CASE/0270/08/24

COMPLAINANT v THERAMEX

Alleged promotion of an unauthorised indication for linzagolix

CASE SUMMARY

This case was in relation to a Theramex-sponsored symposium and exhibition stand relating to Yselty (linzagolix). The complainant alleged that information presented at the World Congress of Endometriosis created the misleading impression that linzagolix had obtained a licensed indication for the treatment of endometriosis.

The outcome under the 2021 Code was:

Breach of Clause 2	**Bringing discredit upon, and reducing confidence in, the pharmaceutical industry**
Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 6.1 (x2)	**Providing misleading information**
Breach of Clause 11.2 (x2)	**Promoting a medicine for an unlicensed indication**

No Breach of Clause 11.1	**Requirement that a medicine must not be promotion prior to the grant of its marketing authorisation**

This summary is not intended to be read in isolation.
For full details, please see the full case report below.

FULL CASE REPORT

A complaint about Theramex HQ UK Ltd was received from a contactable complainant who described themselves as a doctor.

COMPLAINT

The complaint wording is reproduced below:

> "I am writing to express my concern regarding Theramex's promotion of the drug linzagolix at the World Congress of Endometriosis held in Edinburgh in 2023. During a company-sponsored symposium titled 'GnRH Antagonists in the Treatment of Uterine Disorders,' Theramex speakers presented information not only on uterine fibroids but also on endometriosis, referencing data from the phase 3 EDELWEISS trial and other related studies.
>
> My colleagues and I attended this symposium under the impression that it was a promotional and sales-focused session, as it was held by Theramex, a company known

> for its products in women's health. Based on the presentations, we left the meeting with the understanding that linzagolix had obtained a licensed indication for the treatment of endometriosis. However, at the [named gynaecological endocrinology congress] in [location] in 2024, I was informed by Theramex personnel at their allocated booth that linzagolix does not currently hold a license for treating endometriosis.
>
> I was disappointed to learn this, as the information presented at the World Congress of Endometriosis strongly suggested that linzagolix was approved for this indication. This discrepancy raises serious concerns about the accuracy and transparency of the information provided by Theramex during its promotional activities and the risk to patient safety if patients are prescribed products that do not have a licenced indication.
>
> Given that this was a promotional symposium, I am troubled by the apparent omission of clear communication regarding the licensing status of linzagolix for endometriosis. The fact that Theramex had a promotional stand at a congress dedicated entirely to endometriosis further reinforced the belief that linzagolix was being promoted for this condition. The lack of clarification from Theramex during the Edinburgh symposium has left my colleagues and me feeling misled about this product's status.
>
> Please investigate this matter further to determine whether the promotion of linzagolix at the World Congress of Endometriosis complied with regulatory guidelines. Healthcare professionals must receive accurate and transparent information to make informed decisions regarding patient care. Without this principle, patient safety will be placed at risk.
>
> Thank you for your attention to this matter. I look forward to your response and any actions that may be taken to address this issue."

When writing to Theramex, the PMCPA asked it to consider the requirements of Clauses 2, 5.1, 6.1, 11.1 and 11.2 of the 2021 Code.

The case preparation also wrote to Theramex with the following information:

> "[The complaint] relates to matters which pre-date Theramex agreeing to comply with the Code and accept the jurisdiction of the PMCPA. You have, therefore, a choice as to how the complaint is dealt with. The PMCPA does accept such complaints if the matters raised are covered by UK law. However, if Theramex would rather the complaint be dealt with by the MHRA then we would refer the complainant to the MHRA and explain that the activity occurred prior to the company agreeing to comply with the Code/accept the jurisdiction of the PMCPA.
>
> If you do agree for the complaint to be dealt with under the Code, only matters relating to requirements of UK law will be taken forward and any matters relating solely to Code requirements (and not to UK law) will not be taken forward."

