NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 15 April 2025 at 14:30 via Microsoft Teams

PRESENT	APOLOGIES	APPROVED
Ms L Cameron	Dr D Culligan	
Dr V Chieng	Mrs M Galvin (and deputy Mrs S Howlett)	
Ms A Davie		
Ms F Doney		
Mrs E Milne		
Dr L Elliot (Chair)		
Mrs G McKerron		
Mrs S O'Beirne		
Mr M Paterson		
Dr K Simpson		
Mr R Sivewright		

IN ATTENDANCE
Ms Dawn Bruce, Specialist Pharmacy Technician, Formulary Team.
Dr Sarah Wallage, Sexual and Reproductive Health Consultant to discuss item 5.1 Penthrox®.

Note some items were taken outwith agenda order.

ITEM	SUBJECT	ACTION
	WELCOME The Chair welcomed members, opened the meeting, and confirmed that a quorum was present.	
1.	**APOLOGIES** Apologies for absence were requested and noted.	
2.	**MINUTE AND DECISIONS**	
	2.1. DRAFT MINUTE OF THE MEETING HELD 18 MARCH 2025 Members accepted the draft note of the meeting subject to minor typographical changes. The corrected final approved minute will be in the public domain within 21 days of final approval.	**FD**
	2.2. FORMULARY GROUP DECISIONS MARCH 2025 - PUBLISHED 31/03/2025 Members ratified the decisions of the March 2025 meeting as published.	
3.	**MATTERS ARISING**	
	3.1. Action LOG The Action log was noted.	
	3.2. MAVACAMTEN (REPLIES TO QUERIES) Members reviewed the replies to the queries posed at the March meeting. Regarding the sharing of patient's CYP2C19 phenotype status, the requestors confirmed that the result is recorded on TrakCare as a letter from the Genetic Team and would be shared with the patient's GP in a clinical letter from the cardiology consultant. Initial comments from the genetic team in NHS Greater Glasgow and Clyde have suggested that this result is not able to be applied directly to any other drugs, and that each drug would need to be tested individually to assess the level to which this affects	

ITEM	SUBJECT	ACTION

each agent.

Regarding the question of additional coding the requestors considered this would be helpful but did not feel best placed to comment on or decide this.

Regarding the question of contraceptive pathways, there is not a contraceptive pathway with an expectation that the patient will have a discussion with the person that manages their contraception (the expectation being that this would usually be the patient's GP).

Item closed. **FTEAM**

5. NEW PRODUCT REQUESTS

5.2. SMC 2654 LONSURF® (METASTATIC COLORECTAL CANCER (CRC))

There were no declarations of interest recorded in relation to this product.

The Group considered the request for Lonsurf® in combination with bevacizumab for the treatment of adults with metastatic colorectal cancer (CRC) who have received two prior anticancer treatment regimens including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and/or anti-EGFR agents.

The Group noted that:

- Lonsurf®:
  - is a cytotoxic medicine that contains two active substances, trifluridine and tipiracil
  - is already included on the formulary as monotherapy as a third-line treatment option for adults with metastatic CRC (SMC 1221/17) and combination use with bevacizumab will replace Lonsurf® monotherapy
  - [for this indication] meets SMC end of life AND orphan equivalent criteria
  - [for this indication] was accepted for use only in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and the output from the PACE process
- evidence comes from SUNLIGHT (n = 492) an open-label, randomised, phase III study that compared Lonsurf®-bevacizumab with Lonsurf® monotherapy in the third-line setting:
  - the primary objective was overall survival (OS); median OS Lonsurf®-bevacizumab 10.8 months vs. 7.5 months (hazard ratio 0.44 (0.36 to 0.54) p<0.001)
  - secondary objective was progression-free survival (PFS); median PFS Lonsurf®-bevacizumab 5.6 months vs. 2.4 months (hazard ratio 0.61 (0.49 to 0.77) p<0.001)
  - in the study the median duration of treatment was 5 months in the Lonsurf®-bevacizumab group and 2.1 months in the Lonsurf® monotherapy group
- limitations of SUNLIGHT:
  - open label study, so outcomes may be subject to bias
  - limited to fitter patients (ECOG-PS 0 or 1) so may not represent clinical practice
- cost offset is available from Lonsurf® as monotherapy, and there are already costs in the system as Lonsurf®-bevacizumab has been accessed via individual patient requests
- patients' continue therapy until disease progression or unacceptable toxicity, bevacizumab monotherapy was not allowed in the study
- additional costs expected include the cost of bevacizumab, and additional aseptic preparation for Lonsurf® and bevacizumab, consumables etc.

