CASE AUTH/3446/12/20

COMPLAINANT v JAZZ PHARMACEUTICALS

Sunosi website

An anonymous non-contactable complainant who described him/herself as a health professional, complained about misleading information on the Sunosi (solriamfetol) website from Jazz Pharmaceuticals UK. Sunosi was indicated to improve wakefulness and reduce excessive daytime sleepiness in certain adult patients with narcolepsy or obstructive sleep apnoea.

The complainant alleged that pages on the website did not include the mandatory disclaimers about leaving to go to an external website. The complainant referred to two pages: one with a hyperlink in relation to reporting adverse events to the Medicines and Healthcare products Regulatory Agency's (MHRA's) website and another hyperlink from one of the references listed.

The complainant alleged that there was no prescribing information provided on the mobile phone version of the pages for health professionals.

The complainant alleged that a claim, 'Sunosi is a convenient, ONCE-DAILY DOSE in a single tablet' which stated underneath that patients could be titrated up to their most effective, tolerated dose (up to a maximum daily dose of 150mg)* was misleading and not a capable standalone claim. The complainant noted that the claim did not mention the important qualifying information and alleged an increased risk to patient safety.

The complainant alleged that, overall, the websites on desktop and mobile devices were missing critical information and had misleading information which could impact on patient safety. Breaches of the Code were alleged including Clause 2.

The detailed response from Jazz is given below.

In the Panel's view, it was sufficiently clear that the hyperlink mhra.gov.uk/yellowcard would take the user from the Jazz website to an external MHRA website; particularly as the hyperlink was within a highlighted box titled 'Adverse events reporting'. The Panel therefore ruled no breach of the Code in this regard.

In relation to the narcolepsy.org.uk hyperlink, the Panel noted that this link appeared within the clearly labelled references section as part of reference 6 and included 'Narcolepsy UK. Narcolepsy Charter 2019. Available at: www.narcolepsy.org.uk/resources/narcolepsy-charter'. In the Panel's view, a user of the site accessing the link would be clear that he/she was being directed to a narcolepsy.org.uk webpage and that this was not part of the Jazz website. The Panel therefore ruled no breach of the Code in this regard.

With regard to accessing the prescribing information from a mobile phone, the Panel noted Jazz's submission that prescribing information was available and could be found

within the hamburger menu icon lines at the top right of the landing page, and also by clicking on the text of the words 'Prescribing Information' towards the bottom of the page. The Panel had no evidence before it that the prescribing information was not available on the website in question when accessed from a mobile phone and no breach of the Code was ruled in that regard.

The Panel noted Jazz's submission that during its investigation it discovered that the technology used did not keep the prescribing information tab as a 'sticky' static tab on a mobile phone, resulting in the 'Prescribing Information' tab to become 'contracted' into the hamburger menu icon on the top right side of the page. The Panel further noted Jazz's submission that the prescribing information was marked as such towards the end of the webpage, however, that did not meet the requirements of 'a clear, prominent statement' due to its position. The Panel therefore ruled a breach of the Code as acknowledged by Jazz.

In relation to the allegation that the website could have impacted patient safety, the Panel noted its comments and rulings above. The Panel considered that Jazz should have checked the final form of the material to see how the website would appear on a mobile device and should have spotted that the prescribing information tab had become contracted into a hamburger menu icon. High standards had not been maintained in that regard and a breach of the Code was ruled. The Panel noted Jazz's submission that the prescribing information was available when the website in question was accessed from a mobile phone: from the hamburger menu icon on the top right side and at the end of the webpage. The Panel therefore ruled no breach of Clause 2.

The Panel noted the complainant's allegation that the claim 'Patients can be titrated up to their most effective, tolerated dose (up to a maximum daily dose of 150 mg)*' beneath the heading 'Sunosi is a convenient, once-daily dose in a single tablet' within the 'Introducing Sunosi' webpage was misleading and not capable of standing alone as important qualifying safety information from the summary of product characteristics (SPC) was omitted.

The Panel considered that it was not clear what the asterisk in the claim in question was referring the reader to.

