South East London Integrated Medicines Optimisation Committee (SEL IMOC) Meeting
16th January 2025 (Online via MS Teams)
Final Minutes

1. **Welcome, introductions and apologies**
The Chair welcomed attendees to the meeting. Apologies and observers were noted. The meeting was noted to be quorate.

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. **Minutes, detailed action notes of the last meeting, and action log:**
The minutes and detailed action notes were accepted as an accurate record of the meeting subject to the correction of minor typographical errors. An update to agenda item 5 - updated guideline for the off-label use of nebulised antibiotics in the management of pseudomonas aeruginosa in non-cystic fibrosis bronchiectasis and associated formulary request was also requested, in relation to a change of tobramycin "nebulised prefilled syringe" to "nebulised solution in a plastic ampoule".
Members were provided with an update on progress against actions due for this month, these were noted, and items closed were agreed.

4. **Update on IMOC GP vice Chair election**

Following an expressions of interest (EoI) process for the role of IMOC GP vice chair, the role has been successfully recruited to unopposed. No objections were raised by committee members to the outcome of the process and committee members welcomed the IMOC GP member as a new a vice chair.

5. **Treatment pathway and cost modelling for ritlecitinib (Litfulo®) in patients 12 years and older with severe alopecia areata**

The authors were in attendance to present this item on behalf of the dermatology sub-group. The treatment pathway has been developed via the dermatology sub-group of the IMOC following the publication of a technology appraisal (TA) by the National Institute for Health and Care Excellence (NICE) as TA 958.The pathway aims to provide uniformity for the secondary and tertiary care prescribing of ritlecitinib in SEL and covers information about disease severity assessments, eligibility criteria and initiation and on-going monitoring for ritlecitinib.

In terms of the resource impact, the presenters noted as this is a new service and due to the current capacity of the service, implementation of ritlecitinib will be phased over time as the service is established. For this reason, the cost impact may be less than anticipated initially and may not reflect the predicted numbers by NICE. Based on the five-year cost modelling for implementation of the drug only (not service delivery) using the NICE TA resource impact model from year three onwards the cost impact would exceed the IMOC financial threshold delegated to the committee. In line with the committee's terms of reference, this will be escalated to the Executive Committee for information.

Members discussed the guidance and noted that one of the factors for patients who may not have severe alopecia areata but may be eligible for treatment with ritlecitinib is the negative impact of alopecia areata on psychological functioning. They queried how this would be assessed. The presenters clarified that the British Association of Dermatologists (BAD) recommended the use of psychological assessments to holistically review the impact of the disease on patients' lives. Standard mental health patient reported outcome measure (PROMS) are used for psychological assessments. In practice the dermatology life index score is also used. The presenters acknowledged that it would be useful to add detail and context to these measures in the next iteration of the pathway. A query was raised regarding the inclusion of dose optimisation for stable patients in the treatment flowchart and the rationale for this, given it is off-label and not covered by the NICE TA. Members queried if there an evidence base for dose optimisation in this patient cohort and how and when will dose optimisation be initiated. The presenters outlined that dose optimisation would not occur in the first

year of treatment when patients' response is still being ascertained. Whilst the evidence base is mainly anecdotal, the aim of dose optimisation is to reach a minimal dose which maintains remission and also results in less exposure to the drug long term. The presenters agreed to better articulate within the pathway how dose optimisation will be implemented, including the criteria for moving to this regimen and that it is outside of the product licence and NICE guidance. Monitoring of outcomes would be expected through the dermatology sub-group. The presenters confirmed that if there is no improvement in SALT score or a worsening in this score, treatment would not continue despite improvement in psychological factors.

