CASE AUTH/3701/10/22 ***NO BREACH OF THE CODE***

ASTELLAS v JANSSEN

Nurse support service in prostate cancer – Erleada

CASE SUMMARY

This case was in relation to Janssen's provision of a nurse support service for Erleada as part of a package deal which was alleged to be an inducement to prescribe as there were no additional monitoring requirements mandated in the Erleada SPC other than those for the standard management of prostate cancer patients.

The Panel ruled no breach of the following Clauses of the 2021 Code as it did not consider that Astellas had demonstrated that the package deal was inappropriate or was being offered as an inducement to prescribe Erleada as alleged.

No Breach of Clause 2	**Requirement that activities or material must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**
No Breach of Clause 5.1	**Requirement to maintain high standards**
No Breach of Clause 19.1	**Requirement that no gift, pecuniary advantage or benefit may be supplied, offered or promised to health professionals or to other relevant decision makers in connection with the promotion of medicines or as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine.**

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 from Astellas Pharma Ltd about Janssen-Cilag Limited's nurse support service in relation to Erleada (apalutamide) which was offered as part of a package deal.

COMPLAINT

Astellas submitted that it worked both to the letter and spirit of the ABPI Code of Practice and always aimed to address concerns on potential breaches of the Code via inter-company dialogue (ICD). Astellas entered into ICD with Janssen in May 2022, regarding their nurse support service in prostate cancer, and despite numerous correspondence and a meeting with the Janssen team, the ICD proved unsuccessful in relation to the concerns raised by Astellas. Therefore, Astellas formally submitted a complaint regarding the Nurse Support Service Janssen provided for Erleada (apalutamide) for the PMCPA's review.

Summary of complaint:

- Astellas believed the nurse patient support programme for Erleada (apalutamide), provided as a package deal by Janssen exclusively for prostate cancer patients prescribed apalutamide, constituted an inducement to prescribe and breached Clauses 19.1, 5.1 and 2 of the 2021 ABPI Code of Practice.

- Existing nurses provided by Janssen for several years to oversee Zytiga (abiraterone) patients had recently been re-contracted to see patients prescribed Janssen's new launch product Erleada.

- Due to current intense capacity issues in the NHS prostate cancer services, prescribers were being unreasonably induced to prescribe Erleada in order to retain the additional nurse support within the oncology department provided by Janssen, despite several other options being available for patients in this clinical setting.

- Janssen highlighted that its previous Zytiga Patient Support Programme (PSP) and the new Erleada PSP were designed to support the close monitoring and management of adverse events listed in the respective summaries of product characteristics (SPCs). Astellas' complaint was regarding the explicit need for the Erleada PSP within the framework of a package deal; there were no additional monitoring requirements within the apalutamide SPC beyond standard management of adverse events that would most likely occur outside of the nurse clinic setting. Furthermore, Astellas had received reports from NHS Trusts through its own Astellas field members, where the clinical team had felt obligated to exclusively start prescribing Erleada for indicated prostate cancer patients, purely on the basis of the additional clinical nurse support provided by Janssen.

- ICD concluded unsuccessfully as Janssen was unwilling to share the explicit rationale for the nurse PSP for Erleada and the full extent of the work these nurses were providing as fully embedded members of NHS prostate cancer clinics; therefore, a complaint was raised.

Particular details of the complaint

Janssen historically had offered a Nurse Support Service (contracted through a service provider) exclusively for Zytiga (abiraterone) patients as part of a package deal with numerous NHS Trusts; Astellas understood that Janssen had been offering this Zytiga PSP to manage patient follow-up visits in hospital. Janssen had now confirmed that the Zytiga PSP was closing and that a similar PSP for Erleada (apalutamide) had commenced.

Astellas engaged in ICD with Janssen as it had concerns over how the Erleada PSP service was being offered and the nature of this service. The concerns stemmed from the fact that the same nurses who were delivering the Zytiga PSP were now only to start seeing and supporting patients initiated on the newly launched Janssen product Erleada (apalutamide). Astellas believed, and indeed had had feedback, that Trusts facing significant capacity issues were being unduly induced to prescribe Erleada in order to keep the ongoing support of an embedded clinic nurse, provided by Janssen. Janssen discussed that the two PSPs were, in fact, independent. However, Astellas believed the manner in which the nurse service was being transferred was, in

fact, perceived by NHS Trusts as a 'switch' of service, providing commercial benefit to Janssen and was an inducement to prescribe Erleada, breaching Clause 19.1 of the ABPI Code.

