South East London Integrated Medicines Optimisation Committee (SEL IMOC) Meeting
Thursday 18th January 2024 – 2:00pm to 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 Declarations of Interest (DoI) refresh

The DoI summary was noted. 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 minor formatting and typographical corrections. A minor update was requested to the wording of the section covering the pathway for the pharmacological management of excessive daytime sleepiness to clarify that the updated pathway was not approved and is to be re-presented at a future meeting. 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: Eltrombopag (Revolade™) for adults with acquired severe aplastic anaemia

This formulary submission originates from a consultant haematologist at KCH, which is a tertiary centre for the management of aplastic anaemia. The application requests the use of eltrombopag for adults with acquired severe aplastic anaemia (SAA), in three scenarios:

- First line in new patients who are unsuitable for immunosuppressive therapy (IST) or haematopoietic stem cell transplant (HSCT)
- First line in patients who will receive IST (in combination with antithymocyte globulin (ATG) and ciclosporin)
- Second line in patients who have had an inadequate response to IST

The first and third scenarios are in line with the UK product licence, and the second scenario is off-label, though all the scenarios requested are in line with the product licence approved in the United States (U.S). Background to the condition and the rationale for the use of eltrombopag in this setting with a review of the evidence base was provided in the detailed evidence review within the meeting paperwork.

➢ Evidence Review

The formulary pharmacist provided an overview of the evidence base for the use of eltrombopag in this setting. 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 eltrombopag. The information presented also included the estimated resource impact for eltrombopag in this setting. The resource impact of the submission is within the financial threshold that the Committee has delegated authority to approve. Aplastic anaemia is a rare, life threatening autoimmune haematological condition and treatment consists of HSCT or IST with ATG and ciclosporin or eltrombopag treatment. Eltrombopag is a TPO-receptor antagonist and works by stimulating the production of platelets. It is licensed in the UK for the treatment of SAA in patients who are either refractory to prior IST or unsuitable for HSCT. Eltrombopag is licensed in the United States (U.S) as a first line treatment option for SAA. The National Institute for Health and Care Excellence (NICE) terminated their appraisal on the use of eltrombopag in aplastic anaemia in 2016 as the company did not make a submission to NICE. Eltrombopag was formulary included following an interim policy developed by NHS England (NHSE) during the COVID-19 pandemic as a bridging option for patients not able to attend hospital for IST or HSCT. The policy has now been withdrawn.

Several small scale single arm studies and one randomised control trial (RCT) have investigated eltrombopag in SAA as second line, and first line treatment. One study investigating use as second line treatment in 25 patients with SAA refractory to immunosuppression found a response rate

(improvement in either platelets, neutrophils, or red cells) of 44% at 3 months, and a trilineage response (improvement in all 3 cell lines) of 24% at 6 months. The RCT investigating use as first line treatment found improved trilineage response rates when given with immunosuppression vs. immunosuppression alone (22% vs 10%, OR 3.2, 95%CI 1.3-7.8). Overall response rates (single lineage response) were 59% and 31%. Longer term outcomes suggest response is often maintained after treatment cessation, but relapse can occur, which is usually effectively managed with retreatment. Retrospective studies have found broadly similar outcomes. Eltrombopag is generally well tolerated, and no new safety signals are expected from its use compared to the already documented adverse effects. Eltrombopag is a high cost and tariff excluded treatment and Integrated Care Boards (ICBs) are the responsible commissioners for this indication. Eltrombopag is expected to become off patent in late 2025, and costs could decrease significantly should generic versions become available, although generic availability is unclear at present.

Data were shared at the meeting regarding Individual Funding Request (IFR) approvals for eltrombopag since 2018 and the numbers treated under the NHSE interim policy between 2020 -2022, demonstrating a patient cohort. The decision to prescribe eltrombopag in this setting is made through a multidisciplinary approach.