The presenters also agreed to make the following amendments to the treatment pathway:

- At the start of the treatment flowchart (section 7) cross-refer to the initiation criteria outlined in section 6.1
- Update to the wording in reference to the shingles vaccine in line with existing SEL guidelines (for example, the rheumatology guidelines for rheumatoid arthritis and spondyloarthropathies) to ensure recommendations for use are in line with national recommendations.
- Clarify that periodic skin checks will be carried out by the specialist team and will be completed as a baseline check and at each follow up appointment with the specialist team. Patients will also be educated in relation to self-surveillance of skin checks.
- Clarify that responsibility for the full blood counts (at 4 weeks initiation and then regularly every 4 – 6 months) will be under secondary care.
- Correct the point of discontinuation if a SALT score of 20 or less is not achieved from 39 weeks to 36 weeks in section on continuation criteria (section 6.2), which is line with the product information.

Members noted that the implementation and outcomes from the pathway will need to be monitored via the dermatology sub-group, in line with this a monitoring framework for ritlecitinib in alopecia areata will need to be developed thought the dermatology sub-group.

Committee members approved by consensus the treatment pathway for ritlecitinib (Litfulo®) in patients 12 years and older with severe alopecia areata pending amendments to the pathway in line with discussions and escalation of the cost modelling.

ACTION: Author to amend pathway in line with meeting discussions and share with the IMOC team to progress for IMOC Chair's ratification
ACTION: Estimated resource impact based on NICE modelling to be escalated to the Executive Committee for information

6. **Updated urticaria treatment pathway and associated documents:**
    - **Formulary request and cost modelling for omalizumab dose optimisation (off-label) for chronic spontaneous urticaria (CSU) in adults**
    - **Evidence review for omalizumab dose optimisation (off-label) for CSU in adults**
    - **Omalizumab in urticaria outcomes and monitoring framework**

The authors were in attendance to present the updated urticaria pathway on behalf of the dermatology sub-group of the IMOC. The main update is in relation to off-label dose escalation and optimisation of omalizumab in patients over the age of 12 for the management of chronic spontaneous urticaria (CSU). Minor updates have also been carried out within the primary care section of the pathway including updates to the antihistamine treatment options in line with current availability.

Current use of omalizumab for the management of CSU is in line with NICE TA 339, in patients where antihistamines and montelukast have failed. In line with NICE, the use of omalizumab in this patient cohort is restricted to a treatment course of 6 doses, with patients being retreated only if a relapse occurs. Locally, up to 25% of patients have suffered severe relapses between omalizumab courses which has impacted on patient physical and mental health, quality of life and increase in the use of steroids and immunosuppression to manage CSU symptoms. Through options for dose escalation and optimisation of omalizumab, the use of steroids and immunosuppression can be reduced.

Dose escalation or optimisation of omalizumab would be considered (dose escalation via three different dose escalation pathways) in patients with CSU who are unable to achieve optimal primary response at the usual licensed dose and treatment duration based on their urticaria activity score (UAS7). In the event of a response, at 6 months, the updated guidance advocates the following strategies following assessment of post-treatment UAS7 scores:

- 0 (complete response) - stop treatment, treat on relapse
- 1-6 (controlled urticaria) – start treatment break or consider dose escalation of continued 300mg every 4 weeks without a break in treatment (following multidisciplinary team [MDT] discussion). Reviewed every 12 months.
- 7-15 (mild urticaria) – continue at 300mg every 4 weeks
- 7-15 in weeks 1-3 but increases by minimum 10 points in week 4 – consider dose escalation to 300mg every 3 weeks (following MDT discussion). Reviewed after 2 doses.
- >15 but improved by 10 points from baseline – consider dose escalation to 450mg every 4 weeks (following MDT discussion). Reviewed after 2 doses.
- <10 point change from baseline – discontinue

Complex patients (those on dual immunosuppressants and steroids in addition to omalizumab, and those with significant use of steroids or unable to take immunosuppressants) may also be considered for continued treatment at 6 months regardless of UAS7 score. For dose optimisation, this can be considered in patients as alternative to abrupt cessation in those who have had greater than 6 months treatment, or previous relapse. This consists of increasing the dosing interval to 300mg every 5-6 weeks, and then by further 1-2 weekly increases if remains asymptomatic. In the event of relapse of symptoms, treatment is resumed at the last appropriate dosing interval.