Janssen highlighted that both programmes were designed to support the close monitoring and management of adverse events, particularly those listed as side-effects and Special Warnings and Precautions for use in the SPC for each product. Whilst Astellas understood there could potentially be justification for additional monitoring requirements/follow-up visits for abiraterone patients, there were no mandated additional monitoring requirements within the apalutamide SPC other than those required for the usual prostate cancer patient. Additionally, as apalutamide was an oral medication taken by a patient at home, Astellas found it difficult to understand how acute adverse events were to be managed by secondary care nurses.

Astellas engaged in ICD to highlight its concerns and hosted a teleconference to seek clarity on the particulars of the Erleada PSP. Janssen was unwilling to provide any details regarding the Erleada PSP and nature of the clinical work undertaken by either their contracted Zytiga or Erleada nurses and specifically how this related to the Code requirements regarding Package Deals or Patient Support Programmes. Therefore, Astellas remained unsatisfied as to whether these nurses, the work they actually undertook and the way in which they were offered to departments would be acceptable under the Code. More importantly, Astellas failed to see how this provision of an embedded clinical nurse linked exclusively to the prescribing of one particular novel hormonal treatment could not ever be seen as an inducement to prescribe when several therapies existed in this medicinal class. Furthermore, Astellas had reports from its own field members that clearly indicated apalutamide had been selected purely on the basis of the additional nurse that accompanied it.

Following conclusion of the ICD, Astellas was still concerned that the nurse service for Erleada was, indeed, an inducement to prescribe and therefore felt Janssen was failing to maintain the high standards expected of pharmaceutical companies, bringing discredit upon the pharmaceutical industry hence breaching Clauses 19.1, 5.1 and 2 of the 2021 Code of Practice.

RESPONSE

Janssen submitted that it was disappointed that Astellas had chosen to proceed to a formal complaint to the PMCPA. Janssen willingly engaged in the ICD process and made a concerted effort to address their stated concerns. Astellas, however, continued to challenge Janssen's decisions to withdraw the support service related to Zytiga and also to challenge the need for a separate support service (package deal) related to Erleada. Unfortunately, it also became apparent that Astellas was either unwilling or unable to provide any evidence to illustrate or support its claims which appeared to be based solely on verbal statements from sales representatives. Astellas appeared to be seeking information on Janssen's commercial agreements and while Janssen was willing to discuss the monitoring needs described in the SPC on which the support service was based, it was not willing to share details on these agreements beyond those provided in the exchange of letters, nor did it feel it needed to defend Janssen's decision to initiate the programme. This was especially true in the absence of any documentary evidence to support Astellas' claims.

While Janssen was, of course, very happy to engage in the ICD process, it was concerned that proceeding with the formal complaint process, based on verbal reports from sales representatives regarding undocumented conversations with unnamed health professionals, set a precedent for similar inter-company complaints to proceed to formal complaints in the future.

Janssen's response to the five bullet points in Astellas' 'Summary of complaint' was structured below under sections:

1) Rationale for an Erleada patient support programme provided as a package deal under Clause 19.1.

2) Independence of the Zytiga and Erleada patient support programmes:

    1. In reference to their first and fourth bullet points referencing the rationale for a patient support programme for Erleada, Clause 19.1 stated:

        'No gift, pecuniary advantage or benefit may be supplied, offered or promised to health professionals or to other relevant decision makers in connection with the promotion of medicines or as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine, subject to the provisions of Clauses 10.4 and 19.2.'

        And the supplementary information stated:

        'Clause 19.1 does not prevent the offer of package deals which are commercial arrangements whereby the purchase of a particular medicine is linked to the provision of certain associated benefits as part of the purchase price, such as apparatus for administration, the provision of training on its use or the services of a nurse to administer it. Transfers of value made in the course of these package deals would need to be disclosed in accordance with Clause 28. The transaction as a whole must be fair and reasonable, and the associated benefits must be relevant to the medicine involved.'

        The supplementary information made clear that the Clause does not prevent a company offering a commercial arrangement as a package deal for individual products that included the provision of nurse support and training, provided the associated benefits were relevant to the medicine involved.

