South East London Integrated Medicines Optimisation Committee (SEL IMOC) Meeting
Thursday 21st March 2024, 2:00pm-4:30pm (Meeting held via MS Teams)
FINAL Minutes

1. Welcome, introductions and apologies

The Chair welcomed attendees to the meeting. Apologies and observers were noted.

2. Conflict of interests – declarations and DOI refresh

The Chair asked that any conflicts of interest with the meeting agenda be declared and that any outstanding declarations be returned. No conflicts were raised.

3. Detailed action notes of the last meeting, minutes, and action log:

The notes were accepted as an accurate record of the meeting subject to the correction of minor formatting and typographical errors. Members were provided with an update on progress against actions due for this month, these were noted, and items closed were agreed.

4. Formulary submission: Ospemifene for moderate to severe symptomatic vulvar and vaginal atrophy in a select cohort of post-menopausal women

This formulary submission originates from a consultant gynaecologist at GSTT. The application requests the use of ospemifene (Senshio™) for initiation within menopause clinics as a second line treatment option for postmenopausal women with moderate to severe symptomatic vulvar and vaginal atrophy (VVA), which is in line with the licensed indication. The application notes that use would be restricted to those in whom vaginal oestrogen therapy is contraindicated or has failed. The application requests an Amber 2 “Red, Amber, Green, Grey” (RAGG) category.

- **Evidence Review**

The formulary pharmacist provided an overview of the evidence base - a detailed evidence review was provided within the meeting agenda pack covering background to the condition, a review of the evidence base with strengths and limitations and rationale for use of ospemifene in this setting. The information presented also included the estimated resource impact for ospemifene in this setting. The resource impact of the submission is within the financial threshold that the Committee has delegated authority to approve. Ospemifene is licensed for the treatment of moderate to severe symptomatic VVA and reduces symptoms including vaginal dryness and dyspareunia. Currently topical oestrogen is the standard pharmacological treatment for the symptoms of vaginal atrophy related to oestrogen deficiency in postmenopausal women and several preparations are available on the SEL formulary. Some vaginal oestrogen products are not recommended in patients with a history of hormone sensitive cancer, and therefore ospemifene may be suitable in these patients. The formulary application specifically requests use of ospemifene in women not eligible for vaginal oestrogen therapy.

Guidance from the National Institute for Health and Care Excellence (NICE) for the diagnosis and management of menopause was last updated in December 2019 and pre-dates the availability of ospemifene. It recommends vaginal oestrogen is offered to women with urogenital atrophy (including those on systemic HRT) and advises that treatment may be continued for as long as needed to relieve symptoms.

Two pivotal trials found ospemifene was associated with significant improvements in physiological parameters (including vaginal maturation index and vaginal pH), and improved patient-reported symptom scores for vaginal dryness and dyspareunia compared with placebo. A large systematic review (44 studies, of which 6 were randomised controlled trials comparing ospemifene to placebo) found ospemifene was associated with similar efficacy and safety outcomes to vaginal oestrogen preparations, and superior to lubricants for most outcomes. Whilst the pivotal studies were of good quality, limitations include the lack of direct active comparator evidence, and the short-term nature as they were limited to 1-year duration. Overall, ospemifene appears to be a well-tolerated and safe option for women, however, longer term data are presently lacking and therefore the longer-term risks remain to be quantified. Longer term studies are underway and may help further define this. The most commonly reported side effects with ospemifene are vulvovaginal candidiasis and other mycotic (fungal) infections, hot flushes, headache, muscle spasms, mild

vaginal bleeding, vaginal and genital discharge, and rash. The contraindications to the use of ospemifene were noted in the evidence review, in line with the product's summary of product characteristics (SmPC).

- **Applicants' presentation**

The applicant was in attendance to present the submission and field any questions. The applicant's declaration of interest was noted. Ospemifene is an oral treatment and taken at a dose of 60mg daily for VVA, which is commonly associated with other symptoms such as dyspareunia and urinary tract infections. The applicant outlined that use is intended in line with the licensing for patients but in a specific cohort of people where there would be a preference for an oral preparation or it would be advantageous over topical treatments, for example, in those who are not dexterous enough to insert treatments vaginally. Currently ospemifene is not licensed for women with breast cancer, however the hope is that in future, evidence will be available to demonstrate its safety and efficacy in this cohort of patients.

