CASE/0285/09/24 ***NO BREACH OF THE CODE***

COMPLAINANT v ASTRAZENECA

Concerns about misleading claims for Forxiga

CASE SUMMARY

This case was in relation to an advertisement about Forxiga (dapagliflozin) published in a quarterly digital journal intended primarily for pharmacists. The complainant alleged that the advertisement posed significant concern with regard to patient safety and a serious risk of inappropriate use of dapagliflozin due to the statements, "in this complex world", "think dapagliflozin", "co-morbidities and complications", and further alleged a failure to include safety considerations listed within the prescribing information.

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(x3)	**Requirement that information/ claims/ comparisons must not be 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 was received about AstraZeneca, from an anonymous, non-contactable complainant who described themselves as a health professional.

COMPLAINT

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

> "I am very concerned by an advertisement by AstraZeneca within the [named digital journal for health professionals] for which I subscribe. The advertisement is for Forxiga (dapagliflozin). The advertisement states that 'In this complex world', which we certainly do live in particularly within the world of Pharmacy, 'think dapagliflozin'. The text in the middle contains the statement 'co-morbidities and complications' - my interpretation of this is that AstraZeneca are suggesting that I prescribe dapagliflozin for patients with co-morbidities and complications, just 'think dapagliflozin' as the solution for this complex patient. They do not share any of the safety considerations listed within the Prescribing Information, where further consideration should be given, or use not recommended, or recommendations to use with caution, such as Renal Impairment, Hepatic Impairment,

Use in patients at risk of volume depletion and/or hypotension, Diabetic ketoacidosis (DKA), to name just a few. Furthermore, 'co-morbidities and complications' is written next to eGFR, where there is extensive guidance on when and when not to use dapagliflozin in patients with varying eGFR rates. The statement written as a whole is highly suggestive to me that given the complexity of the environment in which we work and the disease area, dapagliflozin can be used in any patient without consideration of serious safety considerations linked to comorbidities and patient complications. This is a significant concern with regards to patient safety and seriously risks inappropriate use of dapagliflozin."

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

ASTRAZENECA'S RESPONSE

The response from AstraZeneca is reproduced below:

"We are writing to you in response to your letter dated 5th September 2024, concerning a complaint from a healthcare professional ("HCP") about misleading claims about Forxiga® (dapagliflozin) in an advertisement ("advert") in [named digital journal for health professionals] that the HCP subscribes to.

Summary of the Allegations

The complainant has made 3 allegations about the advert which AZ will respond to in turn:

1. *"The text in the middle contains the statement 'comorbidities and complications' - suggesting that I prescribe dapagliflozin for patients with co-morbidities and complications, just 'think dapagliflozin' as the solution for this complex patient."*

2. *"They do not share any of the safety considerations listed within the Prescribing Information, where further consideration should be given, or use not recommended, or recommendations to use with caution, such as Renal Impairment..."*

3. *"Furthermore, 'co-morbidities and complications' is written next to eGFR, where there is extensive guidance on when and when not to use dapagliflozin in patients with varying eGFR rates. The statement written as a whole is highly suggestive to me that given the complexity of the environment in which we work and the disease area, dapagliflozin can be used in any patient without consideration of serious safety considerations linked to comorbidities and patient complications."*

AstraZeneca takes compliance with the ABPI Code of Practice (the "Code") seriously and in the response below consideration has been given to Clauses 6.1, 5.1 and 2 of the 2021 Code.

AstraZeneca Response

<u>Background</u>

The advert in question was published in the Summer 2024 edition of [named digital journal for health professionals], a quarterly digital publication intended primarily for pharmacists. The intent of the advert is to encourage HCPs to consider dapagliflozin as an option for patients with the diseases for which it is indicated.

At the top of the advert the full Forxiga indication for Heart Failure (HF), Chronic Kidney Disease (CKD) and Type 2 Diabetes (T2D) is clearly stated. Underneath this, the advert includes the following claim *"In this complex world of T2D, CKD and HF, think dapagliflozin"*. There is a word cloud between *"...and HF*" and "*think dapagliflozin*", which is intended to reflect the complex world of T2D, CKD and HF as referenced in the claim.

Below this is a prominent call to action, directing the reader to the AZ Forxiga website, and a prominent link to prescribing information (PI). The advert was certified by a Nominated Signatory.