Omalizumab dose escalation and optimisation is already in practice locally and the updated pathway aims to formalise this practice. The improved patient outcomes observed to date include an increased duration of patients being completely or partially symptom free, reduction in hospital visits and steroid burden. Patients have also been safely managed via home care with no safety concerns or increased adverse effects reported. Local audits have demonstrated up to 25% of the adult patients at GSTT are currently dose optimised to dosing intervals of every 5 weeks and beyond.

The Formulary Pharmacist provided a brief overview of the evidence base for dose escalation. A main study to note, is a recent observational single centre study reviewed 138 CSU patients on omalizumab over a 12 year period. Of the 138 patients, 70% of patients were responders to omalizumab 300mg every 4 weeks (50% complete response and 21% partial responders) and 9% were non-responders. A total of 48% of partial responders and all non-responders were dose escalated to 450mg monthly, then 600mg monthly, followed by 600mg 2 weekly. Fifty-seven per cent of those partial responders and 33% of the non-responders became responders upon dose escalation. Overall, 69% of patients improved response upon dose escalation and 8% remained non responders. Another study described is a UK single centre review of 357 patients who received omalizumab over a 10 year period with dose escalations based on UAS7 and UCT (Urticaria Control Test). Dose escalations included 300mg – 450mg every 4 weeks and up to 600mg every 4 weeks. Of the full cohort, 36% were managed on doses lower than 300mg every 4 weeks, 22% required higher doses, and 2% had higher and lower doses at some point during their overall treatment with omalizumab. The authors reported if standard doses were used, 22% of the cohort would have needed to switch to immunosuppression rather than be effectively maintained on omalizumab.

From a safety perspective, the studies did not reveal an increase in adverse effects in patients receiving higher doses than patients on the standard 300mg monthly dose. It was also noted that omalizumab is used at higher doses in the management of asthma. From a resource impact perspective, the resource impact of the submission is within the financial threshold delegated to the committee. An omalizumab biosimilar is expected in 2025 which will reduce the cost impact vs. the originator brand. Savings will also be achieved through dose optimisation of patients in line with the updated treatment pathway.

To support the monitoring and review of the patient outcomes associated with the updated treatment pathway, , an outcomes and monitoring framework has also been developed which would be reported on and reviewed at regular intervals via the dermatology sub-group.

In response to a query regarding whether the use of other off-label treatments , such as immunosuppressants, would reduce with the use of escalated omalizumab, the presenter advised that the use of the off-label immunosuppressants is usually reserved for the management of autoimmune urticaria. The main treatment in this patient cohort is methotrexate or ciclosporin. With respect to the use of famotidine in the primary care section of the treatment pathway, the presenters confirmed that if there is partial response to treatments trialled earlier in the pathway and can also be useful as a treatment option whilst patients await specialist review. The presenters also clarified that histamine blockers, such as famotidine, are historically part of the pathway and provide an option to cover mast cell activation. They are useful if there is partial response to treatments trialled earlier in the pathway and also as a treatment option whilst patients await specialist review. The presenters agreed to make the following amendments to the pathway:

- Update to the scope section to include a statement noting that the pathway also covers omalizumab in CSU for 12 years and older.
- Clarify step 3 in the treatment pathway for all types of urticaria by making it clear that montelukast should be trialled in CSU patients before omalizumab and it can also be considered in inducible urticaria's, however this is not a requirement before specialist referral for omalizumab
- The existing GP information sheets for the transfer of prescribing to primary care of danazol, doxepin and naltrexone in urticaria require review and update in line with the pathway.

Committee members approved by consensus the updated urticaria treatment pathway, formulary inclusion of dose escalation /dose optimisation of omalizumab and the omalizumab outcomes and monitoring framework pending amendments in line with discussions.