THERAMEX'S RESPONSE

Theramex confirmed its agreement for the case to be dealt with under the Code. The response from Theramex is reproduced below:

> "Thank you for your letter dated 15 August 2024, regarding a complaint under the Code of Practice by an anonymous individual who stated that he/she is a healthcare professional.
>
> **The Complaint**
>
> The email correspondence sent to PMCPA indicates that the complainant is concerned that Theramex has promoted linzagolix outside its licensed indication at the World Congress of Endometriosis (WCE), at Edinburgh 2023. The complainant believed that they and their colleagues attended a promotional symposium and left with the impression that linzagolix was currently available for patients with endometriosis. The complainant further stated that there was an apparent omission of clear communication regarding the licensing status of linzagolix for endometriosis and that this might have jeopardised patient care.
>
> You asked Theramex to address the requirements of Clauses 2, 5.1, 6.1, 11.1 and 11.2 when responding to the complaint and to provide copies of the presentation at the company-sponsored symposium at WCE, details on how the material was used, the product's SmPC, briefing materials and instructions given to the speakers, and standard operating procedures/ policies.
>
> **Summary response to the complaint**
>
> Patient safety is of paramount importance to Theramex. Accordingly, we have taken this complaint very seriously and conducted a thorough internal review of the issues raised by the complainant and the matters PMCPA has asked us to address in our response.
>
> Theramex takes its obligation under the ABPI Code of Practice very seriously. All of the activities conducted at the WCE congress were intended to be in accordance with Theramex's Sponsorships of Congresses and Educational Events SOPs and the Theramex Code of Conduct.
>
> Following this review and analysis, we have seen no evidence indicating that patient safety has been put at risk. The product (Yselty) was not available anywhere in the world in 2023 and therefore, could not be prescribed to patients.
>
> Importantly, our review shows that robust procedures are currently in place to ensure that all representatives who attend congresses abide by the standards required. However, while we have appropriate policies and procedures in place, it has come to light that some activities carried out at WCE 2023 may not have met the Code's and our own internal requirements in all respects.

The fact that some activities may have fallen short of our required standards had been recognised by us several months before this complaint was sent to PMCPA, and the necessary corrective measures have already been taken.

Our Approval SOP is currently undergoing revision to further strengthen compliance requirements within the organisation. Key changes include better clarity on roles and responsibilities, additional cross functional meetings and introduction of concept document meetings for larger-scale activities, including the organisation of symposia and congress activities.

The licensing status of Yselty (linzagolix)

Yselty (linzagolix) received a license from the European Medicines Agency (EMA) for the treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age on the 14th June 2022. The UK marketing authorisation was subsequently granted by the Medicines and Healthcare products Regulatory Agency (MHRA) via the European Commission Decision Reliance Procedure on the 27th June 2022.

Yselty is currently undergoing assessment by the Committee for Medicinal Products for Human Use (CHMP) use in endometriosis.

The symposium

Theramex sponsored a company symposium during the WCE conference, on the 5th May, 2023, from 12:00–13:00. The symposium's title reads in full: 'The promise of GnRH antagonists in the treatment of endometriosis and related uterine disorders'.

The symposium was certified as a non-promotional event for healthcare professionals (HCPs), to share data related to endometriosis. We have attached both the presentation slides that were used along with the certificate for this activity.

There were four sections to the presentation, which we have included below with a summary:

- Welcome and introduction
    - History and management of endometriosis
- GnRH antagonists – treatment of choice for endometriosis and related uterine disorders
- Efficacy and tolerability of new GnRH antagonists in the treatment of endometriosis and related uterine disorders
- Question and answer session

Since it was our intention to discuss uterine health, slides pertaining to the uterine fibroid indication were also included in this presentation. We acknowledge that this might have given the impression that this was a promotional symposium, when it was intended to be a legitimate exchange of scientific information concerning the current and emerging treatment of endometriosis.

Speaker contracts and briefing for the symposium

All the speakers entered into appropriate contracts and received a speakers' briefing. The speakers' briefing included a section on uterine fibroids. Although this was not the subject of the complaint, we acknowledge that clinical data for an approved indication should not have been included while discussing another that has not.

Person(s) certifying material.

The person certifying the material listed above was:

- [details provided]

Potential breaches of the ABPI Code of Practice

You asked Theramex to consider the provisions of Clauses 2, 5.1, 6.1, 11.1 and 11.2 our response to the complaint. We address these clauses of the Code below.