It appeared to the Panel that the dosing section in question was immediately followed by a reference to consulting the SPC in relation to patients with renal impairment and a section titled 'Cardiovascular monitoring and assessment' with additional information.

The Panel considered the immediate and overall impression to a busy health professional. Context and layout were also important in this regard. Sunosi was a once daily treatment in a single tablet and the maximum daily dose was 150mg. Notwithstanding that it was not clear what the asterisk within the claim in question referred to, in the Panel's view, information in relation to cardiovascular monitoring and assessment as described by the complainant was available in the same section of the website. The Panel queried whether the order and positioning of the information might cause confusion in that the contraindications for use in certain cardiovascular conditions was likely to be read before the information regarding the need to assess blood pressure and heart rate before commencing treatment and to monitor blood pressure and heart rate periodically during treatment and after dose increases. It might

have been clearer to put that information together. However, on balance, the Panel did not consider that the claim 'Patients can be titrated up to their most effective, tolerated dose (up to a maximum daily dose of 150 mg)*' was misleading or incapable of substantiation as alleged. Thus, the Panel ruled no breaches of the Code including no breach of Clause 2.

An anonymous non-contactable complainant who described him/herself as a health professional, complained about misleading information on the Sunosi (solriamfetol) website from Jazz Pharmaceuticals UK. Sunosi was indicated to improve wakefulness and reduce excessive daytime sleepiness in adult patients with narcolepsy (with or without cataplexy) and to improve wakefulness and reduce excessive daytime sleepiness (EDS) in adult patients with obstructive sleep apnoea (OSA) whose EDS had not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP).

COMPLAINT

The complainant alleged that he/she had been provided a link from Jazz medical information to view information on Sunosi and noted that on the bottom of the page which introduced Sunosi (ref UK-SOL-2000055 November 2020), there was adverse event reporting wording which stated 'Adverse events should be reported. Reporting forms and information can be found at mhra.gov.uk/yellowcard'. The complainant stated that when he/she clicked on that hyperlink to the Medicines and Healthcare products Regulatory Agency's (MHRA's) website, the mandatory disclaimer about leaving to go to an external website did not appear. That disclaimer pop-up was also not present on the identical page on the mobile phone version when a reader clicked on the MHRA website hyperlink (ref UK-SOL-2000050, November 2020). The complainant alleged breaches of Clause 28.6 on both the mobile version and the web version. The complainant stated that the website should be viewed on a mobile and desktop view for transparency of the missing disclaimer pop up. That was also the case on a webpage detailing Sunosi in narcolepsy (ref UK-SOL-2000057 November 2020) (link provided); reference 6 provided the reader with a link to the Narcolepsy Charter 2019, accessed August 2020, from Narcolepsy UK (link provided). If a reader clicked on the narcolepsy.org.uk hyperlink as presented on the page, no disclaimer about leaving to go to an external site came up; the complainant alleged a breach of Clause 28.6 twice on yet another page.

The complainant stated that on the desktop version of the website, there was a prescribing information tab at the top right on all of the pages for health professionals. However, there was no prescribing information provided on the mobile phone version of the pages for health professionals. The complainant reiterated that the website should be viewed on the health professional section of any mobile phone and alleged a breach of Clause 4.6 which was clear that in promotional material included on the Internet, there must be a clear, prominent statement as to where the prescribing information could be found. Hence, this was missing on all mobile phone version pages which accounted for a breach of Clause 4.6 and Clause 4.1 on several occasions which was a huge concern as promotional material for Sunosi required the addition of a black triangle and as a health professional, prescribing information access was always needed especially for a new product that required a black triangle.

