CASE AUTH/3917/6/24

COMPLAINANT v JAZZ PHARMACEUTICALS

Allegations about promotional videos

CASE SUMMARY

This case was in relation to allegations relating to two educational, promotional, online presentations for health professionals regarding Epidyolex (cannabidiol).

The outcome under the 2021 Code was:

Breach of Clause 2	**Bringing discredit upon, and reducing confidence in, the pharmaceutical industry**
Breach of Clause 5.1 (x3)	**Failing to maintain high standards**
Breach of Clause 6.1 (x3)	**Making a misleading claim**

No Breach of Clause 9.1	**Requirement that all relevant personnel concerned with the preparation or approval of material or activities covered by the Code must be fully conversant with the Code and the relevant laws and regulations**

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 Jazz Pharmaceuticals UK was received from an anonymous, contactable complainant who described themselves as a health professional.

The complainant has now become non-contactable.

COMPLAINT

The complaint wording is reproduced below:

> "A presentation on Epidyolex (INT-EPX-2300276) by [named academic] omitted important information around discontinuation and/or reduction of valproate and epidyolex due to hepatic transaminases elevation when there is concomitant use of Epidyolex and Valproate. In the presentation at 13 minutes 25 seconds, there was discussion of concomitant use of CBD (Epidyolex) and valproate. However, the speaker did not discuss that if clinically significant increases of hepatic transaminases occur which was known due to usage of valproate and epidyolex in combination, epidyolex and/or concomitant valproate should be reduced or discontinued in all

patients until a recovery of transaminase elevations are observed which was guidance from the Epidyolex SPC [summary of product characteristics]. The speaker had not been appropriately briefed to discuss such important safety information around this concomitant usage of Epidyolex with valproate and discontinuation and/or reduction of Epidyolex relevant to elevation in hepatic transaminases. As this important safety information around Epidyolex reduction and/or discontinuation was not discussed, this was a risk to patient safety and was in breach of clauses 6.1, 5.1 and 2. A second presentation on optimising clinical use of Epidyolex (INT-EPX-2400001) by [named speaker] did not discuss hepatic contraindications. The video content from 18 seconds to 28 seconds showed monitoring of ALT [alanine aminotransferase], AST [aspartate aminotransferase] and bilirubin at the start and periodically after with Epidyolex but did not explicitly state that Epidyolex is contraindicated in patients with transaminase elevations greater than 3 times the upper limit of normal and bilirubin greater than 2 times the ULN [upper limit of normal] as in the SPC. It was important that HCPs knew precisely when Epidyolex was contra-indicated in hepatic dysfunction, especially as the video content discussed hepatic monitoring. The case study presented in the same video on combined use of Epidyolex and Valproate at 4 minutes omitted important information around discontinuation and/or reduction of valproate and epidyolex due to increased elevation of hepatic transaminases when there is concomitant use of Epidyolex and Valproate. The speaker had not been briefed to discuss this important part around hepatic elevations. This was a significant risk to patient safety and was in breach of clauses 6.1, 5.1 and 2 Both videos had been funded by Jazz and aimed at UK HCPs. PMCPA need to investigate safety omissions as significant risk to patients."

When writing to Jazz, the PMCPA asked it to consider the requirements of Clauses 2, 5.1, 6.1 and 9.1 of the 2021 Code.

JAZZ'S RESPONSE

The response from Jazz is reproduced below:

"Thank you for your letter of 7th June 2024, in which you notified us of a complaint from an anonymous contactable Healthcare Professional relating to cannabidiol promotional presentations. We were requested to respond to this matter with consideration to the Clause requirements of 6.1, 5.1 and 2, as cited by the complainant. The complainant stated concerns that Jazz did not adequately address the risk of transaminase elevations when taking Epidyolex and valproate concomitantly and also made allegations about the speaker briefing.

