CASE AUTH/3842/10/23 ***NO BREACH OF THE CODE***

COMPLAINANT v ASTRAZENECA

Alleged missing information from Fluenz Tetra post administration leaflet

CASE SUMMARY

This case was in relation to a document titled "Post Administration Information" and subtitled "Facts about Fluenz Tetra nasal spray suspension Influenza vaccine (live attenuated, nasal)". The complainant alleged that important post-administration requirements listed in the summary of product characteristics were not included in the body of the document and that this presented a risk to patient safety.

The outcome under the 2021 Code was:

No Breach of Clause 2	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**
No Breach of Clause 5.1	**Requirement to maintain high standards at all times**
No Breach of Clause 6.1 (x2)	**Requirement that information must be accurate, up to date and not misleading**

This summary is not intended to be read in isolation.
For full details, please see the full case report below.

FULL CASE REPORT

A complaint about AstraZeneca UK Limited was received from an anonymous, contactable complainant who described themselves as a health professional.

COMPLAINT

The complaint wording is reproduced below with some typographical errors corrected:

> "A post administration document produced by AstraZeneca on Fluenz Tetra nasal spray suspension influenza vaccine is missing key post administration information listed in the SPC. The document is available at [URL provided]. The following two parts are important post administration requirements listed in the SPC (sections 4.4 and 4.5). 1. Vaccine recipients should be informed that Fluenz Tetra is an attenuated live virus vaccine and has the potential for transmission to immunocompromised contacts. Vaccine recipients should attempt to avoid, whenever possible, close association with severely immunocompromised individuals (e.g. bone marrow transplant recipients requiring isolation) for 1–2 weeks following vaccination. 2. Do not use salicylates in children and adolescents for 4 weeks after vaccination unless medically indicated as Reye's syndrome has been reported following the use of salicylates during wild-type

influenza infection. These 2 parts from the SPC are missing in the document produced by AZ, not included on page 2 or 3 of the document. Considering the document is aimed at HCPs and is titled post administration, one would expect to find all important requirements post administration of vaccine as the 2 SPC parts are crucial for HCPs to make patients aware of. Missing the 2 key parts from the SPC in the post administration document page 2 and 3 is a major patient safety risk. ABPI code breaches of 6.1, 5.1 and 2."

When writing to AstraZeneca, the PMCPA asked it to consider the requirements of Clauses 6.1, 5.1 and 2 of the 2021 Code.

ASTRAZENECA'S RESPONSE

The response from AstraZeneca is reproduced below:

"Thank you for your letter dated October 31st 2023, which pertains to the alleged omission of information from the Fluenz Tetra post administration leaflet. A summary of the allegations made by the complainant are:

An online PDF document regarding post-administration information for Fluenz Tetra, accessible on [URL provided], a website catering to healthcare professionals (HCPs) in Great Britain, omits two key pieces of information from the SmPC:

i. Vaccine recipients should be informed that Fluenz Tetra is an attenuated live virus vaccine and has the potential for transmission to immunocompromised contacts. Vaccine recipients should attempt to avoid, whenever possible, close association with severely immunocompromised individuals (e.g., bone marrow transplant recipients requiring isolation) for 1-2 weeks following vaccination.
ii. Do not use salicylates in children and adolescents for 4 weeks after vaccination unless medically indicated as Reye's syndrome has been reported following the use of salicylates during wild-type influenza infection.

Omission of this information in the post-administration booklet poses a patient safety risk.

In our response we will provide evidence that:

a) The information above is key when considering whether the prescription and administration of the vaccine is appropriate for that patient, i.e. pre-administration. As the information is considered pre-administration, it is therefore important to include in pre-administration materials.
b) The prescribing information (PI) for Fluenz Tetra provided on page 4 of the booklet does include this information.

AstraZeneca Response

Background

The document subject to the complaint is titled 'Post-Administration Information' and is accessible on the website [URL provided]. This is a promotional website for Fluenz Tetra, intended for healthcare professionals (HCPs) in Great Britain. Someone

accessing this website must declare that they are an HCP before they can view any promotional information. The homepage of this website explicitly indicates its purpose as being a platform for HCPs actively engaged in the National Immunisation Programme for Childhood Flu.