Response

1. *"The text in the middle contains the statement 'comorbidities and complications' - suggesting that I prescribe dapagliflozin for patients with co-morbidities and complications, just 'think dapagliflozin' as the solution for this complex patient."*

The intent of this advert is to highlight the complexities facing HCPs when managing T2D, HF and CKD, and that dapagliflozin may be considered as a treatment option. This complex environment is represented by the word cloud.

The use of language "*… think dapagliflozin*" implies that dapagliflozin could be considered in these patients in line with the licenced indication, rather than a directive to prescribe dapagliflozin for all of these patients. This text is in relatively small font which carries lower emphasis compared with text below, directing readers to further information about dapagliflozin on the Forxiga website by scanning the QR code (*"To discover how dapagliflozin can be incorporated into your practice, scan here"*) and the link to PI. This is due to the primary intent of the advert being for the HCP to seek further information on dapagliflozin.

The statement directing HCPs to the Forxiga website encourages them to seek further information before incorporating dapagliflozin into their practice (and thus before prescribing). The prominent link to PI is on the same page as the text in question, and therefore would not have been missed by HCPs. At the top of the PI is the statement "Please Consult to Summary of Product Characteristics before Prescribing" and information relating to renal impairment is highlighted on page (1) of the PI. The HCP would have been able to access all safety considerations in the PI.

Please see screenshot of advert below for a good quality copy of the full advert.

[screenshot of advertisement at issue]

Due to the reasons outlined above, we consider that the advert does not mislead the HCP to believe that dapagliflozin should be prescribed for all patients with co-morbidities and complications.

2. *"They do not share any of the safety considerations listed within the Prescribing Information, where further consideration should be given, or use not recommended, or recommendations to use with caution, such as Renal Impairment..."*

The advert does not make reference to efficacy outcomes or dosing requirements for dapagliflozin and therefore it was deemed safety information was not required in the material itself to remain balanced. The HCP was clearly directed to seek further information about Forxiga via the call to action. The link to PI was prominent and included all safety considerations related to Forxiga. The statement "Please Consult to Summary of Product Characteristics before Prescribing" is also clearly included at the top of PI.

Due to the reasons outlined above, we consider that the safety information provided in the PI was sufficient, and additional safety information was not required in the advert itself.

3. *"Furthermore, 'co-morbidities and complications' is written next to eGFR, where there is extensive guidance on when and when not to use dapagliflozin in patients with varying eGFR rates. The statement written as a whole is highly suggestive to me that given the complexity of the environment in which we work and the disease area, dapagliflozin can be used in any patient without consideration of serious safety considerations linked to comorbidities and patient complications."*

As previously described, the word cloud is used to support the claim that the disease areas (HF, CKD and T2D), present complexities to HCPs when treating patients with these conditions. The words selected for the word cloud were all chosen as they are relevant to the disease areas where dapagliflozin is indicated. For T2D the associated words are, 'insufficiently controlled type 2 diabetes'. For CKD, 'chronic kidney disease' and 'eGFR' an indicator of renal function. For HF, 'symptomatic chronic heart failure', 'heart failure with preserved ejection fraction' and 'heart failure with reduced ejection fraction'. The combinations of the disease areas; 'T2D & HF', 'T2D & CKD', 'T2D & CKD & HF', 'CVRM' (cardiovascular, renal, metabolism) are relevant as these diseases can co-exist and be interconnected. Lastly, 'co-morbidities and complications' and 'cardiorenal protection' are relevant to these diseases and speak to the effects of disease progression.

The dosing of dapagliflozin in renal impairment is consistent across all three indications, HF, CKD and T2D; dapagliflozin can be initiated in patients with an eGFR>15min/ml/1.73m^2 at the usual dose of 10mg once daily. As previously mentioned, no dosing information for dapagliflozin was included in the advert, and the HCP was clearly signposted to seek further information on Forxiga before dapagliflozin is *"incorporated into practice"*.

As previously described, a prominent link to PI was included in the advert which could not have been missed by HCPs. At the top of the PI is the statement “Please Consult to Summary of Product Characteristics before Prescribing” and information relating to renal impairment is highlighted on page (1) of the PI. The HCP would have been able to access all safety considerations in the PI.

Due to the reasons outlined above, our position is that the advert does not mislead the HCP to prescribe dapagliflozin for all patients with co-morbidities and complications including renal impairment without access to safety information regarding dosing in varying eGFR categories.