The complainant stated that his/her final concern was on the dosage page (ref UK-SOL-2000055 November 2020) (link provided) and the claim, 'Sunosi is a convenient, ONCE-DAILY DOSE in a single tablet'. Underneath that claim it was stated that patients could be titrated up to their most effective, tolerated dose (up to a maximum daily dose of 150mg)*. That was

misleading and not a capable standalone claim as the Sunosi summary of product characteristics (SPC) stated that blood pressure and heart rate should be assessed before initiating treatment and should be monitored periodically during treatment, especially after increasing the dose. Further, pre-existing hypertension should be controlled before initiating treatment and caution should be exercised in treating patients at higher risk of major adverse cardiovascular events, particularly patients with pre-existing hypertension, known cardiovascular or cerebrovascular disease and elderly patients. The complainant noted that the claim on the webpage simply stated that a patient could be titrated without mentioning the important qualifying information; the complainant alleged an increased risk to patient safety. The complainant noted the use of an asterisk which confirmed that Jazz wanted to hide that information which was of concern as material for Sunosi required the addition of a black triangle. Claims must be able to standalone and not qualified by an asterisk. The complainant alleged breaches of Clauses 7.2 and 7.4, and 9.1.

The complainant alleged that, overall, the above confirmed that the website on desktop and mobile was missing some critical information and had misleading information which could impact on patient safety which was not in accordance with and breached Clause 9.1 and Clause 2

When writing to Jazz, the Authority asked it to consider the requirements of Clauses 2, 4.1, 4.6, 7.2, 7.4, 9.1 and 28.6 of the Code.

RESPONSE

Jazz stated that it took its responsibilities to Code compliance and patient safety seriously. On receipt of the complaint and since an allegation relating to patient safety had been raised, the Sunosi.co.uk website had been taken down pending a detailed investigation. The website was withdrawn from public access on 24 December 2020.

Jazz explained that the website was launched on 1 September 2020 and there was a prescribing information update in October which resulted in recertification in November 2020. The equivalent content had been subject to scrutiny and approval by the MHRA advertising pre-vetting team, in a pdf detail aid version. Jazz stated that it had set out to provide comprehensive information about the clinical trial evidence, the safety and prescribing requirements of the product in the promotional launch material, in order to ensure that prescribers were fully informed when making their decision. From the launch of the website, the prescribing information was available as single-click, at a tab of its own in the header bar of the website (the header and tabs remained in place whilst continuous scrolling on the page content). The prescribing information could also be accessed by a single-click towards the bottom of the home page content. In addition, the website contained a link to the SPC.

Access to the website was via routine online searching. A printed mailer, sent to consultant neurologists, consultant respiratory physicians and hospital chief pharmacists in September 2020, included the website link in the printed text. Digital promotion which included the website link was available via Doctors.net.uk resources; this activity was stopped on receipt of the complaint. Jazz representatives had never had hard copy or digital materials containing the link to the website.

The website pages were certified.

The pages referred to by the complainant represented three separate pages of website content: UK-SOL-2000050 was the website landing page content; UK-SOL-2000055 was the Sunosi introduction page and UK-SOL-2000057 was the file to show open reference list. The unique reference numbers referred to individual website pages, as opposed to a desktop and laptop version. There was only one website created.

Jazz noted the complainant's submission that the link to the website was provided by medical information but stated the link was not and never had been made available through its medical information service. There was no link to the website available via the sole Jazz Pharmaceuticals group corporate website (https://www.jazzpharma.com/) and colleagues in medical information had confirmed that they had not received a request to provide the link.

Jazz noted that the complainant was concerned that the link to the MHRA Yellow Card Adverse Event reporting site found at the bottom of the Sunosi introduction page did not result in a 'mandatory disclaimer about leaving to external website'. That observation was repeated when the complainant used the MHRA Yellow Card hyperlink present on the landing page. Jazz noted that Clause 28.6 did not require a 'mandatory disclaimer', rather that 'It should be made clear when a user is leaving any of the company's sites…'. Further, Clause 4.9, which mandated adverse event reporting from promotional material to the MHRA, allowed for use of a statement in which the web address linked directly to the MHRA Yellow Card website. There was no requirement described in the Code to provide further information about leaving the website in relation to linking to the MHRA Yellow Card website. As described by the complainant, the adverse event reporting wording was clearly provided and the link to the MHRA Yellow Card reporting was clearly hyperlinked and present, as required by Clause 4.9. As such, by the complainant's own description, it appeared that he/she was clear he/she was leaving the website to reach the MHRA Yellow Card Reporting website. Jazz concluded that there was no breach of Clause 28.6.