Committee members requested clarity on the patient cohort in which ospemifene is being proposed for use in, given the difference between the applicant's presentation and what is stated in the application form. If use is intended as first line for those with a preference for oral agents, this could result in a higher number of patients across SEL being treated compared to the estimates in the application and therefore overall costs, as ospemifene has a higher acquisition cost compared to standard topical treatments. The applicant explained a high number of patients is unlikely if used in those where the use of ospemifene would be more practical as treatment is initiated on a risk-benefit basis, and ospemifene also provides a treatment option for patients with a history of oestrogen/hormone sensitive cancer. The applicant agreed to discuss some focused criteria for the use of ospemifene outside of the meeting.

Acknowledging that long-term safety data are lacking, the applicant responded to a query regarding whether there are safety concerns that the drug class is not novel and there is sufficient safety information about drugs within this class (the SERMs, such as raloxifene). The applicant also proposed that the service would audit all patients and include information on safety and side effects and would be happy to report back to the Committee if ospemifene is approved. The applicant confirmed the data returned would include patient numbers initiated on treatment to provide some assurance on patient numbers, following concern that the numbers estimated in the application may be an underestimate.

As the product information for ospemifene notes that it should only be initiated in patients with symptoms that adversely affect quality of life e.g., vaginal dryness and pain during sex, members queried if any quality-of-life criteria would be used to determine which patients are eligible for initiation and what stopping criteria would be applied. The applicant responded that a pre-appointment questionnaire (such as MENQOL - Menopause-specific Quality of Life Questionnaire) will be used to gather quality-of-life information in relation to symptoms, to support treatment initiation. Once treatment is started, patients will be reviewed at 3, 6 and 12 months and treatment discontinued if it is not effective or not tolerated. The request is for an Amber 2 category and primary care would be requested to take on prescribing after the first prescription.
The applicant agreed that if ospemifene is approved for use in this setting the Acute Provider Collaborative menopause guideline will be updated to reflect the approval.

- **IMOC discussion after departure of the applicant**

Members discussed the application and agreed that the current initiation criteria described by the applicant are broader than the application outlined and that more focused criteria required confirmation. In the absence of more defined criteria, Committee members felt that patient numbers would be unpredictable and higher than the number anticipated in the application. Members agreed that an audit will be necessary to review the numbers of patients initiated on ospemifene, whether use in line with any agreed criteria and what the outcomes are (including efficacy and safety). Members discussed the first review and agreed that the first review at 3 months should be conducted by the initiating specialist as discontinuation could be considered by the specialist at this point. Whilst Committee members were mindful to support the approval of ospemifene as Amber 2 for a time limited period of 1 year, members agreed by consensus to defer a final decision pending clarity on the criteria for use.

ACTION: Formulary recommendation to be drafted and presented at a future meeting once there is clarity on the criteria for use

Post meeting note: *Following communication with the applicant outside the IMOC meeting, the following specific criteria have been agreed by the applicant for initiating ospemifene under the Amber 2 category:*

- *Topical lubricants have been adequately trialled and*
- *At least two topical oestrogen preparations have been adequately trialled, and these have failed to control symptoms and improve quality of life*

5. Clinical Effectiveness South East London (CESEL) primary care depression and anxiety adult guideline and associated formulary requests:

- **Categorisation of duloxetine for the treatment of depression and anxiety as Amber 1 and removal of specialist initiation restriction**
- **Categorisation of escitalopram for the treatment of depression, anxiety and panic disorder as Green and removal of specialist initiation restriction**
- **Formulary inclusion of pregabalin as Amber 1 for the treatment of generalised anxiety disorder (third line option)**

The authors were in attendance to present this Guide, which has been developed collaboratively through the CESEL leads and Medicines Optimisation leads. The Guide has been written using the Maudsley depression and anxiety guidelines, published in 2019. Additionally, updated NICE guidelines on depression were published in 2022 and informed the development of the Guide. The Guide outlines the diagnosis and treatment, including monitoring requirements, for patients with depression and anxiety. The request is for the IMOC to approve the medicines components of the guide and to update the SEL formulary with the following associated formulary requests:

