Panel considered that the leavepiece was misleading with regard to the licensed indication of Prevenar 13 and ruled a breach of Clause 7.2. The Panel noted its rulings above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel noted that Pfizer had acknowledged all of these breaches of the Code and had already withdrawn the leavepiece.

The Panel noted that in the copy of the leavepiece submitted by the complainant, the prescribing information was very difficult to read. The complainant had referred to 'very small print'. However, the Panel considered that the legibility of the prescribing information in the original leavepiece provided by Pfizer was not unacceptable noting in particular the advice on legibility set out in the supplementary information to Clause 4.1. The Panel ruled no breach of Clause 4.1.

Complaint received **28 February 2012**

Case completed **17 April 2012**