Clause 6.1

Clause 6.1 of the Code concerns the provision of appropriate and balanced information.

Although the intent of the symposium was to have a legitimate exchange of scientific discussion regarding the current and emerging treatments available for endometriosis and other uterine disorders, we accept that more prominence could have been given to data on the two competing products.

It was our intention to share the latest data concerning Yselty for treatment of endometriosis from a recently completed phase III trial. It is disappointing that additional data from competitors were not discussed to ensure the audience had a comprehensive view of the entire data set available for the class of medicines of which linzagolix is a part.

The data provided during the symposium for Yselty was an up-to-date representation of the phase III clinical trial and does not contravene the above Clause. Nevertheless, the balance of information was not divided equally amongst all members of the class of medicine. We therefore accept a breach of Clause 6.1.

Clause 11.1

Clause 11.1 states that a medicine must not be promoted prior to granting of its marketing authorisation.

Theramex did not seek to promote the use of Yselty in endometriosis. The objective of the symposium at WCE was to legitimately share scientific information for products that are currently used to treat the condition, as well as emerging treatments.

The supporting materials for the symposium were reviewed and certified as non-promotional items. Therefore, we do not believe that we have breached Clause 11.1.

Clause 11.2

Clause 11.2 concerns the promotion of the medicine per its marketing authorisation.

The symposium at WCE was not a promotional event; it was a legitimate exchange of scientific data on current treatment and emergent options for endometriosis. The focus of the meeting was on endometriosis.

The symposium flyer was also reviewed and certified as a non-promotional item as the objective was to share new data for Yselty when used to treat endometriosis. The flyer contained the disclaimer, 'This education symposium has been organized and funded by Theramex', thus clearly indicating Theramex's intent on the nature of this non-promotional activity. Therefore, we do not believe that we have breached Clause 11.2.

Clause 5.1

Clause 5.1 of the Code concerns the obligation to maintain high standards.

While all the material used at the WCE conference was reviewed and certified by the appropriate individuals, we recognise that there may have been instances where more could have been done to meet the standards expected by the Code and by ourselves. This had been recognised, and since Q2 last year, we have introduced compliance trainings, concept meetings, and have conducted a robust review of all our internal policies and SOPs.

While our investigations do not indicate that any patients experienced adverse events, as the product is not yet available on the market, we recognise the highest standards were not met in this instance. Therefore, we accept a breach of Clause 5.1.

Clause 2

Clause 2 of the Code concerns activities which bring the industry into disrepute. A finding of breach of Clause 2 is reserved for the most severe breaches of the Code. We accept that data on an approved indication should not have been included in a presentation to HCPs on data for an unapproved indication, and that a better balance should have been struck between data relating to linzagolix and other GnRH antagonists. However, we do not think that these shortcomings go so far as to bring the industry into disrepute.

All materials currently used by Theramex HQ for international conferences comply with the Code's provisions.

We are not aware of any evidence of patient's safety has been jeopardised as a result of the matters discussed above.

Well before the date of this complaint, we have recognised that while our procedures were robust, improvements could still be made. We have therefore made substantive revisions to our processes. We are confident that the measures we have instituted and are continuing to implement will ensure that our materials and other activities are fully

compliant in the future. Therefore, we do not believe there has been a breach of Clause 2."

FURTHER INFORMATION FROM THERAMEX

After giving preliminary consideration to the case, the Panel asked Theramex to note the complainant's allegation: "*The fact that Theramex had a promotional stand at a congress dedicated entirely to endometriosis further reinforced the belief that linzagolix was being promoted for this condition*" and to provide a copy of the 'promotional stand' in question and the briefing materials for the company employees attending the congress.

The response from Theramex is reproduced below:

"I write further to your request for additional information in Case/0270/08/24 and attach the following in the covering email to this letter:

- A high quality image of the booth panel which related to Yselty
- The briefing document for our employees attending the WCE 2023.

The focus of the exhibition stand is clearly on the licensed indication (fibroids), with no mention of any other indication and no signposting to the completely separate and educational symposium which focused on the topic of endometriosis.