The specific concerns raised by the complainant are outlined as follows:

- An Epidyolex (cannabidiol) presentation that discussed the concomitant use of cannabidiol and valproate/valproic acid (here after referred to as valproate), did not discuss that if clinically significant increases of hepatic transaminases occur cannabidiol and/or concomitant valproate should be reduced or discontinued in all patients until recovery of transaminase elevations are observed which the complainant alleges was guidance from the Epidyolex SPC. This is an incorrect interpretation of the SPC as we will demonstrate in this letter.

- The speaker has not been appropriately briefed to discuss safety information about the concomitant usage of cannabidiol with valproate and discontinuation and/or reduction of cannabidiol relevant to elevation of hepatic transaminases.

- A second presentation did not discuss hepatic contraindications. The video did not explicitly state that cannabidiol is contraindicated in patients with transaminase elevations greater than 3 times the upper limit of normal and bilirubin greater than 2 times the ULN as in the SPC.

- The speaker had not been briefed to discuss hepatic elevations.

As part of Jazz's commitment to provide medical education and to help improve patient care in the specialist management of specific developmental and epileptic encephalopathies, Jazz created two educational promotional presentations for health care professionals. The intended audience for these presentations was physicians, nurses and pharmacists with interest in neuroscience/epilepsy. These were approved as INT-EPX-2300276 and INT-EPX-2400001, referred to in our response as presentation 1 and presentation 2, respectively.

The speakers were chosen due to their expertise in the therapeutic area, they are referred to in our response as Speaker 1 and Speaker 2. Their details are provided in the attachments which for data privacy reasons we request are redacted when this case is written up .

Speaker 1 and Speaker 2 were fully briefed before speaking on behalf of Jazz. The speakers were advised on compliance considerations when preparing slides. This guidance comprised inclusion of adverse events and concomitant medication guidance, as well as the need to be accurate fair and balanced in the use of data.

Therefore, we refute the complainant's allegation that the speakers were not appropriately briefed. In fact, we gave comprehensive, detailed briefings to both speakers, as attached (INT-EPX-2300270).

Presentation 1 was given by a pharmacologist. The main objective of the presentation was to educate on the pharmacology of the endocannabinoid system and the mechanism of action of cannabidiol in treating seizures associated with Lennox-Gastaut syndrome (LGS) and Dravet Syndrome (DS).

The complainant alleges that the presentation breaches clause 6.1 because it did not discuss that 'if clinically significant increases of hepatic transaminases occur … epidyolex and/or concomitant valproate **should be** reduced or discontinued in **all** patients until a recovery of transaminase elevations are observed which was guidance from the Epidyolex SPC'. In fact, this guidance is not given in the Epidyolex SPC.

Section 4.4 of the SPC sets out details of how to manage hepatocellular injury. It outlines **several options** for managing cases of elevations of transaminases. It states: 'Dose adjustment or discontinuation of valproate or dose adjustment of clobazam **should be considered** if transaminase elevations occur.' 'Resolution of transaminase elevations occurred with discontinuation of cannabidiol or reduction of cannabidiol

and/or concomitant valproate in about two-thirds of the cases' (Section 4.4 SPC). The SPC section 4.4 also states that 'In about one-third of the cases, transaminase elevations resolved during continued treatment with cannabidiol, without dose reduction.' Thus, it is clear that the guidance from the Epidyolex SPC does not require that physicians reduce or discontinue the use of cannabidiol in patients with hepatic transaminase elevations. Rather it equips the physician with information and a suggestion of various courses of action to be considered including continuing the treatment.

In addition, the briefing for Speaker 1 expressly requested they highlight the risks when cannabidiol and valproate are used concomitantly. The speaker briefing stated: 'Highlight the potential on liver enzymes and adverse event occurrence when CBD and valproate are used concomitantly'. In the presentation, Speaker 1 does explicitly state that the combination of cannabidiol and valproate is known to be associated with an increased incidence of transaminase elevations: 'Then we have this very specific situation with the combination of cannabidiol and valproic acid. There, it's known that this combination is associated with an increased incidence of transaminase elevation. We do not really have a good explanation for this. The mechanism remains unknown. It might be related to changes in the free unbound concentrations of the drugs, but it has not been really characterized by now'. The purpose of the presentation was not to discuss how to manage this from a clinical perspective. However despite this, the risk of transaminase elevations in the concomitant use of cannabidiol and valproate were still highlighted.