There is a section of the website called 'Administration information' ([URL provided]) which hosts four information booklets and one video resource to support administration of Fluenz Tetra. There is an administration video, Administration Storage Information Booklet, Pre-Administration Information Booklet, During Administration Information Booklet, and Post-Administration Information Booklet.

The Post-Administration Information booklet (subject to the complaint) is four pages long. The booklet is viewable on the website in PDF format and can be downloaded by the HCP. It includes pertinent information regarding the safety profile and efficacy of Fluenz Tetra. The second page refers to the SmPC for more detailed information about adverse reactions. The PI is presented on the fourth page.

Response to allegations

Information about possible transmission to immunocompromised contacts and salicylate use post administration, are essential considerations *prior* to administering the vaccine, to ensure Fluenz Tetra is an appropriate treatment option for that patient. It is important that this information is included in pre-administration materials.
This information is captured in our Pre-Administration Information booklet. Relevant sections are shown in Figure 1, 2 and 3 below.

Figure 1: Excerpt of Pre-Administration Information; page 2
[Points 4 and 6 from a list were highlighted: "4. Is the recipient in close contact with people who are severely immunodeficient?" "6. Is the recipient on salicylate therapy (e.g. aspirin)?"]

Figure 2: Excerpt of Pre-Administration Information; page 4
[Excerpt read:
"4. Is the recipient in close contact with people who are severely immunodeficient?
Vaccine recipients should be informed that Fluenz Tetra is an attenuated live virus vaccine and has the potential for transmission to immunocompromised contacts. Vaccine recipients should attempt to avoid, whenever possible, close association with severely immunocompromised individuals (e.g. bone marrow transplant recipients requiring isolation) for 1–2 weeks following vaccination. Peak incidence of vaccine virus recovery occurred 2–3 days post-vaccination in Fluenz clinical studies. In circumstances where contact with severely immunocompromised individuals is unavoidable, the potential risk of transmission of the influenza vaccine virus should be weighted against the risk of acquiring and transmitting wild-type influenza virus."]

Figure 3: Excerpt of Pre-Administration Information; page 5
[Excerpt read:
"6. Is the recipient on salicylate therapy (e.g. aspirin)?
Children and adolescents receiving salicylate therapy (e.g. aspirin) must not be given this vaccine, as there is an association between the use of salicylates during influenza infection and Reye's syndrome.

For the same reason, salicylates must not be given for 4 weeks following vaccination unless medically indicated."]

As the information is considered at the pre-administration stage, we assert that it will have already been considered by the time of vaccine administration, and therefore not necessary or appropriate to include again in the main text of post-administration materials.

This approach is in line with UKHSA materials (including the UKHSA Consent form, UKHSA training materials) and The Green Book – where information about possible transmission to immunocompromised patients and salicylate use post-administration is included in pre-administration materials rather than post-administration materials. To support full and thorough informed consent these concerns are addressed prior to administration. UKHSA materials are provided to all GB HCPs who have the responsibility of prescribing or administering Fluenz Tetra.

Although we don't deem it necessary to include this information in the main text of the post-administration leaflet, the PI is presented on the fourth page which does include information about potential transmission to immunocompromised contacts (*Warnings and Precautions*), and that Salicylates must not be used for 4 weeks following vaccination (*Contraindications and Drug Interactions*) for completeness.

AstraZeneca believes that we have upheld high industry standards and has maintained patient safety, whilst keeping materials consistent and in line with national guidance.

We therefore strongly deny the alleged breach of clauses 6.1, 5.1, and 2 of the ABPI Code of Practice.

Summary of AstraZeneca's position

AstraZeneca asserts that information in the SmPC relating to possible transmission to immunocompromised patients, and salicylate use post-administration of Fluenz Tetra, are important pre-administration considerations and therefore should be and are included in pre-administration documentation to support HCPs and patients in deciding whether Fluenz Tetra is an appropriate choice for that patient. This is also in line with government materials.

AstraZeneca demonstrates a complete adherence to the ethical and moral principles outlined in the ABPI Code of Practice and upholds its obligations under the code requirements."