The Group accepted the restricted local need for Lonsurf® in combination with bevacizumab for the treatment of adults with metastatic CRC who have received two prior anticancer treatment regimens including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and/or anti-EGFR agents.

ITEM	SUBJECT	ACTION
	SMC 2654 - Lonsurf® 15mg/6.14mg, 20mg/8.19mg film-coated tablets (trifluridine/tipiracil) is routinely available in line with national guidance (SMC 2654). Indication under review: in combination with bevacizumab for the treatment of adults with metastatic colorectal cancer (CRC) who have received two prior anticancer treatment regimens including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and/or anti-EGFR agents. In an open-label, randomised phase III study, the addition of bevacizumab to trifluridine/tipiracil was associated with significant improvements in overall survival. This advice applies only in the context of an approved NHS Scotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/list price that is equivalent or lower. This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting. It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only. Treatment should be prescribed by physicians experienced in the administration of anticancer therapy.	**FTEAM**

4. PRESENTATION/DISCUSSION

The Chair welcomed Dr Sarah Wallage, Sexual and Reproductive Health Consultant to the meeting to discuss the request for item 5.1 Penthrox® as an additional analgesic for gynaecological procedures.

Dr Wallage confirmed that:

- the volatile anaesthetic methoxyflurane, as Penthrox®, is now recommended in the Royal College of Obstetricians and Gynaecologists (RCOG) Green-top Guideline as a patient-controlled inhaled analgesic for use in operative gynaecological procedures, so use is now more mainstream
- initially the service wishes to use Penthrox®, in combination with local anaesthetic, in the operating theatre for people having surgical termination or evacuation of retained products. If successful, the service would look to roll-out use to include gynaecological out-patient areas and possibly at the Health Village and the Sexual Reproductive Health Clinic.
- Penthrox® use will be optional, and use will have been discussed [with consenting patients] before theatre
- Standard Operating Procedures (SOPs), based on the existing Emergency Department SOPs, have been developed. The SOP exclusion criteria include people under 18 years, people on enzyme inducing drugs, those with renal function problems, etc. A particular issue for Sexual Health will be the use of doxycycline prophylaxis, an alternative antibiotic would be chosen if Penthrox® is being used.
- Penthrox® is not a Controlled Drug, and is likely to be stored in the theatre anaesthetic cupboard
- the surgeons will risk assess which patients will be offered Penthrox®
- the anaesthetists are supportive of use of Penthrox® in this setting
- Penthrox® would be prescribed by the clinician performing the procedure on an anaesthetic form. The form will be uploaded to patient's TrakCare Electronic Patient Record.
- patients are expected to only use one device for the procedure
- operating department practitioners/theatre nurses are accustomed to supporting patients through these procedures
- the staff will support/encourage the patient to self-administer Penthrox® correctly, e.g., exhale through the device
- Penthrox® is not replacing another drug but for some people it may avoid the need for a general anaesthetic
- training is available from the manufacturer, the pack insert has clear instructions,

including correct disposal
- patients will be given the Patient Information Leaflet (PIL) before discharge with advice about symptoms to report and to inform clinicians of use if seeking medical care in the next week or so
- there are no ventilation concerns regarding the use of Penthrox® in theatre due to the frequent air changes
- other areas of the UK are also using Penthrox® in ambulatory clinic settling

Dr Wallage highlighted that:
- having an additional method of pain relief would be beneficial for patients and staff
- for some patients the availability of Penthrox® may avoid the need for a general anaesthetic
- should Penthrox® move into gynae clinics more advice would be sought regarding the ventilation requirement for Penthrox®, particularly in relation to pregnant staff

The Chair thanked Dr Wallage for attending the meeting to discuss the request for Penthrox® as an additional analgesic for gynaecological procedures.

5.1. FG1 473/25 – PENTHROX® (OFF-LABEL)

There were no declarations of interest recorded in relation to this product.

The Group considered the request for the off-label use of Penthrox® as an additional analgesic for patients (adults) having surgical abortion or evacuation retained products of conception after abortion with local anaesthetic in theatre at ARI.

