CASE AUTH/3885/3/24

EVER PHARMA UK v BRITANNIA PHARMACEUTICALS

Alleged off-licence promotion of APO-go

CASE SUMMARY

This case was in relation to alleged off-licence promotion of Britannia Pharmaceuticals Ltd's product APO-go (apomorphine hydrochloride) through its Nurse Service and at a sponsored meeting.

The outcome under the 2021 Code was:

Breach of Clause 5.1(x2)	**Failing to maintain high standards**
Breach of Clause 11.2(x2)	**Promoting a medicine for an unlicensed indication**

No Breach of Clause 2	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**

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 EVER Pharma UK Ltd about Britannia Pharmaceuticals Ltd.

COMPLAINT

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

> "We wish to formally register a complaint regarding Britannia Pharmaceuticals Ltd (**Britannia**) concerning the promotion of its product, a prescription-only medicine (**POM**), APO-go® outside the terms of its marketing authorisation (**MA**) and in a manner that is inconsistent with the product's Summary of Product Characteristics (**SmPC**).
>
> We believe Britannia is providing direct support in the form of a company funded nurse service which facilitates the use of their product outside the requirements of the SmPC.
>
> **Background**
>
> APO-go® is approved for the treatment of patients with Parkinson's disease (**PD**) and the active pharmaceutical ingredient is Apomorphine. For all relevant patients with PD, the prescribing HCP decides if a patient should commence treatment on Apomorphine.

Patients must be pre-treated with Domperidone to reduce the risk of severe nausea, and then will be scheduled for an Apomorphine response test to determine if there is a positive clinical effect. A response test is a subcutaneous injection of Apomorphine to evaluate a patient's clinical response and any adverse events. This enables a clinical decision regarding the benefits and risks of long-term treatment to be made by the prescribing HCP. Apomorphine naive patients will be administered Apomorphine for the first time during the Apomorphine response test and the patient is at risk of adverse events such as severe hypotension.

For these reasons and in the interests of patient safety, section 4.2 of the SmPC for APO-go® specifically states that: - *'Apomorphine should be initiated in the controlled environment of a specialist clinic. The patient should be supervised by a physician experienced in the treatment of Parkinson's disease (e.g. neurologist).'*

This letter addresses our concerns regarding reported initiation of patients with PD onto Apomorphine (response tests) outside the controlled environment of a specialist clinic; namely in a home environment by nurses employed by Britannia.

1. **Facilitation of off-licence use by APO-go® nurse team.**

As the only other provider of Apomorphine for the use in PD, EVER Pharma UK Ltd (**EVER**) has been repeatedly asked by NHS clinicians if EVER would be willing to provide Apomorphine response tests to PD patients in the home environment, similar to the service provided by Britannia. Such requests have been in respect of Apomorphine naive patients who will be administered Apomorphine for the first time.

Each SmPC for Apomorphine shares the same wording with regards to initiation of the POM in section 4.2, specifically that: '*Apomorphine should be initiated in the controlled environment of a specialist clinic. The patient should be supervised by a physician experienced in the treatment of Parkinson's disease (e.g. neurologist).'*

Our interpretation of this wording is that the provision of home initiation would not be consistent with the MA and poses a potential patient safety risk. This interpretation was confirmed by the Medicines and Healthcare products Regulatory Agency (**MHRA**) (Appendix 1). The MHRA clearly state that home initiation would indeed be considered an off-label practice.

We engaged in intercompany dialogue with Britannia and were unable to reach a satisfactory conclusion. During the intercompany dialogue, Britannia acknowledged that nurses employed and funded by Britannia do support home initiation of APO-go® at the request of NHS healthcare professionals (Appendix 2).

Britannia confirmed that it does not apply any clinical criteria to assess such requests from the NHS. Given the risks associated with such off-label initiation, we would have expected Britannia to have a process to justify the practice and assess the potential safety risks to each patient.

Britannia did not provide any information regarding the number of patients initiated on APO-go® at home. We were disappointed by this response as we had anticipated that

Britannia would be carefully documenting such requests, and that the information would be readily available.