- Categorisation of duloxetine for the treatment of depression and anxiety as Amber 1 and removal of specialist initiation restriction
- Categorisation of escitalopram for the treatment of depression, anxiety and panic disorder as Green and removal of specialist initiation restriction
- Formulary inclusion of pregabalin as Amber 1 for the treatment of generalised anxiety disorder (GAD) (third line option)

The Guide has been consulted via the SEL IMOC and the main amendment post consultation was the inclusion of detailed information on deprescribing. Additionally, in relation to the withdrawal of antidepressants, this has changed from the 50% dose reduction recommended by NICE to a slower withdrawal of 25% for reducing/tapering antidepressant doses or deprescribing for safety reasons.
In relation to dose tapering, Committee members queried whether the wording around the use of liquids to support dose tapering could enable some flexibility to help avoid the use of unlicensed specials and wastage. The authors explained practically, many patients will need liquid formulations, especially towards the lower dose titration ranges, flexibility will be easier at the higher dose end ranges. There are resources available from Maudsley and Specialist Pharmacy Services (SPS) that give guidance on the practicality of dose reductions. This can be further clarified within the Guide. Additionally, this will be highlighted as part of the education and training for the Guide at borough level.

The authors will add a link to the SEL Joint Medicines Formulary (JMF) to the treatment page of the Guide to signpost individuals to the formulary where the RAGG categories can be accessed. Members requested that the formulary entry on the JMF makes clear that pregabalin is an Amber 1, third line treatment option for GAD. The Amber 1 category also provides safety precautions as pregabalin can be high risk for abuse especially in this patient cohort as the recommendation to initiate will be from a specialist. It was noted that mirtazapine is not currently RAGG categorised on the SEL JMF, the intention is that it can be initiated by a primary care clinician on the advice of a specialist, meaning an Amber 1 category would be ideal. Members agreed with this by consensus.

In relation to the implementation of the Guide, the authors confirmed there are plans for teaching packs and webinars to be made available to support and educate clinicians. The presenters agreed that overprescribing leads would be involved in this process to ensure overprescribing element is supported as part of any training and education. A question was raised regarding the NICE guidance for panic disorder, which includes imipramine and clomipramine. These medications are currently uncategorised on the SEL JMF, but they are in use. The Committee agreed by consensus to categorise imipramine and clomipramine in this setting as

Amber 2. Prescribing tricyclic antidepressants is not routinely encouraged in this setting and initial prescribing by a specialist would be desired.

Committee members agreed by consensus to approve the medicines elements of the Guide and the formulary requests, pending the amendments discussed. Committee members thanked the leads for developing a comprehensive Guide, which will be useful for both primary and secondary care.

ACTION: Authors to agree wording for the use of liquids during tapering doses with Medicines Optimisation leads
ACTION: Authors to update Guide and return to the IMOC team to progress for ratification via Chair's action
ACTION: SEL JMF to be updated with duloxetine as Amber 1, escitalopram as green, mirtazapine as Amber 1 and pregabalin as Amber 1 (third line option) for their licensed indications and removal of specialist initiation restriction once Guide is approved
ACTION: SEL JMF to be updated to categorise imipramine and clomipramine as Amber 2 for panic disorder once Guide is approved

6. Long-acting injectable (LAI) antipsychotic primary care project update

The Mental Health lead for this project was in attendance to update the Committee on progress, which follows from the results of a primary care survey previously discussed at the July 2022 IMOC meeting. Discussions with local primary care clinicians have occurred to understand the barriers to prescribing LAIs in primary care. The clinicians consulted shared that the availability of a pathway on the use of LAIs in primary care would be useful and support LAI prescribing and monitoring in primary care. The initial plan was therefore to create a pathway that covers both primary and secondary care. Action plans were discussed within implementation teams, and it was recommended that before progressing plans some important areas needed to be reviewed and clarified including:

i. Provision of clarity around LAI use in secondary care and by community mental health teams
The future aim is to standardise common good practice guidance across the local mental health Trusts with a view for it to be available for use in primary care too. The guidance will form the basis for the pathway in primary care. The Guide will be shared with borough leads currently involved in the project for comment and review.
ii. Clarity around prescribing decisions i.e. how LAI's are chosen
A decision aid has been produced which incorporates a table with comparative data for each LAI including continuation rate, available outcome data and available safety information including reports of side effects.
iii. Devising a plan for routine step down to primary care
Each borough within SEL is at a different phase of implementation, but work is progressing in Bromley and Southwark and further updates can be provided to the Committee in the future.