ACTION: Author to amend pathway in line with meeting discussions and share with the IMOC team to progress for IMOC Chair's ratification
ACTION: Author to review and update associated GP information sheets for danazol, doxepin and naltrexone

7. Updated Inflammatory Bowel Disease (IBD) pathways, cost tool and outcomes and monitoring framework (24/25)

The GSTT Specialist Gastroenterology Pharmacist was in attendance to present this item which has been updated and approved via the IBD sub-group. The main updates to the IBD treatment pathway include inclusion of recent NICE TAs for the use of etrasimod (TA 956), risankizumab (TA 998) and mirikizumab (TA 925) in moderately to severely active ulcerative colitis (UC). In addition, the terminology of 'biologic therapies has been amended to 'advanced therapies to cover the variety of therapies now available in IBD management. An asterisk has been added to ustekinumab to indicate the availability of ustekinumab biosimilar. The IBD pathway cost tool has also been updated to include the new NICE TA approved treatment options, risankizumab 180mg maintenance dose, estrasimod and ozanimod price reduction and ustekinumab biosimilar. The IBD pathway outcomes and monitoring framework has also been updated for this financial year and one of the audits has already been completed.

In terms of the resource impact of the NICE TAs, it was noted that in line with the NICE resource impact statement for estrasimod, risankizumab and mirikizumab in UC, these treatments are not anticipated to be a significant resource impact as they are a further treatment options for the patient cohorts they cover and the cost is likely to be a substitution. A query was raised regarding dual biologic therapy and whether the use of upadacitinib in this setting is being considered through the sub-group as there have been some individual funding requests? The presenter confirmed that a request for this is being progressed, covering the use of upadacitinib and ustekinumab. A request was made to amend that way in which the name of a Trust was presented in the Trust contact details.

Committee members approved by consensus the updated IBD pathways, cost tool and outcomes and

monitoring framework pending amendments in line with discussions.

ACTIONS: Authors to amend pathway and cost tool in line with meeting discussions and share with the IMOC team to progress for IMOC Chair's ratification

8. Paediatric formulary "Red, Amber, Green, Grey" (RAGG) rating review: Phase 1 – medicines used in cardiology

The authors presented this item, which aims to update the formulary RAGG categories for paediatric medicines used in cardiology in line with their actual use in practice. This is part of a larger ongoing project where a full review is being undertaken to consider the appropriate RAGG categories for medicines used in paediatrics. The process has considered the different indications and specialties the medicines may be used in and liaising with the relevant teams across SEL hospital Trusts. This process is not being used to consider down grading the category i.e. moving Red or Amber 3 medicines, which will remain the same. There are also Green, Amber 1 and Amber 2 medicines which are considered to be appropriate and have not required a change in RAGG category. The summary table was presented and it was explained that in the majority of instances, a move from Green to Amber 2 is being proposed as the first prescription will come from the hospital. These patients may require specific monitoring on initiation and dose titration which is carried out by the specialist team. In general medications within the same class are assigned the same RAGG category, however there are some instances where 2nd or 3rd line agents and or those indications with little experience or use in paediatrics may be given a higher RAGG category meaning a greater amount of specialty input on initiation. The presenter highlighted some corrections to the summary table circulated within in the paperwork for the committee to note.

Overall, the proposals reflect current practice and the request to the committee is to approve the proposed changes in RAGG category for the paediatric medicines used in cardiology.
A query was raised regarding whether the RAGG category for propranolol in portal hypertension (proposed change from Green to Amber 2) should align to the same RAGG category as carvedilol in portal hypertension which is categorised as Red. The presenter agreed to discuss this with the relevant specialists and provide an update to the committee at a future meeting.

Committee members approved by consensus the proposed changes to the RAGG categories for paediatric medicines used in cardiology.