We accept that there may be rare circumstances when a patient with PD may be judged by their supervising clinician to need home initiation of Apomorphine, in a manner inconsistent with the SmPC. We do not believe that off-licence use should be supported or conducted by a pharmaceutical company.

The NHS has limited resources to implement home initiations. It appears to us as though Britannia routinely provides the home initiation service. It appears to us that Britannia has made a commercial decision to facilitate the home initiation of patients on to their APO-go® product, outside the requirements of product's SmPC. This practice gives Britannia a commercial advantage. Further, such conduct amounts to the promotion of APO-go® outside the terms of the MA.

The recent article in the Journal of Neural Transmission by Dr C Kobyleki, full title: *'Home initiation of apomorphine infusion: lessons from the COVID-19 pandemic and implications for current clinical practice'* provides additional context on the number of routine home initiations being undertaken by Britannia in a single centre (Appendix 4).

Breaches of clause

11.2 (3.2) The promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its summary of product characteristics subject to the provisions of Clause 11.3 below.
5.1 (9.1) High standards must be maintained at all times.

2. **Promotion of home initiation of APO-go® (Apomorphine) in Britannia sponsored meetings**

We are aware of a Britannia sponsored promotional symposium that took place during a meeting of the Parkinson's Disease Nurse Specialist Association on [dates] 2022 in [location].
At this meeting, we understand that:

a) a Britannia sponsored speaker delivered a presentation to the audience entitled *'Simplifying the APO-go® (apomorphine hydrochloride) experience for you and your patients';* and
b) an external speaker, spoke for 30 minutes and included data from the APOKADO study, full title *'Feasibility and benefits of home initiation of subcutaneous apomorphine infusion for patients with Parkinson's disease: the APOKADO study')* of which he was an author (Appendix 3). *5.1* (9.1) High standards must be maintained at all times.

We note that the speaker was selected and reimbursed by Britannia and that the content of the presentation should have been reviewed and approved by Britannia. During intercompany dialogue, we requested a copy of the presentation and Britannia refused to provide a copy.

Manifestly, Britannia chose to include details of a study on the topic of home initiation of Apomorphine, which is inconsistent with the SmPC. In our view, this clearly amounts

to promotion of the administration of APO-go® in a manner that is inconsistent with its SmPC.

Breaches of clause

11.2 (3.2) The promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its summary of product characteristics subject to the provisions of Clause 11.3 below.
5.1 (9.1) High standards must be maintained at all times.

Conclusions

It appears clear that Britannia's nurses routinely initiate patients onto Apomorphine at home. This is not consistent with the MA. This is acknowledged by Britannia themselves in intercompany dialogue and is documented in the recently published article by Kobylecki *et al*.

We have also presented evidence that Britannia has actively promoted home initiation using their nurse service in company sponsored meetings.

We believe that Britannia's consistent disregard of the MA brings the industry into disrepute.

Breaches of clause:

Clause 2: Upholding Confidence in the Industry

Activities or materials must never be such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry."

BRITANNIA'S RESPONSE

The response from Britannia is reproduced below:

"Thank you for your letter dated 14th March 2024 notifying Britannia Pharmaceuticals that the Authority has received a complaint from EVER Pharma UK Ltd.

Britannia has taken the allegations made by EVER Pharma very seriously; we understand the importance of inter-company dialogue and the importance of the undertakings committed during such discussions. Britannia has engaged fully and professionally with EVER Pharma in relation to these matters. Our responses were complete, honest and delivered within the specified timeframes. Britannia is concerned that EVER Pharma did not choose to respond to our intercompany communication sent on the 18th January 2024 and opted instead to escalate the matter to the Panel 8 weeks later on the 13th March 2024.

Upon receipt of the initial letter from EVER Pharma on the 29th of November 2023, Britannia conducted an internal investigation, led by the Medical Director and Compliance Officer. Following this Britannia communicated to EVER Pharma that Britannia does not

routinely promote home initiation of APO-go® and provided an undertaking and assurance that this will not happen going forward either.

Britannia is concerned that EVER Pharma have chosen to misrepresent Britannia's response to them and have not given the full context. Please find below our response to the allegations:

1. **Alleged Facilitation of off-licence use by APO-go® nurse team**.