        As discussed in Janssen's exchange of letters with Astellas, the Erleada SPC listed the following in 'Special Warnings and Precautions for Use' (Section 4.4): seizure, falls and fractures, ischaemic heart disease and ischaemic cerebrovascular disorders, Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN), with special care and/or monitoring necessary for patients with recent cardiovascular disease, those at risk of prolonged QT interval, and with certain concomitant medications. Onset of rash in particular requires careful management to avoid progression to the life-threatening and potentially fatal complication of SJS/TEN. The onset of many of these events was concentrated in the first 6 months of use, and therefore additional monitoring and nurse support during this period contributed significantly to patient safety for a medicine only recently made available for the first time to patients within the NHS. Janssen therefore believed that the provision of nurse support and additional monitoring as a package deal provided benefits that were clearly relevant and appropriate

to Erleada. Astellas seemed to suggest that a nurse support programme was acceptable for Zytiga but not for Erleada based on their interpretation of monitoring requirements for each product. While Janssen agreed that there were more specific blood monitoring requirements for Zytiga, there were no requirements in the ABPI Code or other regulations that stipulated the specific monitoring requirements required for this support to be acceptable as part of a package deal, only that '*the associated benefits are relevant to the medicine involved*'.

There was no pecuniary advantage or benefit to the health professional in the provision of this nurse support. However, Janssen felt the benefit to the patients prescribed Erleada was clear, particularly in regard to supporting the appropriate use and monitoring of a product recently available for prescription within the NHS. While Janssen agreed that there were *'intense capacity issues'* in the NHS and there was a secondary benefit to the NHS in the provision of any package deal by companies for their products, this should not influence or prevent Janssen providing appropriate support to patients for each of its products, particularly those services contributing to patient safety, provided they met the package deal requirements as specified in the supplementary information to Clause 19.1.

With regard to the fifth bullet point stating that '*ICD concluded unsuccessfully as Janssen were unwilling to share the explicit rationale for the nurse PSP for Erleada*', the rationale for nurse support and monitoring was explained and repeated during the exchange of letters. During the ICD, an attempt was made to take Astellas through the Erleada SPC to clarify for them the listed safety and monitoring requirements. With regard to the full extent of the work that the nurses were providing, this was part of Janssen's contractual agreement with the service provider and while Janssen was willing to discuss the monitoring needs described in the SPC, it was not willing to share details on Janssen's commercial agreements with the service provider beyond those provided in the exchange of letters, especially in the absence of any documentary evidence to support Astellas' claims.

2. With regard to bullet points two and three, the nurse services for Zytiga and Erleada were separate and independent programmes. Whether to provide a service as a package deal was the choice of a company, as was the decision of when to stop providing that service, provided the requirements of Clause 19.1 were met. The Zytiga programme had been running for a number of years, and there was now significant familiarity with the medicine. Furthermore, Zytiga had lost its exclusivity and as generic formulations of abiraterone acetate become available, it would not be possible to determine whether a patient had been prescribed Zytiga® or a generic version; the patient support programme could not therefore be linked to a particular medicine and hence could no longer be classified as a package deal under Clause 19.1 of the ABPI Code. Janssen understood that the service had provided value to patients and the NHS and felt proud to have provided the Zytiga nurse programme. However, it was reasonable for any company to review the continuation of its programmes especially

with such significant changes in circumstances, and the decision was made to close the program in September 2022, and to communicate the decision to the NHS Trusts and the service provider. Furthermore, Janssen believed it had communicated the closure in an appropriate and constructive way.

An Erleada patient support programme began as a pilot, and the wider programme commenced following a positive National Institute for Health and Care Excellence (NICE) recommendation and therefore its widespread availability on the NHS. Provision of the Erleada service was separate to the provision of the Zytiga service and was subject to a competitive tender process, following which, and in addition to Janssen's satisfaction with the service provided for Zytiga, the same service provider was also awarded the contract to provide an Erleada nurse support service. Some Trusts that participated in the Zytiga nurse support programme requested that the Erleada package deal was provided contractually as an expansion/extension of the existing service initially to simplify the contracting process, given that the service provider was the same for both programmes, but the contracts were subsequently separated. Regardless of the contracting process, the two services were provided independently and at no point did Janssen instruct any of its personnel, including representatives, to connect termination of the Zytiga support with an obligation or inducement to take up the Erleada support programme, and there had been appropriate briefings to representatives.