ACTION: Paediatric formulary to be updated with approved RAGG category changes for paediatric medicines used in cardiology
ACTION: Author to follow up discussions in relation to the proposed RAGG category for propranolol in portal hypertension

9. Updated guidance for prescribing melatonin for sleep disorders in paediatrics (children and adolescents)

The lead authors for this item, including a consultant in paediatric sleep disorders, presented this item. The existing guidance has been updated following approval at the September 2024 IMOC meeting to move melatonin in sleep disorders in paediatrics from a RAGG category of Amber 3 to Amber 2 and inclusion of the Ceyesto™ brand of liquid formulation. The following items were presented to the committee for review and approval:

- Updated melatonin guidance and treatment pathway
- New formulary recommendation for Adaflex™ (melatonin) for use in insomnia in children and adolescents aged 6 -17 years with attention deficit hyperactivity disorder (ADHD) where sleep hygiene measures have been insufficient
- Updated formulary recommendation for Slenyto™

The guideline and treatment pathway have been updated following a consultation process after discussions at the September 2024 IMOC meeting. The main updates include changes in the RAGG category from Amber 3 to Amber 2, terminology within the guideline, specific considerations for switching between melatonin preparations, updated information in relation to brand versus generic

prescribing of melatonin, inclusion of the Adaflex™ brand of melatonin and outlining specialist responsibilities in relation to treatment initiation and treatment breaks. It was noted that a formulary application for Adaflex™ (for use in line with its licensed indication) was initially presented to the committee in March 2023. As part of the application, the committee had requested the existing guidance and shared care guideline is updated. Subsequently, the paediatric teams applied for a change of RAGG category and move away from Amber 3 (shared care). This has resulted in a time lag since the original formulary application for Adaflex™ was made. Committee members noted a review of the original costings associated with Adaflex™ from 2023, (provided within the agenda pack) will be required as melatonin 2mg modified release (M/R) tablets, are now available generically with a significant reduction in price. Committee members discussed the presented guidance and pathway and raised the following comments:

- The original formulary application for Adaflex™ in March 2023 and discussions at the September 2024 IMOC meeting confirmed that the formulary inclusion approval for Adaflex™ was in line with the licensing, however the updated guideline recommends Adaflex™ off label in children where the other listed preparations are not clinically appropriate and/or tolerated. Members queried the rationale for this off-label use, The presenters responded that the off-label use of Adaflex™ outside of its licence would be rare and would be the last treatment option for patients who could not tolerate other melatonin preparations.
- Members requested that as melatonin 2mg M/R tablets are now available generically, this option should appear as the first line preparation of choice within the melatonin prescribing information summary table and prescribing guidance flowchart for all patients, unless they meet the licensed criteria for Adaflex™ or Slenyto™.
- Under the "Other points to note" section of the melatonin prescribing information summary table, the first bullet point should be re-worded to "*Patients who are currently stabilised on this formulation do not necessarily need to be switched, unless it is clinically indicated by the specialist team*" to prevent blanket switching,
- In line with the licence for Adaflex™ and the Adaflex™ formulary inclusion approval previously provided in principle (pending updated guidance), the maximum dose for Adaflex™ within the guideline should be noted as 5mg daily. *The presenters agreed wording can be added to the guideline as follows to enable the off-label use of Adaflex™ above the dose of 5mg which is required in some patients -"The decision to exceed the maximum dose of 5mg is at the clinical discretion of the healthcare provider and would be considered off-label use"*.
- As a follow on, members queried whether for the cohort of patients on Adaflex™ who may require off-label doses above 5mg, could melatonin 2mg modified release (M/R) tablets which is also off-label in this patient cohort be prescribed as an alternative cost-effective preparation? *Adaflex™ is an immediate release preparation which has the advantage of providing quicker sleep onset in comparison to the M/R preparation and has been shown to be beneficial for the cohort of children who really struggle with sleep onset. The presenters agreed to add further information to the guideline that explains the scenario(s) in which the prescribing of off-label Adaflex™ doses above 5mg would be appropriate.*
- At the September 2024 IMOC meeting, it was noted where children are identified as more complex, these patients would remain under specialist care and this would be defined and included in the updated pathway. This is not currently within the guideline and the reasons were queried. *The presenters acknowledged it would be challenging to define complex patients in this clinical setting given the factors that can contribute, however where a patient is deemed complex, they will remain under a specialist service such as the paediatric neurodisability service or neurology service.*
- Correction to the wording "sleep latency reduced by at least 60 minutes, for at least 3 days of the week" to "sleep latency reduced to 60 minutes or less, for at least 3 days of the week" was requested
- In various sections within the guideline there is mention of treatment breaks and treatment discontinuation, members asked if treatment breaks and discontinuation are recommended synonymously or as two separate treatment recommendations? *They occur as separate treatment recommendations, treatment breaks are often recommended to patients on long term melatonin and if the patient is able to sleep well during the treatment break, there would be a consideration for stopping melatonin treatment.* Members requested an update to the wording in relation to