Jazz noted that the complainant was further concerned that a link to Narcolepsy UK from the reference section of the website did not result in a disclaimer message about leaving the website to go to an external website. That was described as being observed both when the website had been viewed from a desktop and from a mobile. Jazz acknowledged that there was a link provided on the website to Narcolepsy UK, but that was provided from within the references list section only. Clause 28.6 required that "… it is made clear when a user is leaving any part of the company's sites…'. The hyperlink in question was within a reference list at the end of the webpage, and in full transparency was clearly identifiable as an external resource from Narcolepsy UK in the text description, the presence of the blue and underlined text and the date it was accessed, presented as follows:

> "Narcolepsy UK. Narcolepsy Charter 2019. Available at: https://www.narcolepsy.org.uk/resources/narcolepsy-charter. Accessed August 2020".

That hyperlink was provided as a factual reference resource and to substantiate content used on the website. Jazz considered that the context in which the hyperlink was provided, as described above, gave full transparency and clarity to readers that it was a reference to an external website, in order to access the resource. The company therefore denied a breach of Clause 28.6.

Jazz noted that the complainant stated that there was no prescribing information provided on the website when he/she viewed it on a mobile phone and that the prescribing information was

available on a tab at the top of all of the pages when viewed on a desktop. Following thorough investigation, Jazz stated that the prescribing information was available on the website, as described by the complainant and was also available on the website when it was accessed via a mobile phone. The prescribing information could be found within the tabs (hamburger menu icon lines) at the top right of the landing page, and also by clicking on 'Prescribing Information' towards the bottom of the page, when viewed on a mobile phone. Jazz stated that as the prescribing information was present, there was no breach of Clause 4.1.

Jazz noted that the complainant had stated that a clear, prominent statement on where the prescribing information could be found 'was missing on all mobile phone version pages' when the website was viewed on a mobile phone; the complainant had indicated that the prescribing information could be easily found at the top of all pages when the content was viewed on a desktop. As described above, and as this was the same website, the prescribing information was present when the content was viewed on a mobile. However, Jazz stated that it had identified that the design technology used within the website development did not keep the prescribing information tab as 'sticky' which resulted in the clearly labelled 'Prescribing Information' tab being 'contracted' into the hamburger menu icon on the top right side of the page. The prescribing information was present and was marked clearly as such towards the end of the webpage, however Jazz acknowledged that that did not meet the requirements of 'a clear, prominent statement' due to its position on the webpage and so was in breach of Clause 4.6.

Jazz noted the complainant's concern about the missing prescribing information from the mobile phone version pages given that promotional material for Sunosi required the addition of a black triangle. As noted above, the prescribing information was not missing and was present with the 'hamburger menu icon lines' at the top of the page. The prescribing information was also available via a link towards the end of the page. In addition, within the website content there was a link to the SPC; that provided information relevant to a prescribing decision and was more comprehensive than prescribing information, from which the prescriber was encouraged to always consult the SPC for more information. Therefore, Jazz considered that readers would readily be able to access all relevant prescribing information sources.

Jazz noted that the complainant had alleged that the dosing page, which included the claim *'*Patients can be titrated up to their most effective, tolerated dose (up to a maximum daily dose of 150mg *' was misleading and not capable of standing alone. Jazz submitted that the claim was accurate, correct and clearly presented in the context of the information on the page. The claim did not advise or recommend that all patients were titrated up to 150mg, but rather spoke to personalisation of the titration ie 'up to **their** most effective*..'*. The claim was on a page that focussed on dosing and was not, in that context, presented as standalone information; it was within the flow of a page that presented comprehensive and clear information about dosing, titration (in two different indications), blood pressure and cardiovascular monitoring requirements and referred to further information being available for dosing in renal impairment. Jazz noted that the complainant further alleged that the use of the asterisk confirmed that Jazz wanted to hide the information. Jazz refuted that allegation, as the blood pressure, heart rate and cardiovascular monitoring recommendations were present three times on the page; the asterisk was used to draw the reader's attention to the related information.