The supplementary information to Clause 19.1 stated that a package deal provides for a '*commercial arrangement whereby the purchase of a particular medicine is linked to the provision of certain associated benefits as part of the purchase price*'. It was therefore appropriate and legitimate for a company to provide support and benefits to patients linked to the prescription of a specific medicine, and this applied to the patient support programme that Janssen provided for Zytiga and for the separate programme related to Erleada. Astellas appeared to take the view that the provision of nurse support as part of a package deal was, in itself, an inducement to prescribe in the absence of any similar provision of nurse support for other company's products, and that this '*leads to pressuring the clinicians to an otherwise un-justified change in prescribing and ultimately, restricting the treatment options that clinicians can offer to newly diagnosed patients*'.

Janssen was surprised and disappointed by Astellas' suggestion that health professionals were making inappropriate treatment choices based solely on the provision of additional nurse services as part of a package deal for individual products. Clearly such support was accepted under Clause 19.1 as an appropriate and legitimate commercial arrangement that benefits both patients and healthcare systems, and Janssen respected and valued clinician's abilities to make clinical decisions in consultation with their patients on the most appropriate treatment for each individual patient.

Janssen failed to see that the inherent nature of the support programme for Erleada or how it was being offered was inappropriate, or that it was inconsistent with the ABPI Code

requirements under Clause 19.1 for a package deal. Nor did Janssen see how the cessation of the Zytiga programme was inappropriate or incorrect. Each programme provided by Janssen was clearly linked to a particular medicine and provided appropriate benefits as part of the purchase price. No pecuniary advantage or benefit was being supplied as an inducement to prescribe Erleada (and the programme and associated support could only be requested following prescription of the product). The transaction as a whole was also fair and reasonable, with the associated benefits being very clearly relevant to patients prescribed Erleada with monitoring and management of potential associated side-effects for a product recently available within the NHS.

No documentary evidence had been provided for the claims that Astellas made, despite repeated requests, and this potentially set a precedent for inter-company complaints based on verbal reports by sales representatives of undocumented conversations to proceed to formal complaints to the PMCPA in the future.

Janssen refuted the suggestion that it was in breach of Clause 19.1, and therefore also refuted the suggestion that it was in breach of Clauses 5.1 and 2.

PANEL RULING

The Panel noted that the complainant bore the burden of proof and therefore that it was for Astellas to provide the evidence to support its complaint. In general terms, in the absence of evidence of wrongdoing from the complainant, it would be difficult for a complainant to establish its case. It was important that the complaints process was not used solely to seek disclosure of otherwise confidential information. In this regard, the Panel noted the relevant provisions of the Constitution and Procedure in relation to the disclosure of material which a respondent company considered confidential. The Panel noted Astellas' submission that Janssen was unwilling to provide any details regarding the Erleada patient support programme and nature of the clinical work undertaken by the contracted nurses and specifically how this related to the Code requirements regarding Package Deals or Patient Support Programmes. The Panel noted Janssen's submission in this regard that Astellas appeared to be seeking information on Janssen's commercial agreements and while Janssen was willing to discuss the monitoring needs described in the SPC on which the support service was based, it was not willing to share details on Janssen's commercial agreements with the service provider, especially in the absence of any documentary evidence to support Astellas' claims, nor did it feel it needed to defend Janssen's decision to initiate the programme. The Panel noted that companies must respond appropriately to complaints and also noted its general comments above regarding confidential material.

The Panel noted that Clause 19.1 states that 'No gift, pecuniary advantage or benefit may be supplied, offered or promised to health professionals or to other relevant decision makers in connection with the promotion of medicines or as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine, subject to the provisions of Clauses 10.4 and 19.2'. The supplementary information to Clause 19.1, Package Deals, states, amongst other things, that 'Clause 19.1 does not prevent the offer of package deals which are commercial arrangements whereby the purchase of a particular medicine is linked to the provision of certain associated benefits as part of the purchase price, such as apparatus for administration, the provision of training on its use or the services of a nurse to administer it. The transaction as a whole must be fair and reasonable and the associated benefits must be relevant to the medicine involved'.

The Panel noted that Janssen described the nurse support service as a patient support programme which was offered as part of a package deal related to Erleada. The Panel noted that the classification of the service was not the subject of the complaint and thus was not ruled upon. The Panel noted that patient support programmes were not a discrete activity classification under the 2021 Code. The Panel noted that, in general terms, such nurse services might be offered as part of a package deal, the only requirement was that the benefit was relevant to the medicine and the package overall was fair and reasonable.

The Panel noted Astellas' concerns over how the Erleada nurse support service was being offered and the nature of the service.