Further, at the bottom of every slide in the presentation, there was a note stating that the prescribing information is shown at the end of the presentation. The prescribing information gives (i) details of the requirement for increased frequency of monitoring liver function in cases where cannabidiol and valproate are used together and (ii) guidance about when to consider interrupting or discontinuing treatment.

Presentation 2 presented a patient case study including the monitoring required when patients receive cannabidiol therapy alongside other anti-seizure medication(s). The objective of this presentation was to discuss practical ways in which cannabidiol treatment can be tailored to each patient and explore the clinical management of adverse events (AEs) and Drug-Drug Interactions (DDIs) in an adult patient with late-onset LGS.

The complainant alleges that the 'presentation did not explicitly state that Epidyolex is contraindicated in patients with transaminase elevations greater than 3 times the upper limit of normal and bilirubin greater than 2 times the ULN as in the SPC. It was important that HCPs knew precisely when Epidyolex was contra-indicated in hepatic dysfunction, especially as the video content discussed hepatic monitoring.'

In the case study presented, there is no suggestion that the patient had any liver enzyme increases at any stage of treatment. In fact, the presentation shows clearly at the outset that the patient's dosing of valproate was reduced before the patient started treatment. The presenter says: 'Before starting Epidyolex we wanted to reduce valproic acid …. We started then cannabidiol as per SmPC'. Therefore, the contraindication that the complainant references was completely irrelevant in this patient case study.

Despite this, because Jazz takes patient safety and the requirements of the ABPI Code very seriously we did brief the speaker to address the risk of hepatic impairment in the concomitant use of cannabidiol and valproate. The speaker briefing for Speaker 2 specifically required that the speaker address: a 'Summary of concomitant medications at initiation [of the case presented] and subsequent dose reductions' and 'Adverse events experienced by the patient and how they were rectified'.

The complainant alleged that 'The case study presented in the … video on combined use of Epidyolex and Valproate...omitted important information around discontinuation and/or reduction of valproate and [E]pidyolex due to increased elevation of hepatic transaminases when there is concomitant use of Epidyolex and Valproate." As stated above, the case study made clear both verbally and in the slides that the dosing of valproate was reduced **before** the start of treatment with cannabidiol.

Despite all this, at the outset of the presentation the dosing regimen for starting cannabidiol is shared, included is the requirement for liver function monitoring in patients commencing cannabidiol, along with details of the routine and intensive monitoring requirements. There are clear references to the full monitoring details being available in section 4.4 of the SPC. And the SPC was shown at the end of the presentation. Details for dose adjustments in patients with liver impairment are also given and again an instruction to consult the SPC. Furthermore, during the case study presented there are statements, given both verbally and on the slide, warning that the concomitant use of cannabidiol and valproate can cause side effects, including liver enzyme elevations, diarrhoea and decreased appetite and giving guidance on the increased liver enzyme monitoring requirement.

'Information, claims and comparisons must be accurate, balanced, fair, objective and unambiguous and must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. They must not mislead either directly or by implication, by distortion, exaggeration or undue emphasis. Material must be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine.'

The following statement was clearly presented at the start of the presentation: 'Medicines must always be prescribed in line with their SmPC, which contains full prescribing information, including monitoring, warnings/precautions and adverse event profiles.'

Also, visible in the bottom right-hand corner of the page throughout the presentation is the following statement: cannabidiol (cannabidiol) Prescribing Information [PI] for Great Britain is available at the end of the video. The PI was shown in full at the end of the video.