The Group noted that:
- Penthrox® is licensed for the emergency relief of moderate to severe pain in conscious adult patients with trauma and associated pain, this request would be off-label use
- *Clinical effectiveness*: there is evidence of efficacy as an analgesic when used for moderate to severe pain in conscious adults
- *Cost effectiveness*: there are no QALY estimates, but the expected patient numbers are not significant and Penthrox® is not a high-cost item [one bottle 3mL inhalation vapour liquid costs £18.46 (£22.15 including VAT)]
- *Health gain*: there are potential health gains for patients and the Health Board; health gains related to improved analgesia, and potential to avoid general anaesthetic (reduced recovery time and need for supervision; avoids risks and recovery associated with general anaesthetic)
- *Service impact*: for this indication there were no service impacts identified, no impact on current infrastructure; small financial cost with significant cost-offset if general anaesthetic avoided and reduced supervision required post procedure
- *Equity*: Penthrox® is used for this (and other indications) in other areas of the UK
- *Safety*: no new or unexpected safety issues identified; with administration in theatres there were no concerns with ventilation and (unknown potential for) cumulative effect from volatile gas on staff.
  Locally patients will be advised not to drive for 24 hours post procedure.
- *Green prescribing*: this is a volatile anaesthetic in a single use delivery device, some of the environmental impact is offset by some users avoiding a general anaesthesia and all the disposable equipment used for general anaesthesia.

The Group was reassured that the service was taking a measured approach to introduction, and accepted the restricted local need for an additional method of pain relief. The off-label use of Penthrox®, in combination with local anaesthetic, for adults having surgical termination of pregnancy or evacuation of retained products of conception was supported with use limited to theatre at ARI.

ITEM	SUBJECT	ACTION
	FG1 473/25 - Methoxyflurane 99.9% inhalation vapour, liquid (Penthrox®) is routinely available in line with local guidance. **Indication under review: [off-label use] in combination with local anaesthetic for adults having surgical termination of pregnancy or evacuation of retained products of conception** **Restriction: limited to use in theatre at ARI.** **It was classified 3b - licensed product available for restricted off-label use and 8b - recommended for hospital use only.**	**FTEAM**

5.3. SMC 2667 - DABRAFENIB (PAEDIATRIC GLIOMA)

There were no declarations of interest recorded in relation to these products.

The Group considered the request for dabrafenib dispersible tablets used in combination with trametinib powder for oral solution for the treatment of paediatric patients with glioma with a BRAF V600E mutation.

The Group noted that:

- dabrafenib (Finlee®) [for this indication] meets SMC orphan and end of life (high-grade glioma only) criteria, and it was accepted for use only in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and the output from the PACE process
- September 2024, following a full submission assessed under the end of life and orphan medicine process, dabrafenib (Finlee®) was accepted for use within NHS Scotland in combination with trametinib (Spexotras®) for the treatment of paediatric patients aged 1 year and older with:
  - low-grade glioma with a BRAF V600E in the first-line setting
  - high-grade glioma with a BRAF V600E mutation who have received at least one prior radiation and / or chemotherapy treatment.
- gliomas are a heterogeneous group of primary central nervous system (CNS) tumours arising from glial cells. Gliomas are classified into low-grade or high-grade based on how fast it grows.
- surgery is the primary treatment of most low- and high-grade gliomas. Further management depends on whether resection was complete or incomplete and may include observation, chemotherapy and radiotherapy (which may be limited because of neurocognitive toxicity). The chemotherapy regimens are all used off-label. Carmustine implants and temozolomide are available for newly diagnosed high-grade glioma.
- glioma tumour cells with the BRAF mutation produce an abnormal form of a protein called BRAF. The abnormal BRAF protein activates another protein called MEK that is involved in stimulating cell division, resulting in uncontrolled division of cells and thus development of cancer.
- dabrafenib, works by blocking the action of the abnormal BRAF protein in patients with the BRAF mutation and thereby helps slow down the growth and spread of the cancer
- trametinib, works by blocking the activity of the MEK proteins, thereby slowing down the growth and spread of the cancer
- evidence for efficacy and safety comes from TADPOLE an open-label, phase II study comprising two cohorts one randomised, active-controlled cohort in unresectable low-grade glioma and one single-arm cohort in relapsed or refractory high-grade glioma
  - TADPOLE low-grade (n = 110 children, low-grade glioma with the BRAF V600E)
  - among paediatric patients with low-grade glioma with BRAF V600 mutations, dabrafenib plus trametinib resulted in significantly more responses, longer progression-free survival, and a better safety profile than standard chemotherapy as first-line therapy
  - TADPOLE high-grade glioma (single-arm cohort in relapsed or refractory high-grade glioma) 41 children with high-grade glioma with the BRAF V600E mutation received Finlee® combined with trametinib. Of these children, 56% (23/41)

achieved a complete or partial response to treatment which lasted for an average of 22 months. In the treatment of high-grade glioma, Finlee® was not compared with any other treatment or placebo.