Jazz considered that the complainant's assertion that the 'qualifying' information was not present was incorrect. The wording on the page in question and the visual representation of the dosing guidance and additional recommendations were an accurate reflection of the materials

approved by the MHRA during the pre-vetting process. As the information in the claim, and the overall page content, was provided with substantiation and in an accurate and comprehensive way, such that the reader had sufficiently complete information, Jazz submitted that there had been no breaches of Clauses 7.2 or 7.4.

Jazz stated that it always took great care to accurately present comprehensive information relating to product efficacy and safety and it considered that that was reflected in response above, and also in its decision to withdraw the material immediately and allow time to conduct the detailed review. Therefore, the complainant's assertion that, overall, the website 'could impact on patient safety' was without basis since safety information was sufficiently complete and high standards were maintained throughout. Jazz refuted the alleged breaches of Clauses 9.1 and 2.

Jazz stated that it took its responsibilities seriously and was fully committed to operating in an ethical and compliant manner. In addition to its commitment to the Code, the company also ensured high standards through its internal Code of Conduct, training plans and standard operating procedures. Jazz regretted the omission of a prominent statement to guide towards the prescribing information on a mobile device; that was a technical error which would be corrected in all future versions.

PANEL RULING

The Panel noted that Clause 28.6 stated that it should be made clear when a user was leaving any of the company's sites, or sites sponsored by the company, or was being directed to a site which was not that of the company. The Panel further noted that the Code did not stipulate how, exactly, this should be done just that it should be made clear. In the Panel's view, it was sufficiently clear that the hyperlink mhra.gov.uk/yellowcard would take the user from the Jazz website to an external MHRA website; particularly as the hyperlink was within a highlighted box titled 'Adverse events reporting'. The Panel therefore ruled no breach of Clause 28.6 in this regard.

In relation to the narcolepsy.org.uk hyperlink, the Panel noted that this link appeared within the clearly labelled references section as part of reference 6 which stated 'Narcolepsy UK. Narcolepsy Charter 2019. Available at: www.narcolepsy.org.uk/resources/narcolepsy-charter. Accessed August 2020'. In the Panel's view, a user of the site accessing a link from the references section which had a narcolepsy.org.uk URL would be clear that he/she was being directed to a narcolepsy.org.uk webpage and that this was not part of the Jazz website. The Panel therefore ruled no breach of Clause 28.6 in this regard.

The Panel noted the complainant's allegation that when the sunosi.co.uk website was accessed from a desktop, there was a prescribing information tab at the top right of all the healthcare professional pages, but when accessed from a mobile phone there was no prescribing information provided. The Panel noted Jazz's submission that prescribing information was available on the website when it was accessed via a mobile phone and could be found within the hamburger menu icon lines at the top right of the landing page, and also by clicking on the text of the words 'Prescribing Information' towards the bottom of the page, when viewed on a mobile phone. The Panel had no evidence before it that the prescribing information was not available on the website in question when accessed from a mobile phone and no breach of Clause 4.1 was ruled in that regard.

The Panel noted Jazz's submission that during its investigation it discovered that the technology used within the website development did not keep the prescribing information tab as a 'sticky' static tab on a mobile phone, resulting in the 'Prescribing Information' tab to become 'contracted' into the hamburger menu icon on the top right side of the page. The Panel further noted Jazz's submission that the prescribing information was marked as such towards the end of the webpage, however, that did not meet the requirements of 'a clear, prominent statement' due to its position. The Panel therefore ruled a breach of Clause 4.6 as acknowledged by Jazz.

In relation to the allegation that the website could have impacted patient safety, the Panel noted its comments and rulings above. The Panel considered that Jazz should have checked the final form of the material to see how the website would appear on a mobile device and should have spotted that the prescribing information tab had become contracted into a hamburger menu icon. High standards had not been maintained in that regard and a breach of Clause 9.1 was ruled.

Clause 2 was a sign of particular censure and reserved for such use. The Panel noted Jazz's submission that the prescribing information was available when the website in question was accessed from a mobile phone: from the hamburger menu icon on the top right side and at the end of the webpage. The Panel therefore ruled no breach of Clause 2.