The presentation showed the need for monitoring transaminases. There was a clear statement that prior to starting treatment, serum transaminases and total bilirubin should be obtained, and referred to later in the patient case study in the context of potential interaction with valproate. The message to monitor transaminases was clearly described in the presentation.

As demonstrated above, in both presentations Jazz believes it has complied with the requirements of clause 6.1. The complainant alleges a breach of Clause 5.1 and Jazz

also refutes this allegation. Jazz has maintained high standards throughout the engagement. Jazz takes patient safety very seriously. Further Jazz provided a clear briefing to both speakers in advance of the recording specifically addressing the need to provide factual, accurate and balanced information.

All materials for these presentations were certified by a GPhC registered Pharmacist Signatory. In both presentations, the content was reviewed and certified and deemed to be accurate, fair and balanced. Each presentation had different objectives and served the balanced criteria within their objectives. Patient safety has not been compromised in either of the presentations. In fact, patient safety was a key consideration both in the briefing of our speakers and the review and approval of the final presentations. This is clearly demonstrated because despite the fact that the patient's dosing of valproate had been reduced in the second presentation, the presentation still clearly highlights the key safety risks when using Epidyolex: 'Epidyolex interactions:1 Concomitant use of Epidyolex and VPA increases the incidence of transaminase enzyme elevations, diarrhoea and decreased appetite.' Therefore, we refute the breach of Clause 5.1.

The complainant also alleges a breach of Clause 2 with regard to the allegations. Clause 2 is a sign of particular censure and is reserved for such circumstances, we believe that these presentations have been prepared and presented in line with the requirements of clauses 6.1 and 5.1 and therefore we refute a breach of Clause 2.

At Jazz, we take our commitment to upholding industry standards through our activities and interactions seriously, and I hope that the information provided will lead to resolution of the allegations made in this case."

PANEL RULING

The complaint concerned two online presentations; titled:

1. Understanding the Pharmacology of Epidyolex (cannabidiol).
2. Optimise the Clinical Use of Epidyolex (cannabidiol).

Epidyolex was indicated for use as an adjunctive therapy of seizures associated with Lennox-Gastaut Syndrome (LGS), Dravet Syndrome (DS) or tuberous sclerosis complex (TSC). Jazz submitted that they had created two educational, promotional presentations for health professionals, particularly physicians, nurses and pharmacists with an interest in neuroscience/epilepsy. The intention was to provide medical education and help improve the specialist management of specific developmental and epileptic encephalopathies. Jazz submitted that the speakers in each video presentation were chosen due to their expertise within the therapeutic area.

Presentation 1 – Understanding the Pharmacology of Epidyolex (cannabidiol)

The complainant alleged that the presentation omitted important information regarding the discontinuation and/or reduction of valproate and Epidyolex due to hepatic transaminases elevation when there is concomitant use of Epidyolex and valproate, as reflected in the Epidyolex Summary of Product Characteristics (SPC). It was also alleged that the speaker was not briefed appropriately on the use of Epidyolex and valproate concomitantly.

This presentation was delivered by a pharmacologist. The Panel noted Jazz's submission that the main objective was to educate health professionals on the pharmacology of the

endocannabinoid system and the mechanism of action of cannabidiol in treating seizures associated with LGS and DS.

The complaint referred to the data presented in the presentation at 13 minutes 25 seconds, where the speaker presented a slide titled 'Drug interactions' which they introduced as a summary slide, although it was not headed as such. The slide in question was divided into two sections:

1. The first section was headed 'Current state of knowledge-pharmacokinetic interactions between CBD and other ASMs' and also included four bulleted medicines or classes of medicine, which the speaker used to summarise the drug interaction data presented on the preceding slides. In discussing this section, the speaker referred to the need to watch out for changes in tolerability, adverse events and referred to dose adjustment, albeit the first section of the slide was silent on this point. However, the Panel did note that the first section of the slide concluded with 'Caution: list is not exhaustive: potential interaction with ASMs and other drugs possible (see Epidyolex SPC)'.