It was agreed that the project would be discussed at the various borough implementation groups to raise the profile of this work and to inform boroughs about the plans. It was agreed that the project would also be included within the SEL Transforming and Integrating Medicines Optimisation (TIMO) 5 Year Forward view.
Post meeting note: *It has been confirmed that this project is already noted in the TIMO Forward View.*

ACTION: Update on long-acting antipsychotic injections (LAI) primary care project to be presented to the Committee in 6 months

7. Updated glucagon-like peptide (GLP-1) analogue pathway for adults aged 18 years and over with Type 2 Diabetes (T2DM) Mellitus (with inclusion of tirzepatide)

The lead authors were in attendance to present this item. The GLP-1 pathway has been updated to incorporate tirzepatide, in line with NICE technology appraisal (TA) 924. The pathway has also been revised following updates to the national advice on managing the GLP-1 analogue shortages. Tirzepatide has dual mode of action as it stimulates the receptors for both glucose dependent insulinotropic polypeptide (GIP) and GLP. The NICE TA for tirzepatide recommends the same criteria for use as the GLP-1 receptor agonists (RAs). The proposed RAGG rating is Amber 2 in line with the other GLP-1 RAs already noted on the formulary. The cost modelling prepared for tirzepatide estimates that the implementation cost in Year 1 (24/25) will exceed the delegated financial threshold that the Committee is authorised to approve. The impact

is estimated to be higher in year 1 due to the impact of the shortages and people being switched to tirzepatide. After Year 1, the cost impact is estimated to fall to within the Committee's delegated financial threshold. As the cost impact in Year 1 exceeds the financial threshold delegated to the Committee, this will need to be escalated to the Executive Committee for information.

The pathway updates included within the agenda paperwork were summarised. The presenter highlighted that additional updates have been made to both the pathway and information sheet after the circulation of the versions within the agenda paperwork. The updates reflect the revised national GLP-1 RA Medicine Shortage Notification (MSN), published on 18th March 2024. The main updates were shared and summarised on screen within the meeting as follows:

- In line with the updated MSN, the pathway and information sheet now note both semaglutide oral tablets (Rybelsus™) and tirzepatide sub-cutaneous injection (Mounjaro™) as alternative GLP-1 analogues for both new patient initiation and for patients unable to access supplies of their existing GLP-1 analogue therapy. The previous MSN only included oral semaglutide tablets.
- Information advising avoidance in patients with personal or family history of medullary thyroid carcinoma and in those with multiple endocrine neoplasia syndrome type 2 (MEN 2), has been moved from the caution section to the contra-indication section in line with the literature.
- Updated information on monitoring of thyroid function with semaglutide tablets.

In response to a query, the presenters confirmed the intention is that in line with the Amber 2 category, specialist teams would initiate the medication and stabilise patients before prescribing is transferred to primary care. Committee members agreed by consensus to approve the updated pathway and information sheet and an Amber 2 category for tirzepatide.

ACTION: Cost modelling on tirzepatide to be escalated to Executive Committee for information

8. Formulary re-categorisation of rivaroxaban and apixaban for left ventricular thrombus (LVT) from Red to Amber 2: presentation of further information

Specialist pharmacists and cardiologists from the three acute Trusts were in attendance to present this item. The use of rivaroxaban in this setting was discussed and approved as Red (hospital only) by the Committee in 2021 and apixaban was subsequently approved for the same indication as Red via the hospital Joint Formulary Committee process (as the application at the time was for hospital prescribing only). In February 2023 an application was made to recategorise rivaroxaban and apixaban from Red to Amber 2, however, the Committee requested further data on use. This is a re-presentation of the request and audit data have been provided in the agenda pack. It was noted that referral pathways have been updated and all patients will be seen in a cardiology clinic within 3 months of discharge. The presenters described that although rivaroxaban and apixaban are used off-label as a 2nd line treatment option in this setting, recent evidence demonstrates that rivaroxaban and apixaban are as effective as warfarin in this setting. This is especially in the post myocardial infarction cohort who tend to also be prescribed dual antiplatelets.