It is important to understand the difference in the nature of the Nurse Service provided by Britannia to that provided by EVER Pharma which perhaps has led to the confusion on the part of EVER Pharma. The Britannia Nurse Team operate under the clinical governance of the NHS Trust that they have an individual and named Honorary Contract with and they are therefore subject to the NHS Trust's clinical governance, including, but not limited to, Care Quality Commission (CQC) registration, and quality assurance arrangements, with Britannia making the Specialist Nurses available and covering the costs. As stated, this service is covered under an Honorary Contract (Enclosure 1) which is a legal agreement between Britannia Nurse and an NHS Trust which allows a named Britannia's Specialist Nurse to work directly with patients for the NHS providing therapy support. The Specialist Nurse is clinically responsible to, and accountable to, the NHS Trust's prescribing physician (and Specialist Nurse, where applicable) in the relevant service for Parkinson's disease. For employment and administrative matters, the Specialist Nurse reports to the Medical Director at Britannia, but Britannia do not direct, influence or control the clinical services provided by the Specialist Nurse to the NHS Trust's patients.

We believe the Nurse service that EVER Pharma provide is a commercial agreement, which is not declared as a Transfer of Value, provided via a third party who have a service level agreement with the Trust as a company and not individual Honorary Contracts and thus, the EVER nurses operate under the Company's own governance rather than that of the Trust. We believe this impacts the type of service these nurses can offer.

Britannia's Nurse Service works alongside Healthcare Professionals (HCPs) in the individual Trusts to provide on-going support to Parkinson's patients only after they have been selected for APO-go® therapy. The nurse service is led by a Nurse Manager, who reports to the Medical Director. Following the PMCPA audit from June 2023, the Nurse service has been reclassified as a package deal (Enclosure 2). Subsequent to this reclassification, Britannia would like to reiterate that the service delivery is independent of the Sales team and the Commercial functions of the business and continues to report into the Medical function.

As pioneers of apomorphine in the UK, we concur that *'Apomorphine should be initiated in the controlled environment of a specialist clinic. The patient should be supervised by a physician experienced in the treatment of Parkinson's disease (e.g. neurologist).'*

As a result of the restrictions in place due to the COVID-19 pandemic, access to hospital day-case facilities was not available, and face-to-face appointments were restricted. There were long waiting lists to start apomorphine infusion treatment and other device-aided therapies were unavailable due to the need for surgery or other procedures. These challenges required a rethink and change of process at [Named

Hospital], initially, to ensure advanced Parkinson's Disease patients could receive the treatment they urgently needed to provide them with an acceptable quality of life. To avoid significant delays in patients receiving treatment and the consequent exacerbation of debilitating Parkinson's Disease symptoms, the Trust implemented protocols for initiation of apomorphine infusion therapy in the patient's home. Britannia Nurse team were part of the multi-disciplinary team that ensured continuity of care and thus, we do not believe that patient safety has been compromised at any point by Britannia. Please find enclosed an example of a home initiation request received (Enclosure 3).

Britannia provides assurance that its personnel do not actively promote home initiations as routine procedure. A Britannia Nurse operating under a named Honorary Contract with the relevant trust may only provide home initiation of APO-go® in response to an unsolicited request in writing by the prescribing HCP; and under no circumstances proactively offer home initiation of APO-go® as routine procedure. As a result, Britannia has no policy or procedural documents in place that define the clinical circumstances where we believe home initiations would be appropriate as this decision lies with the prescribing HCP and not the Britannia nurses.

With regards to the number of home initiations performed, Britannia do not hold any data on the total number of home initiations as this is not a routine practice for our nurses as treatment not initiated by them. Whilst a limited number of individual nurses receive requests for home initiation the total number of requests received is not readily available as this is not recorded by Britannia. It is also worth noting that not all requests received result in an initiation.