Further, the company briefing clearly directs staff to remain on label; and to redirect any off-label questions to the medical team for reactive management. You will also not that the information in the briefing regarding endometriosis is focused completely on the facts related to the symposium and medical poster and that this information is immediately followed by a reminder about the SPC content, including the licensed indication and key safety data.

For these reasons and those stated in our letter six months ago, we categorically refute any breaches of promotion outside the licensed indication."

PANEL RULING

This case concerned a Theramex-sponsored symposium and exhibition stand relating to Yselty (linzagolix) at the World Congress of Endometriosis in May 2023.

Yselty (linzagolix) was a gonadotropin-releasing hormone (GnRH) receptor antagonist indicated for the treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age.

The Panel noted that the event took place before Theramex had accepted the jurisdiction of the PMCPA. Nonetheless, the Panel bore in mind the well-established principle that if the subject matter of a complaint might fall within the scope of UK law, such as the promotion of a medicine in a manner inconsistent with its summary of product characteristics, the matter would be considered under the Code in the usual way.

Sponsored symposium

The complainant alleged that information presented at the Theramex-sponsored symposium created the misleading impression that linzagolix had obtained a licensed indication for the treatment of endometriosis.

The symposium at issue was titled “The promise of GnRH antagonists in the treatment of endometriosis and related uterine disorders”. The presentation comprised 96 slides in total, divided into the following sections:

- Title slide, disclosures, faculty and agenda (4 slides) – Speaker 1
- “Introduction – history of the management of endometriosis” (12 slides) – Speaker 1
- “GnRH antagonists – treatment of choice for endometriosis and related uterine disorders” (36 slides) – Speaker 2
- “Efficacy and tolerability of new GnRH antagonists in the treatment of endometriosis and related uterine disorders” (41 slides) – Speaker 3
- Q&A, summary slide and thank you slide (3 slides)

The Panel had no information about what the presenters said during the presentation and could rule only on the content of the slides and briefing materials. Of the 96 slides, 39 made explicit mention of linzagolix or details of a linzagolix trial, with a further 18 slides making explicit mention of GnRH antagonists. The briefing for Speaker 2 included the instruction to “Discuss the 3 agents – for the treatment of UF, Adenomyosis and Endometriosis”. The briefing for Speaker 3 included no mention of uterine fibroids (it was focused on endometriosis and adenomyosis) and included the instruction to include a “Summary of new data for the three products”, which the Panel understood to be linzagolix, elogolix and relugolix.

The Panel examined the content of the symposium slide deck and considered whether the presentation complied with the requirements of Clause 6.1 which included, among other things, that information, claims and comparisons must not mislead.

The Panel noted a number of references referred to linzagolix being “approved in EU and UK for treatment of moderate-to-severe symptoms of uterine fibroids in adult women of reproductive age”.

Slide 20, which was almost identical in content to slides 63, 67, 71 and 74, was titled “Oral GnRH antagonists” and displayed a prominent visual layout presenting chemical structures of three GnRH antagonists: elagolix, relugolix and linzagolix. Corresponding footnotes for the structures of elagolix and relugolix included that they were licensed in the US for moderate to severe pain associated with endometriosis, while the footnote for linzagolix stated that it was “approved in EU and UK for treatment of moderate-to-severe symptoms of uterine fibroids in adult women of reproductive age.” The Panel noted slides 67, 71 and 74 preceded slides on clinical trials for the three GnRH antagonists in endometriosis, none of which appeared to have a UK licence for that indication at the time of the symposium. In the context of a congress and symposium focused on endometriosis, the Panel considered that positioning linzagolix in such a manner with two other oral GnRH antagonists licensed for endometriosis in the US, may have implied that linzagolix would also be suitable for such use.

Slide 29 and 75 described linzagolix as “approved in Europe & UK for the treatment of moderate-to-severe symptoms of uterine fibroids in adult women of reproductive age” and also included that it was “in development for the treatment of endometriosis associated pain”, with

slide 75 stating linzagolix was the “only GnRH antagonist being developed with two dose options”.

