NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 21 November 2023 at 14:30 via Microsoft Teams

PRESENT	APOLOGIES	APPROVED
Ms L Cameron	Miss R Anderson	
Dr V Chieng	Mrs S Howlett	
Dr D Culligan until item 8.1	Mrs E Milne	
Ms A Davie	Mr M Paterson	
Ms F Doney (Vice-Chair)		
Dr L Elliot (Chair)		
Mrs G McKerron until item 8.3		
Dr M Metcalfe (Vice-Chair) until item 6.1		
Mr R Sivewright		

IN ATTENDANCE
Dr Callum Duncan, Consultant Neurologist, and Dr David Watson, GP with Extended Role (GPwER), for item 3.
Mrs Christine Standen, Formulary and Medicines Management Pharmacist.

Note some items were taken outwith the agenda order.

ITEM	SUBJECT	ACTION
	WELCOME The Chair welcomed members, opened the meeting, and noted that a quorum was present.	
1.	**APOLOGIES** Apologies for absence were requested and noted.	
3.	**PRESENTATION/DISCUSSION** The Chair welcomed Dr Callum Duncan, Consultant Neurologist, and Dr David Watson, GPwER, to discuss two new oral small molecule calcitonin gene-related peptide (CGRP) antagonists, and potential changes to the current triptan and CGRP monoclonal antibody (CGRP mAb) choices. Dr Duncan confirmed that the national headache pathways are now published and educational sessions for General Practice are planned for the new year. He discussed the triptan choices and treatment options for the prevention of migraine, including the possible use of the oral small molecule CGRP antagonists for high frequency episodic migraine (HFEM) and chronic migraine (CM), and erenumab [a CGRP mAb] for HFEM. Dr Duncan and Dr Watson proposed aligning the triptan choices based on efficacy and cost-effective prescribing options. Sumatriptan at a dose of 100mg should be the first-line oral triptan [NNT* 4.7 versus 6.1 for sumatriptan 50mg], with rizatriptan 10mg second-line. Rizatriptan 5mg is needed mainly for patients on propranolol, but it is quite expensive. The orodispersible formulation is more of a convenience, mainly absorbed in the stomach, it does not improve effectiveness, and there is a question if this formulation should be included on the formulary. Zolmitriptan oral could be replaced by eletriptan [40mg], because of its higher efficacy. Frovatriptan is a long-acting triptan that is particularly useful for menstrual migraine, for prolonged attacks or attack recurrence, and is useful for those that do not tolerate alternative triptans. Similarly, almotriptan is useful to have on the formulary.	

* NNT = Number-Needed-to-Treat

ITEM	SUBJECT	ACTION

For the nasal sprays, zolmitriptan is better and more cost-effective than sumatriptan. For the injections, there are occasional people that do not tolerate 6mg sumatriptan, and the 3mg injection would be useful, although use is expected to be very small.

There is an established prescription route for Primary Care initiated oral preventive treatments. These treatments have to be titrated to the target dose.

The Secondary Care preventative pathway is established, and unlicensed flunarizine is commonly used by the Headache Clinic. It is useful particularly for vestibular migraine, and is generally used before moving to other preventative treatments. Dr Duncan discussed the potential to move flunarizine to primary care prescribing and outlined the pros and cons of a change.

Dr Duncan confirmed that mAbs targeting the CGRP pathway are available, and it would be useful to have mAbs that block CGRP at different points. Formulary inclusion of erenumab for HFEM will mean that the specialist service has CGRP mAbs that target the receptor and ligand for both CM and HFEM.

The small molecule CGRP antagonists are oral tablets that block the CGRP receptor. They do not require dose titration and have short half-lives so present a number of advantages over the CGRP mAbs.
Locally use for most patients is likely to be after Botox®.
Dr Duncan and Dr Watson felt that rimegepant and atogepant, used as preventative treatments for HFEM or CM, should be prescribed in Primary Care on the advice of the Headache Clinic.