- **Applicants' presentation**

The applicant was in attendance to present the submission and field any questions. The applicant's declaration of interest was noted. It was outlined that SAA is an extremely rare condition, affecting 2-3 people per million population. The use of eltrombopag is intended as per the three cohorts described in the application. In the U.S., the Food and Drug Administration (FDA) approved data to support the use of eltrombopag in aplastic anaemia in the first line setting. It was noted that success has been seen with eltrombopag from experience of use thus far within their Trust, which is a tertiary specialist centre. Eltrombopag has proven effective within the respective patient cohorts being requested in the application. The patient response rate significantly improves when eltrombopag is given in addition to ATG and ciclosporin and patients who are refractory or ineligible for IST are responsive to eltrombopag monotherapy. Routine monitoring is conducted for patients when they are seen in clinic. For patients who do not respond to eltrombopag in either the 1st or 2nd line setting, a suitable treatment plan is decided for the individual patient, some patients would receive a second cycle of ATG, those who are eligible for transplant and have a donor would receive transplant and some patients would be given blood transfusions. The benefits of having eltrombopag available for SAA are a reduction of blood product usage, reduction of transfusion related iron overload and resource saving from reductions in haematology day care and in-patient beds.

In response to a query regarding whether all patients would technically be suitable for first line treatment with eltrombopag, the applicant explained that the request is for eltrombopag to be first line in all patients who are not suitable for HSCT, including those who are suitable or unsuitable/refractory to IST with ATG and ciclosporin. If eltrombopag is used as first line in this way it eliminates the need to use eltrombopag second line for patients who have had an inadequate response to IST with ATG and ciclosporin. It was confirmed that for use in the first line setting, patients with aplastic anaemia would need to be unsuitable for *both* IST and HSCT. With respect to treatment duration, the applicant clarified that there may be patients who do not get an optimal response in all 3 cell lines, in such cases treatment has previously been extended to 9 months and in rare cases up to 12 months, however, treatment would not go beyond this. This would relate to a small proportion of patients. Committee members were informed that updated guidelines on the management of aplastic anaemia from the British Society of Haematology (BSH) have been drafted and are due for publication imminently. The draft version of the updated BSH guideline includes the addition of eltrombopag in the first line setting. The existing version from 2015 only supports use in the 2nd line setting. From a value perspective, the applicant outlined that value and benefits can be monitored by presenting factors such as reduction in transfusion burden and reduction in hospitalisation and that they would be willing to monitor this, if eltrombopag is approved.

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

Members discussed the application and queried why ICB's were responsible commissioners for such a rare condition and not NHSE; clarity on this will be sought from NHSE. Evaluations of the NHSE policy were queried with the NHSE Pharmacy specialised commissioning representative, who will follow up if any outcome data are available.

Committee members discussed the available evidence, it was acknowledged that there is more evidence available in the U.S. for first line use of eltrombopag and the FDA has approved first line use. Members acknowledged that within the UK, as patient numbers are lower, it may take some time to gather the same level of data as the US. Additionally, this is a very rare condition and therefore randomised controlled trials in large numbers are unlikely. A point was raised that there does need to be a local position in place for eltrombopag treatment as the submission of IFRs where a cohort of patients exists is time and resource consuming and can create inequalities between patients from different geographical areas. Members agreed it would be helpful to have further information on outcomes seen from the existing experience of use to determine the value and support the decision-making process.

Committee members agreed by consensus that the decision for this formulary submission should be deferred and further information requested from the applicant on outcomes, including any value to the healthcare system. The report could include (but not limited to): impact on the need for blood transfusions, iron chelation therapy, patient complications, inpatient, and day-case bed days and hosiptalisations. Members also agreed that it would be preferable if the applicant returns once the updated national guidance from the BSH is published.

ACTION: Formulary applicant to provide an outcomes report to support the Committee's decision making
ACTION: NHSE specialised commissioning representative to follow up if any evaluation of the NHSE interim policy is available or can be produced

5. **Updated formulary recommendations:**

- **Formulary recommendation 101 Buvidal™ (buprenorphine weekly or monthly solution for injection) for the treatment of opioid dependence**
- **Formulary recommendation 102 Nyxoid™ (naloxone nasal spray) for the immediate emergency treatment of known or suspected opioid overdose**
- **Formulary recommendation 138 - Pitolisant for the treatment of cataplexy in adult patients with type 1 narcolepsy**

The formulary recommendations were updated following the presentation of their outcome reports at the November and December IMOC meetings, where the Committee agreed by consensus the removal of the time limit on the approvals for all three recommendations. The "Red, Amber, Green, Grey" (RAGG) category for all three updated recommendations remains as Red. A revised version of recommendations 101 and 102 were shared on screen as the versions in the agenda pack have had minor updates following comments from the Triage Panel review.