To clarify and provide context to the assertions made by EVER Pharma in their complaint, home initiation is not routinely undertaken by Britannia Nurse Team. Of the over 169 hospitals that Britannia Nurse team have individual Honorary Contracts with, only 17 have requested home initiation. Britannia strongly disagree with EVER Pharma's allegation that Britannia has made a commercial decision to facilitate the home initiation of patients on to its APO-go® product, outside the requirements of the product's SmPC to gain a commercial advantage. We regard this as a serious and unfair allegation from EVER Pharma, despite the fact the Britannia has repeatedly tried to clarify and undertake that we do not promote home initiations. This is an unsubstantiated allegation and Britannia is unclear why EVER Pharma believes that we proactively initiate patients at home as routine procedure. This was also made clear during the inter-company dialogue with EVER Pharma.

The clinical paper referred to by EVER Pharma in Appendix 4: '*Home initiation of apomorphine infusion: lessons from the COVID-19 pandemic and implications for current clinical practice'* authored by Dr Christopher Kobyleki and Lucy Partington-Smith states n=27 patients had their treatments initiated at home during the COVID-19 pandemic (June 2020 to June 2022) with the help of the Britannia nurse service. The paper is the authors' independent experience with home initiations. The authors specify in the clinical paper that during the COVID-19 pandemic, day-case facilities were unavailable. Thus, to avoid significant delays in patients receiving treatment and the consequent exacerbation of debilitating Parkinson's disease symptoms, the NHS Trust had developed a new procedure for initiation of apomorphine therapy in the patient's home with assistance from the Britannia Nurse Service.

Britannia thus refutes the alleged breach of clauses 11.2 and 5.1, as we have not promoted APO-go® outside of its license because we do not proactively promote or initiate patients on APO-go® treatment at home and have provided an undertaking to EVER Pharma to that effect.

2. Alleged Promotion of home initiation of APO-go® (Apomorphine) in Britannia sponsored meetings:

We note EVER Pharma's concerns regarding a Britannia sponsored symposium that took place during the Parkinson's Disease Nurse Specialist Association meeting on [date] 2022 in [location].

Britannia would like to clarify that the title of the slide set from the external speaker at the symposium, Professor [name], was '*Simplifying the experience for you and your patients*' and not '*Simplifying the APO-go® (apomorphine hydrochloride) experience for you and your patients*'. The objective of the symposium was to share knowledge (based on clinical studies) on how the physician and patient experience can be simplified. As part of this presentation, Professor [name] presented 10 clinical studies, one of which was published data from the APOKADO study. Professor [name] described their experience with home initiations in France during the COVID-19 pandemic, which at the time of the symposium in [date] 2022 was shortly after the UK's COVID Alert Level was downgraded. This data was also relevant to the UK where home initiation of apomorphine for infusion/injection was also performed during the pandemic in the interest of uninterrupted patient care.

Following EVER Pharma's request, Britannia approached the speaker to request [their] permission to share the presentation with EVER Pharma, but the request for permission was denied. Without this consent, Britannia was unable to share the slides with EVER Pharma. However, as per Clause 8.6, upon request from the PMCPA, Britannia is sharing this presentation with the PMCPA (Enclosure 4), along with the consent evidence from Professor [name] (Enclosure 5)

Britannia selected Professor [name] as a speaker and reimbursed [them] and consequently the content of [their] presentation was reviewed and approved by Britannia. A verbal briefing only was provided to Professor [name]. This was identified during an internal spot check by the Compliance Team in November 2022. On further investigation, the Marketing Team had clarified that due to time constraints, a verbally binding briefing and written agreement (Enclosure 6) was completed before Professor [name] had commenced slide preparation. This ensured relevant compliance checks on the Professor's slide deck could be completed before the event took place. The spot check report was provided to the PMCPA during June 2023 reaudit (Enclosure 7). Britannia disagrees with EVER Pharma's allegation that we had chosen the APOKADO study for Professor [name] to present at the symposium. Professor [name] is a leading expert in Movement Disorders and in Apomorphine Therapy. [They are] therefore well suited to presenting on 'Simplifying the experience for you and your patients'. [Their] choice of material for the presentation reflects [their] personal experience and knowledge and in the case of the APOKADO study [nature of involvement].