Further information including 2023 European Society of Cardiology acute coronary syndrome guidance, a tertiary centre study conducted in Leeds and a 2021 'No-LVT Trial' was briefly shared and suggests that direct oral anticoagulants (DOACs) are a suitable consideration in this setting, and in some cases pose less risks and complications when compared to warfarin. Since the original request in February 2023, this request has also been supported by the cardiovascular sub-group, who are in support of a recategorisation to Amber 2. The presenters clarified that follow up would be conducted by specialists and prescribing only transferred if patients require longer term treatment. In line with advice from the cardiovascular sub-group, members agreed that there should be a stipulation in the formulary that secondary care will supply until cardiology review (generally 3 to 5 months).

The Committee approved by consensus the recategorisation of apixaban and rivaroxaban from Red to Amber 2 in this setting, in line with the discussions.

ACTION: SEL JMF to be updated to recategorise abixaban and rivaroxaban from Red to Amber 2 in this setting once the formulary recommendation for rivaroxaban has been updated and approved
ACTION: Formulary recommendation 122 rivaroxaban for the treatment of LVT to be updated to Amber 2 in line with discussions

9. Formulary inclusion of Nutrizym 22™ (pancreatin) capsules as Amber 1 to replace Pancrease® HL for the treatment of pancreatic endocrine insufficiency

The formulary pharmacist presented this item and explained that the request was to include Nutrizym 22™ to the formulary as Amber 1 for pancreatic endocrine insufficiency to replace Pancrease® HL on the formulary as it has been discontinued. Creon™ would usually be used as a first line option, however, there have been significant shortages hence the current request. The Committee agreed by consensus to approve the formulary inclusion of Nutrizym 22™ in this setting as Amber 1.

ACTION: SEL JMF to be updated to include Nutrizym 22™ (pancreatin) capsules as Amber 1 to replace Pancrease® HL for the treatment of pancreatic endocrine insufficiency

10. Inclusion of Meflynate XL™ to the paediatric formulary for the treatment of attention deficit hyperactivity disorder (ADHD) in children 6 years and over

The paediatric formulary pharmacist presented this item along with a paediatric consultant who was in attendance. Meflynate XL™ (modified release methylphenidate capsules) will be an additional option to Medikinet XL™, to be prescribed in accordance with its license. It will be considered in new patients that need to be commenced on methylphenidate. By initiating new patients on Meflynate XL™, the remaining supply of other brands could be protected for existing patients. This request was initially prompted by shortages; however, specialists feel Meflynate XL™ would be beneficial as a permanent addition to the formulary as it has some clinical advantages, including more flexible administration options (as it can be taken without food). There is no additional cost expected in primary care from including Meflynate XL™ on the paediatric formulary as it is similarly priced to the existing alternative already on the formulary.
The Committee approved the inclusion of Meflynate XL™ to the formulary by consensus, pending an update to the paediatric shared care guideline for ADHD.

ACTION: Meflynate XL™ to be added to the paediatric formulary for the treatment of ADHD once the shared care guideline has been updated and approved
ACTION: Paediatric ADHD shared care guideline to be updated to include Meflynate XL

11. Standing items/Items for information only

- Formulary submissions tracker
  Noted.
- NICE TA Guidance Summary - ICS & NHS England attributed medicines:
  The summary was noted, and RAGG categories were agreed by consensus, where it was possible to confirm the RAGG status.

- For information and noting:

- RMOC update - SEL response to NHS England London Region proposals on a successor to the London RMOC
- Updated resources to support practices in managing the shortages of GLP-1 receptor agonists – approved via the urgent Triage Panel process 04/03/2024 – to note the pathway has been further updated as discussed earlier in this meeting.
- Adult and paediatric formulary updates

These were noted by Committee members.

12. Any Other Business
Nil items raised.

IMOC dates for next 3 months:

Date	Time	Venue
Thursday 18th April	2:00pm-4:30pm	MS Teams
Thursday 16th May	2:00pm-4:30pm	MS Teams
Thursday 20th June	2:00pm-4:30pm	MS Teams