While the Panel noted reference to the licensed indication on seven slides, along with two slides that included that linzagolix was in development for the treatment of endometriosis associated pain, the Panel considered the overall impression of the slides. The Panel noted the second section of the symposium was titled “GnRH antagonists – **treatment of choice for endometriosis** and related uterine disorders” (emphasis added by Panel) and 22 of the 36 slides in this section explicitly mentioned linzagolix. Notably, one of the final slides, slide 92, included the statement “Endometriosis is not completely curable but there **are** NEW treatment options for related pain and infertility” (emphasis added by Panel).

In the Panel’s view, the small number of references to linzagolix being indicated for treatment of uterine fibroids and being only in development for treatment of endometriosis associated pain did not negate the misleading impression given that linzagolix was a suitable treatment option in endometriosis. The Panel therefore ruled a **breach of Clause 6.1**.

While the Panel noted Theramex acknowledged a breach of Clause 6.1, this was on the basis that “the balance of information was not divided equally amongst all members of the class of medicine”. The Panel noted the complainant’s allegation with regard to Clause 6.1 was in relation to the misleading impression that linzagolix was licensed for endometriosis, as ruled upon above. The Panel therefore made no ruling of Clause 6.1 regarding the balance of information.

In relation to Theramex’s submission that the symposium was certified as non-promotional, the Panel noted its findings above and took particular account of the content of the section of the symposium titled “Efficacy and tolerability of new GnRH antagonists in the treatment of endometriosis and related uterine disorders”. The Panel noted that slides 74 to 82, 84, and 86 to 89 were dedicated to linzagolix. For example:

- Slide 76 showed a screenshot of a scientific journal article titled “Treatment of endometriosis-associated pain with linzagolix, an oral gonadotropin-releasing hormone-antagonist: a randomized clinical trial” and slide 77 presented data from this trial.
- Slide 78 showed a screenshot of a scientific journal article titled “Profile of Linzagolix in the Management of Endometriosis, Including Design, Development and Potential Place in Therapy: A Narrative Review” and slides 79 (titled “Linzagolix and endometriosis (Phase 3)”), 81 and 82 presented data from this trial (the EDELWEISS trial referred to by the complainant).

The Panel noted Theramex’s submission that the sponsored symposium was intended to be “a legitimate exchange of scientific information concerning the current and emerging treatment of endometriosis”.

The Panel noted the Code permitted companies to undertake certain activities with regard to unlicensed medicines, such as the legitimate exchange of medical and scientific information during the development of a medicine, provided that this did not constitute promotion. To avoid being seen as disseminating data to expand the product’s use, i.e. promotional and in breach of the Code, the activity must not be a one-way flow of information.

The symposium had taken place in the context of a scientific congress and while the Panel considered that this was an appropriate setting, this alone did not guarantee compliance with the Code.

The Panel noted Yselty (linzagolix) had a license for the treatment of uterine fibroids and that of the 1-hour symposium, 50 minutes related to presentation time with only 10 minutes for "Q&A and Close" which would have been in relation to the content presented. In this regard, the Panel considered the symposium which discussed the use of linzagolix for endometriosis was such that it could not benefit from the exemption in the Code in relation to the legitimate exchange of medical and scientific information.

The Panel took account of the circumstances, including the content of the slides, and considered the symposium could not be seen as anything other than the promotion of Yselty (linzagolix) for endometriosis. Yselty (linzagolix) was not licensed for use in endometriosis at the time of the symposium. In the Panel's view, the symposium had promoted linzagolix outside of the terms of its marketing authorisation. The Panel ruled a **breach of Clause 11.2**.

Clause 11.1 related to the promotion of a medicine prior to the grant of its marketing authorisation. Noting that Yselty had a marketing authorisation at the time of the symposium, the Panel ruled **no breach of Clause 11.1**.

Exhibition stand

The Panel noted the allegation that Theramex's promotional exhibition stand at a scientific congress dedicated entirely to endometriosis reinforced the impression that linzagolix was being promoted for this unlicensed indication.