The Panel noted the complainant's allegation that the claim 'Patients can be titrated up to their most effective, tolerated dose (up to a maximum daily dose of 150 mg)*' beneath the heading 'Sunosi is a convenient, once-daily dose in a single tablet' within the 'Introducing Sunosi' webpage was misleading and not capable of standing alone as important qualifying safety information from the SPC was omitted.

The Panel did not know how exactly the webpage in question appeared to the complainant. The material before the Panel included a PDF created by the case preparation manager of the 'Introducing Sunosi' webpage which was accessed from the link provided by the complainant, the job bag certificate and a photograph of that section of the website provided by Jazz (ref UK-SOL-2000055).

The 'Introducing Sunosi' webpage referred to, *inter alia*, Sunosi's indications, mode of action, safety profile, special warnings and precautions which included a statement that treatment with Sunosi increased blood pressure and heart rate in a dose dependent fashion and stated that use in patients with unstable cardiovascular disease, serious heart arrhythmias and other serious heart problems was contraindicated. The section then referred to other contraindications and pharmacodynamic drug interactions. This was followed by the claim at issue.

The Panel considered that it was not clear what the asterisk in the claim in question was referring the reader to. Below the claim in question, the page was divided into two, with one side referring to the indication in patients with obstructive sleep aponea and the other patients with narcolepsy. Further down there were two boxes: a purple box related to dosing for patients with obstructive sleep apnoea and a green box related to dosing for patients with narcolepsy. Both these boxes also contained asterisks with different footnotes. Therefore, it appeared that the asterisk in the claim in question 'Patients can be titrated up to their most effective, tolerated dose (up to a maximum daily dose of 150 mg)*' did not have a corresponding explanatory note.

It appeared to the Panel that the dosing section in question was immediately followed by a reference to consulting the SPC in relation to patients with renal impairment and a section titled 'Cardiovascular monitoring and assessment' which stated:

- 'Blood pressure and heart rate should be assessed before initiating treatment with Sunosi and should be monitored periodically during treatment, especially after increasing the dose.
- Pre-existing hypertension should be controlled before initiating treatment with Sunosi and caution should be exercised in treating patients at higher risk of MACE [major adverse cardiovascular event], particularly patients with pre-existing hypertension, patients with known cardiovascular or cerebrovascular disease and elderly patients (see section 4.4 of SmPC).
- Use in patients with unstable cardiovascular disease, serious heart arrhythmias and other serious heart problems is contraindicated (see section 4.3 of SmPC).
- The need for continued treatment with Sunosi should be periodically assessed. If a patient experiences increases in blood pressure or heart rate that cannot be managed with dose reduction of Sunosi or other appropriate medical intervention, discontinuation of Sunosi should be considered. Caution should be exercised when using other medicinal products that increase blood pressure and heart rate (see section 4.5 of SmPC).
- Long-term use: The need for continued treatment and the appropriate dose should be periodically assessed during extended treatment in patients prescribed Sunosi.'

The Panel considered the immediate and overall impression to a busy health professional. Context and layout were also important in this regard. Sunosi was a once daily treatment in a single tablet and the maximum daily dose was 150mg. Notwithstanding that it was not clear what the asterisk within the claim in question referred to, in the Panel's view, information in relation to cardiovascular monitoring and assessment as described by the complainant was available in the same section of the website. The Panel queried whether the order and positioning of the information might cause confusion in that the contraindications for use in certain cardiovascular conditions was likely to be read before the information regarding the need to assess blood pressure and heart rate before commencing treatment and to monitor blood pressure and heart rate periodically during treatment and after dose increases. It might have been clearer to put that information together. However, on balance, the Panel did not consider that the claim 'Patients can be titrated up to their most effective, tolerated dose (up to a maximum daily dose of 150 mg)*' was misleading or incapable of substantiation as alleged. Thus the Panel ruled no breach of Clauses 7.2 and 7.4. The Panel consequently ruled no breach of Clauses 2 and 9.1 in this regard.

Complaint received **21 December 2020**

Case completed **15 June 2021**