treatment breaks and discontinuation, to note that if a patient is sleeping well without melatonin during their treatment break, discontinuation can be considered.

- Primary care prescribing data shows a large variety of melatonin products being prescribed locally, is there any work underway to review and rationalise this variable prescribing of melatonin products? *The presenters advised that this will be reviewed through the primary care medicines value group , in particular the melatonin products which do not have a product licence.*

Formulary recommendations:

- **Updated - melatonin 1mg and 5mg prolonged release tablets (Slenyto™) for managing insomnia in children and adolescents (aged 2 years to 18 years)**

The existing formulary recommendation has been revised in line with the updated guidance for prescribing melatonin including the updated RAGG category of Amber 2, stating the time frame for dose stabilisation before transfer of care to primary care and adjustments to the wording in relation to switching between melatonin preparations. A comment was received via the virtual Triage Panel review process to align the wording around treatment initiation and discharge information as per the wording used within the new Adaflex™ recommendation. Committee members approved the formulary recommendation by consensus pending this change.

- **New - melatonin immediate release tablets (Adaflex™) for managing insomnia in children and adolescents (aged 6 years to 17 years) with attention deficit hyperactivity disorder (ADHD)**

This formulary recommendation outlines the approval of Adaflex™ following discussion in September 2024 and presentation of the updated guidance and treatment pathway at this IMOC meeting. It was noted that the cost impact section of the recommendation requires updating in line with changes in the product prices for melatonin 2mg M/R release tablet. The presenters will follow this up and advise on the entry. Committee members approved the formulary recommendation by consensus pending update to the costing section.

Committee members approved the following by consensus, pending amendments in line with discussions:

- Updated guidance for prescribing melatonin for sleep disorders in paediatrics
- Updated formulary recommendation - melatonin 1mg and 5mg prolonged release tablets (Slenyto™) for managing insomnia in children and adolescents (aged 2 years to 18 years)
- New formulary recommendation - melatonin immediate release tablets (Adaflex™) for managing insomnia in children and adolescents (aged 6 years to 17 years) with attention deficit hyperactivity disorder (ADHD) pending updated costings

ACTION: Authors to amend guideline in line with discussions and share with the IMOC team to progress for IMOC Chair's ratification
ACTION: Authors to provide updated costing information for the Adaflex™ formulary recommendation for approval via IMOC Chair's ratification

10. Standing items/Items for information only

- Formulary submissions tracker

Noted.

- NICE Technology Appraisal (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:

- Adult and paediatric formulary updates
- Information note on the acute management of potential adverse treatment effects of lecanemab – this document is based on a version drafted by NHS England (NHSE), which NHSE had suggested ICS areas may wish to circulate locally to highlight the potential adverse effects from lecanemab. The manufacturer of lecanemab has made lecanemab available in the UK via

independent clinics and patients may present to NHS services with side effects associated with lecanemab. The document has been cascaded through the emergency cascade system across the ICS.

The above items were noted by committee members.

11. Any other business
Nil items raised

IMOC dates for next 3 months

Date	Time	Venue
Thursday 20 February 2025	2pm – 4:30pm	MS Teams
Thursday 20 March 2025	2pm – 4:30pm	MS Teams
Thursday 17 April 2025	2pm – 4:30pm	MS Teams