In relation to Astellas' concerns about the way the service was offered, the Panel noted that Astellas' concerns stemmed from the fact the same nurses who were delivering the nurse support service for Zytiga , which was closing, were now only to start seeing and supporting patients initiated on the newly launched Janssen product Erleada , when, in Astellas' view, there were no additional monitoring requirements within the Erleada SPC beyond standard management of adverse events that would most likely occur outside of the nurse clinic setting. The Panel noted that, according to Astellas, it had feedback that Trusts facing significant capacity issues were being unduly induced to prescribe Erleada in order to keep the ongoing support of an embedded clinic nurse, provided by Janssen and the manner in which the nurse service was being transferred was, in fact, perceived by NHS Trusts as a 'switch' of service, providing commercial benefit to Janssen and was an inducement to prescribe Erleada.

The Panel noted that Astellas referred to a switch to the Erleada patient support programme as having a commercial benefit to Janssen. The Panel noted that package deals were an integral part of a commercial offering and might legitimately result in a commercial benefit. The package deal, nonetheless, had to comply with the relevant supplementary information.

The Panel noted Janssen's submission that the two patient support programmes were independent; some Trusts that participated in the Zytiga nurse support programme requested that the Erleada package deal was provided contractually as an expansion/extension of the existing service initially to simplify the contracting process given that the service provider was the same for both programmes, but the contracts were subsequently separated. According to Janssen, regardless of the contracting process, the two services were provided independently and at no point did Janssen instruct any of its personnel, including representatives, to connect termination of the Zytiga support with an obligation or inducement to take up the Erleada support programme, and there had been appropriate briefings to representatives in this regard. The Panel further noted that it appeared that Astellas could provide no evidence in relation to its claims with regard to the feedback received from trusts and bore the burden of proof in this regard. The Panel also bore in mind that Clause 19.1 applied to inducements to individuals, rather than organisations. The Panel noted Janssen's submission that there was no pecuniary advantage or benefit being supplied as an inducement to prescribe Erleada (and the programme and associated support could only be requested following prescription of the product).

In relation to Astellas' concerns about the nature of the service, the Panel noted that whilst Astellas understood that there could potentially be justification for additional monitoring requirements/follow-up visits for abiraterone patients, there were no mandated additional monitoring requirements within the Erleada SPC other than those required for the usual prostate cancer patient. Additionally, as Erleada was an oral medication, taken by a patient at home,

Astellas found it difficult to understand how acute adverse events were to be managed by secondary care nurses.

The Panel noted Janssen's submission that the Erleada SPC listed the following in 'Special Warnings and Precautions for Use' (section 4.4): seizure, falls and fractures, ischaemic heart disease and ischaemic cerebrovascular disorders, Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN), with special care and/or monitoring necessary for patients with recent cardiovascular disease, those at risk of prolonged QT interval, and with certain concomitant medications. Onset of rash in particular requires careful management to avoid progression to the life-threatening and potentially fatal complication of SJS/TEN. The onset of many of these events was concentrated in the first 6 months of use, and therefore additional monitoring and nurse support during this period contributed significantly to patient safety for a medicine only recently made available for the first time to patients within the NHS. Janssen therefore believed that the provision of nurse support and additional monitoring as a package deal provided benefits that were clearly relevant and appropriate to Erleada.

The Panel noted that Astellas queried the explicit need for the Erleada patient support programme within the framework of a package deal. The Panel noted that the relevant supplementary information did not require there to be an explicit need for the service, the benefits of the nurse service merely needed to be relevant to Erleada and for the transaction as a whole needed to be fair and reasonable. The Panel noted Janssen's comments above in relation to certain monitoring requirements in the SPC. The Panel noted from Janssen's documentation that the Erleada patient support programme was briefly described as delivering the patient support programme and patient monitoring in line with the SPC; acting as a specialist resource on Erleada to the Trust and providing patient-facing support and education on treatment with Erleada. It appeared to the Panel that the general benefits of the patient support programme were relevant to Erleada.

The Panel noted its comments above and did not consider that Astellas had demonstrated that the package deal was inappropriate or was being offered as an inducement to prescribe Erleada as alleged. The Panel therefore ruled no breach of Clause 19.1. The Panel noted its comments and rulings above and consequently ruled no breach of Clauses 5.1 and 2.

Complaint received **24 October 2022**

Case completed **3 August 2023**