- patient numbers are expected to be very small
- the aims of treatment for glioma include stopping or delaying progression and improving neurological function and quality of life
- treatment options for glioma are limited and dabrafenib plus trametinib offers a new targeted treatment option for people with a BRAF mutation
- this combination would provide a licensed, targeted, oral treatment option that could be taken at home. This would provide advantages to patients and carers, as regular travel to hospital is not required, resulting in reduced costs, and a substantial reduction in the time commitment required to attend for infusions.
- there are limited data in patients older than 18 years of age with glioma, therefore continued treatment into adulthood should be based on benefits and risks to the individual patient as assessed by the physician
- the SMC advice takes account of the benefits of PASs that improve the cost-effectiveness of treatment

Members acknowledged that combination treatment with dabrafenib plus trametinib offered the opportunity for children and adolescents with glioma with a BRAF V600E mutation to have longer before their condition gets worse.

The Group accepted the restricted local need for dabrafenib dispersible tablets used in combination with trametinib powder for oral solution for the treatment of paediatric patients with glioma with a BRAF V600E mutation, in line with SMC 2667.

SMC 2667 - Dabrafenib mesilate 10mg dispersible tablets (Finlee®)▼ is routinely available in line with national guidance (SMC 2667)
Indication under review: in combination with trametinib oral solution (Spexotras®) for:

- **the treatment of paediatric patients aged 1 year and older with low-grade glioma with a BRAF V600E mutation who require systemic therapy**
- **the treatment of paediatric patients aged 1 year and older with high-grade glioma with a BRAF V600E mutation who have received at least one prior radiation and / or chemotherapy treatment**

In an open-label, phase II study, dabrafenib plus trametinib significantly improved overall response rate compared with standard chemotherapy in the first-line treatment of unresectable low-grade glioma and resulted in an overall response rate of 56% in patients with relapsed or refractory high-grade glioma.
This advice applies only in the context of an approved NHS Scotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/list price that is equivalent or lower.
This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.
It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only.
Treatment should be initiated and supervised by a qualified physician experienced in the use of anti-cancer medicinal products. **FTEAM**

5.4. SMC 2684 - ZANUBRUTINIB (MARGINAL ZONE LYMPHOMA)

There were no declarations of interest recorded in relation to this product.

The Group considered the request for zanubrutinib as monotherapy for the treatment of adults with marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based therapy.

The Group noted that:

- zanubrutinib [for this indication] meets SMC orphan criteria, and it was accepted for use in NHS Scotland only in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and the output from the PACE process
- November 2024, following a full submission assessed under the orphan medicine process, zanubrutinib was accepted for use within NHS Scotland as monotherapy for the treatment of adults with MZL who have received at least one prior anti-CD20-based therapy (SMC 2684)
- MZL is a group of rare, slow-growing non-Hodgkin lymphomas. MZL develops from B lymphocytes, a type of white blood cell normally found at the edges of lymph node tissue. People are commonly diagnosed at about 75 years and relapse typically occurs within 5 years. [ref NICE]
- MZL is incurable and the 5-year (>90%) and 10-year (75% to 80%) survival rates for gastric EMZL highlight the good prognosis for these patients. Survival rates at 3 to 6 years of >86% for SMZL and >83% for NMZL have also been reported. [ref SMC]
- asymptomatic patients undergo a watch and wait approach
- treatment options include off-label use of medicines - rituximab (CD20 monoclonal antibody) used alone or in combination with chemotherapy
- zanubrutinib is an irreversible inhibitor of Bruton's tyrosine kinase (BTK). BTK is a signalling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. These pathways are involved in the pathogenesis of several B-cell lymphomas. By blocking the action of BTK, the medicine is expected to slow the progression of the disease.
- zanubrutinib is the first medicine licensed for MZL
- evidence for efficacy and safety comes from MAGNOLIA an international, open-label, single-arm phase II study, n = 66) and AU-003 an international, open-label, multiple-dose, multi-cohort phase I/II study. The relevant disease-specific cohort enrolled 20 patients with MZL in the single-arm, part 2 (dose expansion) of the study.
- the primary outcome in both studies was overall response rate (ORR)
- MAGNOLIA was the main study in MZL, in patients (66) whose cancer had come back or did not respond to previous treatment targeting CD20. Overall, around 68% (45 out of 66) had at least a partial response after an average of 28 months of treatment: 26% (17 out of 66) had a complete response (no signs of cancer) and 42% (28 out of 66) had a partial response.
- patient numbers are expected to be small, but costs would be cumulative as the median duration of treatment in MAGNOLIA was 24.2 months (May 2022 data cut-off)
- some cost offset is available from the displacement of rituximab plus chemotherapy
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of zanubrutinib
- zanubrutinib is an oral treatment that can be taken at home, so has some service benefits (no chair time, aseptic prep, consumables etc.,) and has time and cost savings for patients/carers who do not have to travel to hospital to receive treatment.
- the service has experience prescribing zanubrutinib for other indications

Members acknowledged that MZL is an incurable, rare condition that can have a negative impact on quality of life for people with MZL, and their families and carers, and that zanubrutinib is the first medicine licensed for MZL, and it is an oral treatment that would allow treatment at home.