The Panel reviewed the visual material provided which included a booth panel that appeared to be approximately 3 metres tall and 2 metres wide. The panel featured a prominent Yselty brand logo along with Theramex's corporate logo at the top. In the centre of the booth panel was the following text in a font with a capital height of approximately 1.5 cm:

"This medicine is authorised for use in the European Union.
Yselty is indicated for the treatment of moderate to severe
symptoms of uterine fibroids in adult women of reproductive age."

Towards the bottom of the panel, in similar font size, was the adverse events reporting statement and the statement "Prescribing information is available at the booth", along with the job code and date of preparation.

The Panel noted that the booth text made no reference to endometriosis and that the licensed indication for uterine fibroids was included. However, the Panel considered that the reference to the indication appeared in small text, in a manner that was not prominent, and may have been overlooked in the wider context of the endometriosis congress.

It was not clear to the Panel what other information, if any, was presented or provided on Theramex's promotional stand. In this regard, the Panel reviewed the briefing slides provided by Theramex for employees attending the congress.

The Panel noted that the employee briefing slides displayed the title and agenda of the Theramex sponsored symposium, ruled upon above, along with an image of a flyer. It was unclear to the Panel how, where, or whether this material would be disseminated from the booth.

Similarly, while images of a "Linzagolix Booth Infographic" titled "Considering the diverse needs of women with uterine fibroids" were included in the briefing, no information was provided on its use. The Panel considered this appeared to be a leavepiece offered at the stand, noting the inclusion of the note "Bijuve and Zoely LP also available".

The briefing document went on to highlight an oral and poster presentation, which included authors from Theramex, that were being presented at the congress and related to linzagolix phase 3 clinical trial data for endometriosis-associated pain; no written instructions were provided in relation to these, such as whether visitors were to be directed to these.

The Panel noted that representatives were instructed to remain on-label, and that any "unsolicited questions relating to unlicensed use" would be redirected to medical teams for reactive management. However, the Panel considered, in the context of an endometriosis-focused congress, Theramex's booth would, on the balance of probabilities, solicit questions about Yselty in endometriosis.

In the Panel's view, the presence of the exhibition stand at issue, at a congress themed entirely around endometriosis, promoted Yselty (linzagolix) for the treatment of endometriosis and created a misleading impression that it was licensed for that indication which was not so. The Panel ruled **breaches of Clauses 6.1 and 11.2**.

Overall

The Panel noted its rulings above that the overall impression from both the symposium and the exhibition stand was that Yselty (linzagolix) was approved and suitable for the treatment of endometriosis, which was not so; at the time of the symposium, linzagolix was only authorised for the treatment of moderate to severe symptoms of uterine fibroids. The Panel considered Theramex had failed to maintain high standards in this regard and ruled a **breach of Clause 5.1**.

The supplementary information to Clause 2 listed prejudicing patient safety as an activity likely to lead to a breach of this clause. The Panel took account of Theramex's submission that there was no evidence that patient safety had been put at risk as Yselty was not available anywhere in 2023 and, therefore, could not be prescribed to patients. However, the Panel was concerned about the appropriateness of promoting a medicine prior to its availability, particularly where that promotion related to an unlicensed indication.

The Panel noted that Yselty had been promoted at a scientific congress dedicated to endometriosis. The sponsored symposium was partly focused on discussing the use of linzagolix and other GnRH antagonists in endometriosis – the speakers had been specifically briefed to discuss linzagolix outside of its marketing authorisation.

The Panel noted with concern that Theramex had certified the symposium as non-promotional, yet it included extensive discussion and presentation of data regarding the use of linzagolix – in both its licensed indication and in endometriosis. The company had failed to recognise that the

content of the symposium was clearly promotional. In the Panel's view, the failure to recognise the distinction between promotional and non-promotional activities demonstrated a lack of awareness of the Code.

Taking into account the cumulative effect of its comments and findings above, the Panel considered that Theramex's promotion of Yselty outside of its marketing authorisation at a scientific congress dedicated to endometriosis fell short of competent care; an unlicensed indication had been promoted to health professionals and this brought discredit upon and reduced confidence in the pharmaceutical industry. The Panel ruled a **breach of Clause 2.**

Complaint received **14 August 2024**

Case completed **14 May 2025**