PANEL RULING

The complaint related to a document titled "Post Administration Information" and subtitled "Facts about Fluenz Tetra nasal spray suspension Influenza vaccine (live attenuated, nasal)" which was intended for GB health professionals. The complainant alleged that important post-administration requirements listed in the summary of product characteristics were not included in the body of the document and that this presented a risk to patient safety.

AstraZeneca submitted that the information cited by the complainant was key when considering whether the prescription and administration of the vaccine was appropriate for the patient – pre-administration. AstraZeneca submitted that, for this reason, the information was included in their pre-administration materials.

The Panel noted that the booklet at issue was available on a webpage titled "Administration Information" and was one of a set of four information booklets: "Administration Storage Information", "Pre-administration Information", "During Administration Information" and "Post Administration Information".

The "Post Administration Information" booklet was four pages in length. The first page included, in addition to the title, logos, etc., the product indication and the adverse events reporting statement. Page two presented a summary of the safety profile and information on the side effects that can occur with Fluenz Tetra. Page three contained a statement on vaccine effectiveness, which explained how the effectiveness of influenza vaccines varies from year to year, and a list of references. The final page was the prescribing information.

The two statements from the summary of product characteristics that the complainant alleged should have been included in the booklet were as follows:

From the traceability section of Section 4.4 Special warnings and precautions:
"Vaccine recipients should be informed that Fluenz Tetra is an attenuated live virus vaccine and has the potential for transmission to immunocompromised contacts. Vaccine recipients should attempt to avoid, whenever possible, close association with severely immunocompromised individuals (e.g. bone marrow transplant recipients requiring isolation) for 1–2 weeks following vaccination."

From Section 4.5 Interaction with other medicinal products and other forms of interaction:
"Do not use salicylates in children and adolescents for 4 weeks after vaccination unless medically indicated as Reye's syndrome has been reported following the use of salicylates during wild-type influenza infection."

Having reviewed the materials provided by both parties, the Panel accepted AstraZeneca's submission that both statements were included in the main body of the "Pre-administration Information" booklet and that they were also included in the Fluenz Tetra prescribing information in both the "Pre-administration Information" and "Post Administration Information" booklets.

The Panel considered it was well established that material had to be capable of standing alone and sufficiently complete to enable prescribers to form their own opinion of the therapeutic value of the medicine.

The Panel noted that the "Post Administration Information" booklet was part of a suite of four information booklets all available from the same webpage, along with a video resource. The Panel considered that the two statements at issue were important information relevant to patient safety. In the Panel's view, however, they were points that would be dealt with at the pre-administration stage, and that the focus post-administration was likely to be on possible side effects.

The Panel noted that the vaccine was provided as part of the national immunisation programme. In the Panel's view, the vaccine's seasonality meant that it was likely that health professionals

would refresh their knowledge each year, and that health professionals commonly considered special warnings and interactions when prescribing and administering medicines. In relation to the statement about salicylates, in the Panel's view, the association with Reye's syndrome was well established and there was an expectation that health professionals would exercise caution in this regard.

While noting the requirement for material to be capable of standing alone, the Panel noted that the two statements at issue were present in the "Pre-administration Information" booklet, in the prescribing information (included in the "Post Administration Information" and "Pre-administration Information" booklets), and in the patient information leaflet. The Panel note this approach was consistent with the UKHSA flu vaccination consent form and the Green Book chapter on Influenza which treated both points as pre-administration considerations. In the particular circumstances of the case, the Panel did not consider that the complainant had established that the omission of the two statements from the main body of the "Post Administration Information" booklet meant it was incomplete or misleading. The Panel therefore ruled **no breach of Clause 6.1** in relation to the statement about transmission to immunocompromised contacts, and **no breach of Clause 6.1** in relation to the statement about salicylates.

Noting its rulings of no breaches of Clause 6.1 of the Code, the Panel did not consider that the complainant had demonstrated that AstraZeneca had failed to maintain high standards and ruled **no breach of Clause 5.1** of the Code. The Panel consequently ruled **no breach of Clause 2**.

Complaint received **30 October 2023**

Case completed **16 December 2024**