Committee members approved the formulary recommendation by consensus.

6. **Apomorphine (APO-go®) shared care guideline for the treatment of Parkinson's disease in adults – amendment made to timeframe in appendix 1 (Shared Care Request letter, Specialist to Primary Care Prescriber)**

The formulary pharmacist presented this item and explained that this shared care guideline (SCG) was recently approved and a small discrepancy has since been highlighted. The wording in Appendix 1 of the SCG and the wording under the GP responsibilities section in relation to the timeframe for transfer of prescribing to primary care are not aligned. Historically, since this SCG has been in place, the transfer to primary care occurs 2 weeks after the patient has been initiated by the specialist team, and this is noted in the GP responsibilities section. However, the template letter in Appendix 1 notes the

transfer timeline as 1 month. The request is to amend the 1-month transfer period noted in Appendix 1, to 2 weeks to align with the agreed transfer period noted under the GP responsibilities section.

The Committee approved by consensus the amendment of 1 month to 2 weeks in Appendix 1.

7. **Updated guideline for the use of dapagliflozin and empagliflozin for treating patients with chronic heart failure with preserved ejection fraction (HFpEF) or with mildly reduced ejection fraction (HFmrEF) without diabetes**

The author was in attendance to present this item and explained that the existing guideline has been updated to include empagliflozin following the recent publication of NICE TA 929 'Empagliflozin for treating chronic heart failure with preserved or mildly reduced ejection fraction'. It was confirmed that the RAGG category of empagliflozin would be Amber 2, this was agreed by the Committee at a previous meeting and is in line with the category for dapagliflozin in this setting. With respect to the cost impact, cost estimates from NICE indicate that there will not be a significant additional cost impact expected as the use of empagliflozin in this setting would be a substitute for dapagliflozin, which is similarly priced. The estimated cost impact is within the financial threshold delegated to the Committee.

The Committee approved by consensus the updated guideline for the use of dapagliflozin and empagliflozin for treating patients with chronic HFpEF or with HFmrEF without diabetes.

8. **Updated shared care guidelines (SCG) for the continuation of the following treatments for the prevention of organ rejection in adult liver transplant recipients:**

- **Mycophenolate mofetil**
- **Prograf™ (immediate release tacrolimus)**
- **Advagraf™ (tacrolimus modified release {MR} capsules)**
- **Azathioprine**

The formulary pharmacist presented this item alongside a specialist liver pharmacist in attendance for the item. The four existing SCG's have been updated onto the most recent version of the IMOC shared care prescribing guideline template. It was clarified that the guidelines only cover those patients where the GP has historically been prescribing these agents post liver transplant. It does not cover new patients.

Other minor amendments include the addition of administration details, drug background information, initial stabilisation, and initial monitoring sections for each drug and formatting. A new tacrolimus formulation - Envarsus™ - has also been noted within the guidelines to update the guidelines with new tacrolimus formulations that are now available. It was confirmed that Envarsus™ is not part of the shared care as the shared care only covers historical patients – who would either be prescribed Prograf™ or Advagraf™. With respect to this inclusion, (noting Envarsus™ is not for prescribing in primary care), members requested that reference to this preparation is removed from the guidelines as otherwise it could lead to confusion for primary care clinicians. The author agreed to review this. Members agreed that the initial stabilisation and initial monitoring sections would not be relevant in the guidelines, given they are for historical patients already being prescribed these agents. The authors agreed to remove this information.

The Committee approved by consensus the updated shared care guidelines pending amendments in line with discussions.

ACTION: Authors to update shared care guidelines and return to the IMOC team to progress for ratification via Chair's action

9. **Progress with the SEL IMOC workplan for 2023/24 – quarter 3 update**

The Committee was informed that there has been good progress in achieving the areas in the work plan, including two areas that have been completed - the menopause treatment pathway and the guidance for the management of osteoporosis. Members noted the update.