2. The second section of the slide was headed 'Concomitant use of CBD and valproate' above four bullet points which read:
   - 'Increased incidence for transaminase elevations
   - No evidence for impact on drug and metabolite exposure
   - Mechanism remains unknown
   - Increased incidence of diarrhoea and events of decreased appetite'.

The speaker speculated that the increase in transaminase elevations might be related to changes to the free unbound concentrations of the drugs, but made clear that the reason was unknown. Neither this section of the slide, nor the speaker, referred to dose adjustment or discontinuation in relation to Epidyolex and valproate.

The Panel noted that the SPC stated:

- Section 4.3 (Contraindications) - Epidyolex was contraindicated in patients with transaminase elevations greater than three times the upper limit of normal and bilirubin greater than two times the upper limit of normal.
- Section 4.4 (Special warnings and precautions for use, Hepatocellular injury) - referred to elevations of liver transaminases and that in clinical trials the majority of liver transaminases occurred in patients taking concomitant valproate, discontinuation and/or dose adjustment of valproate should be considered if transaminase elevations occur. Intensive monitoring was required with concomitant valproate if baseline transaminase levels were elevated.
- Section 4.5 (Interaction with other medicinal products and other forms of interaction, under the heading "Valproate") - if clinically significant increases of transaminases occur, cannabidiol and/or concomitant valproate should be reduced or discontinued in all patients.
- Section 4.8 (Undesirable effects) - in cannabidiol-treated patients receiving doses of 10, 20, and 25 mg/kg/day, the incidence of ALT elevations greater than 3 times the upper limit of normal was 23% in patients taking both concomitant valproate and clobazam,

19% in patients taking concomitant valproate (without clobazam), 3% in patients taking concomitant clobazam (without valproate), and 3% in patients taking neither drug.

The Panel bore in mind that the presentation at issue was about pharmacology but nonetheless noted overall the slides referred to some clinical matters. For example:

- Slide 11 (titled 'Pharmacokinetics: CBD metabolism'), beneath a heading 'Potential effects of other drugs on CBD?' stated that 'Dose adjustment may be necessary' and 'Only some of the investigated interactions seem to be of clinical relevance'.
- Slide 12 (titled 'Pharmacokinetic drug interactions: CBD and clobazam') referred to a 'Clinically relevant interaction with impact on tolerability'.
- Slide 13 (titled 'CBD pharmacokinetic drug interaction') stated in bold font that:
    - 'Patients should be closely monitored for adverse drug reactions' in relation to CBD and stiripentol, the speaker stating that one should watch out for these types of interactions and referred to it being necessary in some cases to adjust the dosing.
    - 'When initiating everolimus in patients taking CBD, caution should be taken and monitoring of the mTOR/calcineurin inhibitor blood levels should be considered' and the speaker referred to the importance of monitoring and that it might be necessary to adjust the dosing.

Whilst acknowledging the comments of the speaker that accompanied the slides, in the Panel's view, the slides should be capable of standing alone in relation to the requirements of the Code. Whether, and the extent to which, a pharmacology presentation should refer to or signpost clinical matters must be decided on a case-by-case basis.

Clause 6.1

The Panel noted that Clause 6.1 required, amongst other things, information to be balanced, fair, objective and unambiguous, based on an up-to-date evaluation of all the available evidence and not misleading. Given the risks associated with the concomitant use of valproate, the Panel was concerned that this combination was not treated similarly to other combinations within the presentation where preceding slides made limited references to clinical matters such as dose adjustment and monitoring. Noting the contraindication, the risks of hepatocellular injury and Sections 4.4 and 4.5 of the SPC, the Panel considered that the absence from the slides of any reference to dose adjustment and/or discontinuation in relation to concomitant valproate and Epidyolex was misleading. That absence implied that there was no need to be concerned about such matters compared with the other combinations within the presentation and that was not so. The Panel considered that the slide in question was therefore misleading and ruled a **breach of Clause 6.1** accordingly.