Britannia accepts that inclusion of the APOKADO study in a Britannia sponsored symposium may give the impression that the intent was to promote home initiation. This was an oversight by Britannia and we would reassure the PMCPA that Britannia has come a long way in its compliance journey since November 2022 and with the significant improvements in our knowledge and our processes related to the code and compliance in general its unlikely that there would be an incident like this again.

Britannia would like to highlight that the [name of symposium] 2022 meeting was a part of the review and within the scope of the PMCPA audit (between November 2021 to June 2023). Britannia would like to reiterate that since the first PMCPA audit in November 2021, Britannia has made significant improvements to our procedures, culture and activities related to Compliance. All the learnings from the audits have been taken onboard by Britannia. Notably:

- The transition of the nurse service to a package deal has been completed as per the nurse service recategorisation action and implementation plan provided to the PMCPA in September 2023 as part of the June 2023 audit response. The contractual agreement and job descriptions of nurses have been updated to reflect the non-promotional nature of their roles and inherent limitations. The nurse service SOP has been updated to reflect the new categorisation and provide appropriate guidance to staff. Britannia's [Senior employee] has been responsible for the implementation of the revised nurse service.
- Integrity is one of the four STADA Corporate values in addition to Agility, Entrepreneurship and One STADA. It is at the core of the organisation, and Britannia continues to demonstrate this by our proactivity in communicating areas of process improvements through our internal deviation log, internal monitoring processes across a wide range of areas and raising awareness of Speak up, Speak out.
- PMCPA comments from all 3 audits regarding SOPs have been noted and incorporated in SOP reviews. The updated SOPs have been rolled out to the wider teams and we have ensured appropriate training has been provided.
- We have continued to provide training and share knowledge and learnings on a regular basis e.g. Clever Nelly as a Compliance learning tool. Our Compliance Champions meetings have members nominated across all functions, which reinforces the cross-functional accountability we have embedded, where compliance is a shared responsibility and highlights our commitment to compliance throughout the business. Compliance Champions meetings are held regularly to provide additional opportunity to train, learn and also Speak Up.
- We continue to build upon our internal monitoring processes and have included this as an integral part to our Compliance Framework which will be rolled out completely in 2024. We are currently analysing the key compliance areas and specific materials/activities e.g. contracts, advisory boards and congress activities to determine trends and common issues. This has thus allowed us to focus our efforts to areas where further improvement may be needed.
- With the Compliance Framework being rolled out in 2024, Britannia have scheduled actions (e.g. Compliance structure, Appropriate policies and procedures, Monitor, Review, Due Diligence & Audit, Trainings, Effective

Communications etc.) based on priority and opted for continuous improvement rather than a quick fix approach. This would further strengthen the cultural change and allow everyone to engage at a optimum pace whilst being attentive to the needs of our patients and the business at large. This framework results in a robust and effective compliance programme with the correct structure and attitude to supporting and enabling the business needs.

In summary, we would like to reassure the PMCPA that Britannia has undertaken extensive measures and improvements and will continue to do so. We absolutely understand the seriousness of our obligation to compliance in relation to the ABPI Code and other regulations. Integrity is at the core of the organisation and we have been proactive in communicating areas of process improvements through our internal deviation process and, where needed, through voluntary submissions. We have and continue to be dedicated in our commitment to make necessary changes in our processes, culture and the support and skill of our people and believe we have demonstrated this throughout the audit process and our learnings. We are transparent in our approach and are mindful that we need to continually evolve and review our processes to ensure our quality of materials and activities are Code compliant as an ongoing standard.

We believe this would demonstrate to the PMCPA the improvements that have been made and give the confidence that Britannia continues to remain committed to the process, and always acts with high integrity for the ultimate benefit to the patients.

Summary

Britannia queries EVER Pharma's intentions when they concluded the intercompany dialogue as unsuccessful. Britannia have responded to EVER Pharma's allegations and have repeatedly provided assurances that we do not proactively initiate patients on APO-go® at home. With regards to the symposium, we have provided an undertaking in both our responses dated 18th December 2023 and 18th January 2024 that we will not promote home initiations at any meetings. Britannia would like to point out that historically EVER Pharma has been in several intercompany dialogues with Britannia and the approach adopted has been inflammatory with allegations appearing to be made with an intention to disparage Britannia as a competitor which does not align with the spirit of the Code nor as a member of the ABPI.