10. Outcome data on the use of dienogest (Zalkya™) for the treatment of endometriosis (review of time limited approval):

- GSTT outcome data
- LGT outcome data
- KCH outcome data (verbal feedback)

The formulary pharmacist presented this item, which provides feedback from the acute Trusts as requested by the Committee following a time limited approval to use dienogest in this setting in September 2022. A total of around 40 patients have been treated with dienogest at the acute Trusts. The data for GSTT covered over half of these patients (n =22) and found that around two-thirds of patients reported an improvement in their symptoms. The average reduction in the pain score (ranging from 1 – 10, 1 being slight pain and 10 being severe pain) was 3 points. Approximately two thirds of patients continued dienogest after initial follow up – this resulted in less use of staff capacity and time from use of alternative treatments (injectable gonadorelin analogues). With respect to side effects, just under 70% of patients experienced side effects, although the majority were "common" or "very common" side effects as per the product literature. Fewer patients were treated at KCH and LGT and follow up time is limited but overall patients found dienogest to be beneficial in improving pain symptoms.

Based on the primary care prescribing data provided, 112 patients have been prescribed dienogest in primary care and members queried whether dienogest is being initiated in primary care (the RAGG category is Amber 2 – initiation and first prescription from a specialist). Members agreed that boroughs may want to remind prescribers in primary care of the Amber 2 status of dienogest in SEL.

Committee members agreed by consensus to remove the time limit for dienogest in this setting.

ACTION: Formulary recommendation to be updated to remove time-limit and presented at a future meeting

11. Update on the national genomics programme

The Pharmacy Lead for NHS South East Genomic Medicine Service Alliance was in attendance to present an overview of the regional genomic medicine services under the Genomic Medicine Service Alliances (GMSA) and how these link into medicines optimisation (MO). A 5-year action plan has been developed to help embed genomics in the NHS – this consists of 13 commitments across 4 key themes. There is a commitment to enable a pharmacogenomics programme as part of the 13 commitments.

The presentation provided an update on the following areas:
1. NHS Genomics Strategy
2. NHS Genomic Networks of Excellence
3. Establishing Genomics Medicines Optimisation Governance
4. NHS PROGRESS Pharmacogenomics Implementation Project
5. The National Genomic Test Directory
6. NICE assessments and technology appraisals
7. BNF & Genomic Notes (an online resource to support clinicians)

Committee members noted the presentation and thanked the presenter for sharing the update. Further updates will be arranged in the future.

12. Standing items/Items for information only

- Formulary submissions tracker
  Noted.
- NICE Technology Appraisal (TA) Guidance Summary - ICS & NHSE/I attributed medicines:

The summary was noted and RAGG categories were agreed by consensus, where it was possible to confirm the RAGG status.

- December 2023 RMOC Update

A meeting of the London Regional Medicines Optimisation Committee (RMOC) took place in December 2023. The agenda outline was shared with Committee members within the agenda pack and a short summary of the discussions was provided:

- There are plans underway to restructure the RMOC to a Committee that is more driven by the five London ICS areas with a focus on delivery. Proposals are expected be published in due course by NHSE.
- There was discussion on the use of Free of Charge Schemes and the varied approaches across London, with a presentation focusing on schemes for cancer medicines. NHSE has published recommendations on the use of these schemes and a local approach will be developed via the Medicines Value Group.
- There was also an update on the national Medicines Optimisation opportunities for 2023/24 where ICS leads fed back on which priorities they had chosen.

Committee members were informed at this point on the plans for the priority MO opportunity areas in SEL Originally 5 opportunities were chosen for focus in SEL and these were presented at the additional IMOC meeting held in November 2023. Subsequent to this, the national dashboard for the MO Opportunities was published and showed that SEL has significant improvement to make in the following two opportunities:

- Reducing the course length of antimicrobial prescribing - total amoxicillin prescriptions as 5-day courses
- Improving respiratory outcomes while reducing the carbon emissions from inhalers

In view of the SEL position for these two opportunities, these have both also been chosen as priority areas for SEL in addition to the 5 already selected - SEL has now selected 7 priority MO Opportunity areas. The Medicines Value Group will hold oversight of this work.

- For information and noting:
- Adult and paediatric formulary updates

This was noted by Committee members.

13. Any Other Business

Nil.

IMOC dates for next 3 months

Date	Time	Venue
15th February 2024	2:00pm-4:30pm	MS Teams
21st March 2024	2:00pm-4:30pm	MS Teams
18th April 2024	2:00pm-4:30pm	MS Teams