The Group accepted the restricted local need for zanubrutinib as monotherapy for the treatment of adults with MZL who have received at least one prior anti-CD20-based therapy.

SMC 2684 - Zanubrutinib 80mg capsules (Brukinsa®)▼ is routinely available in line with national guidance (SMC 2684).
Indication under review: as monotherapy for the treatment of adults with marginal

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	zone lymphoma (MZL) who have received at least one prior anti-CD20-based therapy. **In a single-arm, open-label, phase II study, zanubrutinib monotherapy resulted in an overall response rate of 68% in patients with MZL who had received at least one prior anti-CD20-based therapy.** **This advice applies only in the context of an approved NHS Scotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/list price that is equivalent or lower.** **This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.** **It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only.** **Treatment with this medicinal product should be initiated and supervised by a physician experienced in the use of anticancer medicinal products.**	**FTEAM**

6. FORMULARY REVIEW

None.

7. PUBLISHED ADVICE

7.1. SCOTTISH MEDICINES CONSORTIUM ADVICE PUBLISHED APRIL 2025

The Group noted the SMC advice published April 2025.

Following publication of the negative SMC recommendation, for tebentafusp (Kimmtrak®)▼ SMC 2746, this medicine will not be included on the Grampian Joint Formulary for the indication in question.

The following SMC accepted medicines have not been processed within a 60-day timescale:

- SMC 2749 alectinib (Alecensa) (submission expected)
- SMC 2698 bimekizumab (Bimzelx®)▼ (submission received)
- SMC 2763 dapagliflozin (Forxiga®) (submission expected)
- SMC 2714 elafibranor (Iqirvo®)▼ (submission received)
- SMC 2755 eplontersen (Wainzua®)▼
- SMC 2661 futibatinib (Lytgobi®)▼

Local advice for these medicines and indications will be included in the April 2025 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts'. **FTEAM**

8. PROVISIONAL ADVICE

8.1. SCOTTISH MEDICINES CONSORTIUM ADVICE ISSUED APRIL 2025

The Group noted the SMC provisional advice issued April 2025.

If the negative SMC recommendations and non-submission statements are published next month, these medicines will not be included on the formulary for the indication in question.

8.2. NATIONAL CANCER MEDICINES ADVISORY GROUP (NCMAG) ADVICE ISSUED MARCH 2025

The Group noted the NCMAG provisional advice issued March 2025.

ITEM	SUBJECT	ACTION

8.3. FINAL DRAFT GUIDANCE FOR USE IN MOLNUPIRAVIR FOR TREATMENT OF COVID-19

The Chair reported that the final draft guidance for use of molnupiravir for treatment of COVID-19 has been published by the National Institute for Health and Care Excellence (NICE). The SMC has had direct input into the decision-making committee that produced the final draft guidance. SMC advice will be aligned with NICE final guidance. SMC will issue a collaborative advice document to boards following publication of the NICE final guidance (expected 16 April 2025). The advice will have the same status for health board consideration as other SMC advice on new medicines.

9. OTHER BUSINESS

9.1. FORMULARY GROUP ANNUAL REPORT 2024/25

The Chair reported that the Formulary Group annual report is being drafted ready for review at the June meeting. If members wish to have items highlighted in the report feedback should be sent to Ms Doney by 23 May. **ALL**

10. DOCUMENTS FOR INFORMATION

Items 10.1 (MHRA Safety Roundup March 2025), 10.2 (Antimicrobial Management Team (AMT) meeting minute January 2025), 10.3 (AMT meeting minute February 2025) and 10.4 (Acute and Mental Health Medicines Safety Group meeting minute December 2024) were noted.

11. AOCB

None.

DATE OF NEXT MEETING

Tuesday 20 May 2025 starting at 14.30 via Microsoft Teams.

Signature on file

CHAIR'S SIGNATURE **Dr Louise Elliot** **DATE 20 MAY 2025**