To conclude, Britannia hopes that we have sufficiently addressed all the concerns raised by EVER Pharma and we continue to make every effort to engender a culture of Compliance and to adhere with the ABPI Code requirements in all its interactions and not repeat any of our historical mistakes. We firmly therefore refute EVER Pharma's suggestion of a breach of Clause 2."

PANEL RULING

This complaint relates to alleged off-licence promotion of Britannia Pharmaceuticals Ltd's (Britannia) product APO-go (apomorphine hydrochloride) through its Nurse Service and at sponsored meetings. The complaint to the PMCPA follows intercompany dialogue between Britannia and EVER Pharma UK Ltd (EVER Pharma) both of whom provide a product with the

active pharmaceutical ingredient, apomorphine, for the treatment of Parkinson's Disease. For both companies, support of a Nurse Service may be offered in connection with the treatment.

The Panel noted that Britannia made references to previous PMCPA audit's and considered the present case solely on the evidence before it.

Britannia's Nurse Service

The Britannia Nurse Service operates under the clinical governance of the NHS. Specialist nurses are employed by Britannia and individually contracted to NHS Trusts to provide therapy support to patients with Parkinson's Disease. The Specialist Nurses report to the Medical Director at Britannia solely for employment and administrative purposes; Britannia submit that they do not direct, influence or control the clinical services provided by the Specialist Nurse to the NHS Trust's patients stating that they make the Specialist Nurses available and cover the costs. This arrangement is classified as a package deal.

For relevant patients with Parkinson's Disease, the prescribing healthcare professional decides if the patient should commence treatment on apomorphine. Patients are pre-treated with domperidone to reduce nausea and then undergo a response test to determine positive clinical effects. The response test is a subcutaneous injection of apomorphine to evaluate a patient's clinical response and any adverse events. Section 4.2 of the SmPC for APO-go states:

> "Apomorphine should be initiated in the controlled environment of a specialist clinic. The patient should be supervised by a physician experienced in the treatment of Parkinson's disease (e.g. neurologist)."

Britannia submitted that the COVID-19 pandemic created a number of challenges around the provision of apomorphine treatment and there were long waiting lists to start the treatment. To avoid delays in patients receiving treatment, one NHS Trust implemented protocols for initiation of apomorphine infusion therapy in the patient's home. The Britannia Nurse Service were part of the team ensuring continuity of care and in response to an unsolicited request in writing by the prescribing healthcare professional, would provide home initiation. Britannia submitted that under no circumstances must the Nurse Service proactively offer home initiation of APO-go. Britannia further submitted that home initiation is not routine and that out of the 169 hospitals that the nurse team have contracts with, only 17 have requested home initiation.

EVER Pharma allege that Britannia have made a commercial decision to facilitate the home initiation of patients on to its APO-go product outside the requirements of the SmPC, which Britannia strongly refutes.

The Panel acknowledged the unique circumstances of the COVID-19 pandemic and the need for health professionals to adapt to ensure continuity of care. It considered however, that the UK was no longer beholden to those restrictions and that it could not be used as a reason to circumvent the Code.

Both Britannia and EVER Pharma agree that a home setting would not be considered a "controlled environment of a specialist clinic". This interpretation is further supported by an email from the MHRA to EVER Pharma confirming this position and that this would be considered off-label practice. Britannia provided assurance that its personnel do not actively promote home initiations as routine procedure.

Clause 11.2 is clear that promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its summary of product characteristics. The Panel noted, in general terms, that a package deal was a commercial arrangement and therefore promotional.

The Panel considered the evidence available to them. Home initiation began by certain NHS Trusts in response to a unique set of circumstances during the COVID-19 pandemic but it appeared that this approach had continued after the pandemic. Britannia was aware of this continued practice because of the ongoing requests to its Nurse Service for home initiation. Brittania confirmed in their response that 17 Trusts have requested home initiation but were unable to provide further data around how many patients this includes explaining that Britannia does not hold any data on the total number of home initiations as this is not a routine practice for its nurses as treatment is not initiated by them. The Panel also bore in mind Britannia's submission that not all requests received would result in an initiation. It appeared to the Panel that approximately 10% of the hospitals the nurse team have contracts with had requested home initiation.