The information provided in the advert is accurate, balanced, fair, objective and unambiguous. It is not misleading. The material is complete with prominent signposting to further information before being incorporated into practice. There was prominent link included to the PI. It is in line with high standards of the Code and does not bring discredit upon, or reduce confidence in, the pharmaceutical industry.

AstraZeneca therefore refute breach of Clause 6.1, 5.1 and 2 pertaining to this allegation.

Summary

It is AstraZeneca’s position that:

- This advert indicates that dapagliflozin may be considered as a treatment option for indicated patients, and clearly and prominently directs HCPs to find further information about the product. The advert is balanced and does not mislead the HCP to prescribe dapagliflozin in all patients.
- HCPs are encouraged to seek and consider further information before incorporating dapagliflozin into their practice, by scanning the QR code. This takes the HCP to the Forxiga website.
- The advert contains the prescribing information containing all of the safety and dosing considerations for dapagliflozin which is made available through a clear and prominent, direct, single click link.

AstraZeneca takes its responsibilities under the ABPI Code very seriously. Based on the above detailed response, we maintain that the advert is not misleading, that high standards have been maintained and this activity has not brought the industry into disrepute. Therefore, **we refute breaches of Clause 6.1, 5.1 and 2.**”

PANEL RULING

This complaint about AstraZeneca was received from an anonymous, non-contactable complainant who described themselves as a health professional. The complaint related to an advertisement about Forxiga (dapagliflozin) published in the summer 2024 edition of a quarterly digital journal intended primarily for pharmacists.

The complainant alleged that the advertisement posed significant concern with regard to patient safety and a serious risk of inappropriate use of dapagliflozin due to the statements, “in this

complex world", "think dapagliflozin", "co-morbidities and complications", and further alleged a failure to include safety considerations listed within the prescribing information (PI).

The Panel noted that the advertisement at issue included the indication at the top in white font on a blue background, "FORXIGA (dapagliflozin) is indicated in adults for the treatment of chronic kidney disease (CKD); symptomatic chronic heart failure (HF); and insufficiently controlled type 2 diabetes (T2D)".

Beneath this appeared a large, dense word cloud in black font, in the shape of a right kidney, covering the top half of the advertisement. In the middle of the 'kidney' appeared text in white font, "In this complex world of T2D, CKD and HF". There was a smaller word cloud in black font adjacent to this text, outside the 'kidney', which included the second statement at issue, "co-morbidities and complications", and the following words and statements:

- Insufficiently controlled type 2 diabetes
- T2D + HF
- Symptomatic chronic heart failure
- eGFR
- cardiorenal protection
- heart failure with preserved ejection fraction
- CVRM
- T2D + CKD
- TDB + CKD + HF
- Chronic kidney disease
- Heart failure with reduced ejection fraction

To the right of the smaller word cloud, the third statement at issue, "think dapagliflozin" appeared in white font, followed by a picture of a yellow diamond shaped tablet engraved with '10'.

Below the word clouds, in the middle of the advertisement appeared a prominent white banner, stating, "To discover how dapagliflozin can be incorporated into your practice, SCAN HERE", and a large, prominent QR code. AstraZeneca submitted this linked to the Forxiga website.

The QR code was followed by a prominent link to GB (Great Britain) prescribing information. The bottom section of the advertisement included an adverse event reporting box, a statement that this is a promotional piece from AstraZeneca for GB healthcare professionals only, an explanation of abbreviations listed in the word clouds, an AstraZeneca and Forxiga brand logo and the job code and date of preparation.

The Panel noted the complainant's allegation that the statements, "in this complex world" and "think dapagliflozin", with the words "co-morbidities and complications" appearing between the two statements meant that the advertisement suggested that dapagliflozin should be prescribed for any complex patient with comorbidities and complications, without consideration of serious safety considerations linked to comorbidities and patient complications.

The Panel noted AstraZeneca's submission that the intent of the advertisement was to highlight the complexities facing health professionals when managing type 2 diabetes (T2D), heart failure

(HF) and chronic kidney disease (CKD), that dapagliflozin may be considered as a treatment option and that the word cloud represented this complex environment.

The Panel took account of AstraZeneca's submission that the text in the word clouds was relatively small and therefore carried less emphasis compared with the prominent text in the middle of the advertisement, directing readers to further information about dapagliflozin by scanning the QR code.