Speaker in Presentation 1 had not been briefed appropriately - Clause 5.1

The complaint included an allegation that the speaker had not been briefed appropriately to discuss such important safety information around the concomitant usage of Epidyolex with valproate and discontinuation and/or reduction of Epidyolex relevant to elevation in hepatic transaminases.

The Panel reviewed the briefing document produced by Jazz and noted that in relation to the slide at issue it stated: 'Briefly summarise the key messages of the previous slides' and 'Highlight the potential effects on liver enzymes and adverse event occurrence when CBD and valproate are used concomitantly.'

The Panel considered it would have been helpful if the briefing document referred to the relevant requirements of the Code and the importance of treating the combination treatments equally. The briefing document provided the pharmacologist with very general instructions and the Panel did not consider that to be sufficient in relation to signposting clinical matters, given it might have been beyond the speaker's expertise. Given that the slides overall included references to monitoring and dose adjustment, the Panel considered that further briefing information ought to have been provided to the pharmacologist, such that the references in the slides were consistent across the combinations and complied with the Code.

In relation to the slide in question, on balance the Panel considered that, in addition to briefing about adverse events, further detail ought to have been provided to the speaker in relation to dose adjustment and/or discontinuation i.e. how adverse events should be managed. The Panel concluded that Jazz had not evidenced that the speaker had been briefed sufficiently, and the Panel therefore ruled a **breach of Clause 5.1**.

Presentation 2 – Case Study Video 'Optimise the clinical use of Epidyolex'

The complainant alleged that this presentation at 18-28 seconds did not explicitly state that Epidyolex was contraindicated in patients with transaminase elevations greater than three times the upper limit of normal (ULN) and bilirubin greater than 2 times the ULN as in the SPC. The complainant considered that it was important that health professionals knew precisely when Epidyolex was contraindicated in hepatic dysfunction, especially as the video content discussed hepatic monitoring. The complainant also alleged that at 4 minutes, the presentation omitted important information around discontinuation and/or reduction of valproate and Epidyolex due to increased elevation of hepatic transaminases when there is concomitant use. The complainant further alleged that the speaker was not briefed to discuss such contraindications.

This presentation video was presented by another speaker who discussed a patient case study which included the monitoring needed when patients on cannabidiol therapy were also taking anti-seizure medications. The Panel noted Jazz's response that the objective of the presentation was to discuss practical ways in which cannabidiol could be tailored to each patient as well as exploring clinical management of adverse events and drug-drug interactions in an adult patient with late-onset LGS.

The Panel noted the content of Sections 4.3, 4.4, 4.5 and 4.8 of the SPC as set out above.

Slides at 18-28 seconds – Clause 6.1

The Panel considered the presentation at 18-28 seconds which covered two slides. The first slide was titled 'GB indication and dosing for Epidyolex (cannabidiol).' The slide detailed dosing and titration information for Epidyolex in combination with clobazam as adjunctive therapy in seizures associated with LGS or DS, or as adjunctive therapy of seizures associated with TSC. Small print, beneath the dosing table:

- advised the reader to consider the risks/benefits of and adherence to the full monitoring schedule found in section 4.4 of the SPC if the dose was increased above 10mg/kg/day,
- referred to both routine and intensified monitoring of transaminase and bilirubin levels, and

- stated that Epidyolex can cause dose related elevations of liver transaminases.

The second slide, shown at 24 seconds, was also titled 'GB indication and dosing for Epidyolex (cannabidiol)' but specifically addressed dose adjustments in patients with hepatic impairment. Small print beneath the dosing table included:

- reference to hepatic impairment and caution should be used in patients with moderate/severe hepatic impairment and
- a lower starting dose was recommended in patients with moderate/severe hepatic impairment.