Britannia provided a template package deal agreement between Britannia and an NHS Trust dated March 2024 setting out the scope of the package deal. The section headed Referral Process Reference stated that the NHS Clinical Team will direct whether the service should be provided in the NHS Trust clinic or in the patient's home. A subsequent bullet point referred to the Britannia pre-treatment review on suitability for referral and referred to initiation at the patient's home if directed by the prescribing health professional. The Panel noted that the agreement appeared to attach equal weight to clinic and home initiation although the latter only took place at the request of the prescribing health professional. Whilst the Panel accepted that the nurse service operated under the governance of the NHS Trust the agreement indicated that it was offered to the NHS Trust on the basis that home initiation was an acceptable option in certain circumstances. The Panel concluded that Britannia were therefore aware at the outset of the arrangements that a Trust might initiate apomorphine in the home environment as reflected in the agreement which was inconsistent with its marketing authorisation.

The Panel was mindful that apomorphine required careful evaluation on initiation in a clinical setting due to the serious nature of potential adverse effects. The Panel considered whether this was a truly arm's length arrangement in relation to home initiation given the reference to it in the agreement irrespective of reporting lines. Although it was solely the Trust's decision to provide home initiation, it was a service provided by Britannia as part of a commercial package deal on the basis that home initiation was an acceptable option in certain circumstances. The Panel concluded, on balance, that Britannia had thereby promoted APO-go in a manner that was inconsistent with the particulars listed in its SPC and therefore ruled **a breach of Clause 11.2**.

<u>Britannia sponsored meetings</u>

EVER Pharma also raised concerns about off licence promotion of APO-go at a Britannia sponsored symposium that took place during the Parkinson's Disease Nurse Specialist Association meeting in [date] 2022. The speaker shared 10 slides, one of which was published data from the APOKADO study and others which detailed the speaker's own experience with home initiations in France and the UK. The title of the APOKADO study was "Feasibility and benefits of home initiation of subcutaneous apomorphine infusion for patients with Parkinson's disease: the APOKADO study". Britannia accepted that the inclusion of the APOKADO study

may have given the impression that the intent was to promote home initiation. The Panel agreed.

Having concluded that home initiation of APO-go was inconsistent with the particulars listed in the SmPC the Panel considered that the presentation of data from the APOKADO study at a promotional meeting was contrary to the requirements of Clause 11.2 and the Panel ruled a **breach of Clause 11.2** accordingly.

Clauses 5.1 and 2

Turning to the conduct of the company and whether Britannia had maintained high standards, the Panel noted its rulings of breaches of Clause 11.2 above. The Panel was concerned that home initiation had been referred to in the template agreement with the NHS Trust despite the safeguards in the SPC about initiation in a clinical setting. The Panel considered that high standards had not been maintained and ruled a **breach of Clause 5.1.**

The Panel also considered the allegation of a failure to maintain high standards in relation to the Britannia sponsored symposium. Overall, the Panel; was concerned that the inclusion of the APOKADO study in the presentation may have given the impression that the intent was to promote home initiation, bearing in mind that it promoted a prescription only medicine for an initiation method that was not licensed. The Panel considered it was apparent in managing the arrangements for this meeting that Britannia had failed to maintain high standards and ruled a **breach of Clause 5.1**.

The Panel noted that the complainant alleged a global breach of Clause 2 in relation to all matters raised. A ruling of a breach of Clause 2 is a sign of particular censure and is reserved for such circumstances. The Panel noted the steps taken by Britannia to ensure changes have been made since the symposium took place. The Panel also took into consideration the unusual structure of the Nurse Service including that the nurses reported into the Trust for all governance and clinical matters. The Panel considered that its ruling of a breach of Clause 5.1 was therefore proportionate and sufficient to cover the concerns raised in the complaint. The Panel ruled **no breach of Clause 2**.

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Complaint received **13 March 2024**

Case completed **4 June 2025**