The Panel noted that the GB PI for dapagliflozin stated, in bold font, "Consult Summary of Product Characteristics (SmPC) before prescribing".

The Panel further noted that the advertisement at issue was printed on what appeared to be the inside cover of the digital journal, adjacent to the Contents page. The advertisement appeared only once in the journal. The Panel took account of the seven articles published in this issue of the journal, none of which related to dapagliflozin, heart failure, diabetes or kidney disease.

Noting the context of the advertisement, the Panel considered the inclusion of the text "To discover how dapagliflozin can be incorporated into your practice, SCAN HERE" immediately beneath the word clouds, sufficient to alert prescribers that more information was available for the prescribers' consideration before determining the suitability of the product for an individual patient.

The Panel considered the content, layout and impression created by the advertisement as a whole within the digital journal; it determined that its purpose was to enable health professionals to discover more information about dapagliflozin by scanning the prominent QR code, to discover how dapagliflozin could be incorporated into their practice.

In the Panel's view, the complainant had not established that the statements included in the word clouds, "in this complex world" and "think dapagliflozin", with "co-morbidities and complications" appearing between the two statements, meant that the advertisement suggested that dapagliflozin should be prescribed for any complex patient with comorbidities and complications, without safety considerations. The Panel ruled **no breach of Clause 6.1** in this regard.

The Panel noted the complainant's allegation that safety considerations listed in the PI which required further consideration, or use not recommended or use with caution, such as renal and hepatic impairment, use in patients at risk of volume depletion and/or hypotension and diabetic ketoacidosis, were not included in the advertisement at issue and therefore there was a serious risk of inappropriate use of dapagliflozin.

The Panel noted the special warnings and precautions for use listed in the dapagliflozin SPC in relation to renal and hepatic impairment, use in patients at risk of volume depletion/hypotension, and diabetic ketoacidosis, however, the Panel took account of AstraZeneca's submission that the advertisement did not make reference to efficacy outcomes or dosing requirements for dapagliflozin.

The Panel noted that the advertisement did not include any efficacy or safety claims.

In the Panel's view, as noted above, the purpose of the advertisement was to encourage health professionals to discover more information about dapagliflozin, and enabled them to do so via

the linked information. The Panel considered it unlikely that a health professional would make prescribing decisions based on the information in the advertisement alone.

Noting the clear signposting to discover more information about incorporating dapagliflozin into practice, and the prominent link to the GB PI, the Panel considered that the complainant had not established that the absence of safety information in the advertisement, from the PI, meant that the advertisement would lead to a risk of inappropriate prescribing of dapagliflozin by readers, and the Panel ruled **no breach of Clause 6.1** in this regard.

The Panel noted the complainant's allegation that the text within the small word cloud, "co-morbidities and complications" was adjacent to "eGFR", which had extensive guidance on when and when not to use dapagliflozin in patients with varying eGFR rates, suggesting that dapagliflozin can be used in any patient without consideration of comorbidities and complications.

The Panel noted AstraZeneca's submission that the words selected for the word cloud were all chosen as they are relevant to the disease areas where dapagliflozin is indicated and the combinations of the disease areas; 'T2D & HF', 'T2D & CKD', 'T2D & CKD & HF', 'CVRM' (cardiovascular, renal, metabolism) are relevant as these diseases can co-exist and be interconnected. AstraZeneca further submitted that the dosing of dapagliflozin in renal impairment is consistent across all three indications, HF, CKD and T2D; dapagliflozin can be initiated in patients with an eGFR>15min/ml/1.73m^2 at the usual dose of 10mg once daily.

Noting the Panel's view above regarding the purpose of the advertisement, and the clear signposting to seek further information, the Panel considered that the complainant had not established that the words "co-morbidities and complications" adjacent to "eGFR" in the smaller word cloud meant or implied that dapagliflozin can be used in any patient with varying eGFR rates without consideration of comorbidities and complications, and the Panel ruled **no breach of Clause 6.1** accordingly.

Based on its rulings of no breaches of the Code above, the Panel did not consider that it had been established that AstraZeneca had failed to maintain high standards or had brought discredit upon, or reduced confidence in, the pharmaceutical industry. The Panel ruled **no breaches of Clauses 5.1 and 2**, accordingly.

Complaint received **4 September 2024**

Case completed **23 October 2025**