On balance, the Panel considered that whilst the two slides referred to the importance of monitoring given the potential incidence of high transaminase levels and bilirubin above the upper limit of normal as set out in the SPC, the contraindication in Section 4.3 of the SPC was particularly relevant and ought to have been included on the slides in question, as alleged. The omission was such that the slides were misleading and the Panel therefore ruled a **breach of Clause 6.1** in relation to these slides.

Case study slide at 4 minutes – Clause 6.1

In relation to the allegation regarding the case study slide omitting information around discontinuation and/or reduction of valproate and Epidyolex due to increased elevation of hepatic transaminases when there is concomitant use of Epidyolex and valproate, the Panel considered the case study section of the presentation at 4 minutes. The slide was titled, "Reduction of concomitant medication with Epidyolex initiation." The content of the slide indicated that the 'reduction' referred to in the slide heading did not refer to dose reduction as a result of elevated transaminase levels but rather dose reduction of valproate at the point of Epidyloex initiation. The slide included a highlighted box beside the patient case study headed with a warning sign which stated that concomitant use of Epidyolex and valproate increased (amongst other things) the incidence of transaminase levels; and set out the monitoring schedule in such patients of transaminase and bilirubin levels.

Whilst the Panel accepted that information about raised transaminase levels with the Epidyolex and valproate combination was an integral part of the slide, and was within a clear warning section, it considered that the warning section ought to have also referred to dose reduction/discontinuation, as alleged. This was particularly so given that, despite the contraindication at Section 4.3 of the SPC, the slide stated (under a heading 'Safety considerations') that, other than drowsiness, there were 'No safety concerns'.

The Panel noted Jazz's submission that there was no suggestion that the patient in the case study had elevated liver enzymes at any stage of treatment and therefore the contraindication was irrelevant. However, the Panel concluded that, as with the monitoring information, Jazz should have provided the information as part of the slide without implying that the patient in this case study had experienced such matters. The Panel considered that the omission from the warning box was misleading and ruled a **breach of Clause 6.1**.

Speaker in Presentation 2 had not been briefed appropriately – Clause 5.1

The complainant alleged that the speaker had not been sufficiently briefed in relation to the case study section of the presentation. Upon reviewing the video, it was apparent that the speaker had not referenced the highlighted box containing the warnings about dose alteration or

termination of treatment. In considering the briefing document, the notes for this slide provided the following:

- "Summary of concomitant medications at initiation and subsequent dose reductions
- Overview of Epidyolex dosage and titration schedule
- Adverse events experienced by the patient and how they were rectified"

The Panel was concerned that the speaker had not sufficiently highlighted the warnings contained in the box on the slide which were relevant, considering the patient in the case study was using valproate concomitantly with Epidyolex. The speaker was not given any briefing or direction about the information in the warning box. Given the lack of detail provided in the briefing document and the importance of highlighting this key information, the Panel concluded that the speaker had not been briefed sufficiently, and a **breach of Clause 5.1** was ruled.

Clause 9.1

Although the case preparation manager had also cited Clause 9.1 in this case, the Panel considered that the rulings above and below adequately covered this matter. The complainant had alleged that the speakers had not been sufficiently briefed but had not further alleged that either speaker needed to be fully conversant with the Code and/or relevant laws and regulations and further had not satisfied their burden of proof in this regard. The Panel therefore ruled **no breach of Clause 9.1**.

Clause 5.1 and Clause 2

Noting its rulings of breaches of the Code above in relation to both presentations, the Panel considered that Jazz had failed to maintain high standards in this matter. A **breach of Clause 5.1** was ruled.

The Panel considered that patient safety was of the utmost importance, particularly in the context of this case where there were risks related to hepatocellular injury. Examples of activities likely to lead to a breach of Clause 2 included prejudicing patient safety. The Panel considered that the information relating to the concomitant use of Epidyolex and valproate, was important given the risk to patients on this treatment and should have been included/highlighted in the presentations. Jazz had therefore brought discredit upon and reduced confidence in the pharmaceutical industry and a **breach of Clause 2** was ruled.

Complaint received **1 June 2024**

Case completed **19 May 2025**