Responding to questions from members Dr Duncan and Dr Watson confirmed that:
- they expect the main use of rimegepant will be as an acute treatment, but it would be useful to also have it available for preventative use
- the number of people with HFEM is very small, and patients should not get into the scenario where they were using rimegepant on an almost daily basis. These patients would be moved to another treatment option.
- the need to check bloods before prescribing - is it necessary in a young fit person, probably not, so reasonable that it can be targeted. It is about safety, so being aware in people with established liver problems. It can be highlighted in the prescribing pathway to consider if someone might have an underlying liver problem.
- patients on small molecule CGRP antagonists for prevention will be followed-up at the Headache Clinic, this is not a new patient group just another preventive treatment option for the Clinic

The Chair thanked Dr Duncan and Dr Watson for attending the meeting and clarifying the current and proposed use of triptan and CGRP inhibitors. Dr Duncan and Dr Watson left the meeting before decision-making.

8.1. MEDICINES FOR THE MANAGEMENT OF MIGRAINE

8.1.1. ATOGEPANT AND RIMEGEPANT FOR THE PREVENTION OF MIGRAINE

Dr Culligan declared a person, non-specific interest in Abbvie Ltd.

The Group noted the differences in licensing between atogepant and rimegepant, and that only the SMC advice for atogepant takes account of the benefits of a PAS that improves the cost-effectiveness of treatment.

The Group accepted the restricted local need for the oral small molecule CGRP receptor antagonists for the prevention of migraine, with atogepant an additional treatment option for the prevention of HFEM and CM, and rimegepant an additional treatment option for

ITEM	SUBJECT	ACTION

the prevention of HFEM.

SMC 2599 - Atogepant 10mg, 60mg tablets (Aquipta®)▼ is routinely available in line with local guidance.
Indication under review: for the prevention of migraine in adults with:
1) chronic migraine (headaches on at least 15 days per month of which at least 8 days are with migraine) whose condition has failed to respond to three or more prior oral prophylactic treatments
2) high frequency episodic migraine (headaches on 10 - 14 days per month) whose condition has failed to respond to three or more prior oral prophylactic treatments
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.
It was classified 1b - available for restricted use under specialist supervision and 8d - treatment may be initiated in community on the recommendation of a consultant/specialist. **FTEAM**

SMC 2603 - Rimegepant 75mg oral lyophilisates (Vydura®)▼ is routinely available in line with local guidance.
Indication under review: for the prevention of migraine in adults with high frequency episodic migraine (headaches on 10 - 14 days per month) whose condition has failed to respond to three or more prior oral prophylactic treatments.
It was classified 1b - available for restricted use under specialist supervision and 8d - treatment may be initiated in community on the recommendation of a consultant/specialist. **FTEAM**

8.1.2. ERENUMAB (HFEM)

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

The Group agreed that it is useful to have CGRP mAbs that target different parts of the CGRP pathway, and the Group accepted the restricted local need for erenumab as an additional treatment option for the Headache Clinic in the management of HFEM.

Erenumab 70mg, 140mg solution for injection in pre-filled pen (Aimovig®)▼ is routinely available in line with local guidance.
Indication under review: for the prevention of migraine in adults with high frequency episodic migraine (headaches on 10 – 14 days per month) whose condition has failed to respond to three or more prior oral prophylactic treatments.
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.
It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only.
Treatment should be initiated by physicians experienced in the diagnosis and treatment of migraine. **FTEAM**

8.1.3. TRIPTANS FOR THE ACUTE RELIEF OF MIGRAINE

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

The Group discussed the Headache Service's proposed changes to the current triptan choices.

SUMATRIPTAN 3MG/0.5ML SOLUTION FOR INJECTION IN PRE-FILLED PEN

The Group considered the request to include a lower strength sumatriptan injection on the formulary for the acute relief of migraine attacks in adults.

ITEM	SUBJECT	ACTION

The Group noted:

- sumatriptan given by injection is particularly useful for patients who suffer with nausea and vomiting during an attack. A lower dose preparation would be beneficial where patients respond to the 6mg dose but have significant side-effects at this dose.
- the 3mg/0.5mL injection is outwith remit for the SMC, and is only licensed for migraine [6mg injection is also licensed for cluster headache]
- inclusion would be cost minimising, as cost offset is available from displacement of the 6mg injection (£39.50 versus £45.00 for two injections (Nov 2023 SDT))
- in line with the use of simple analgesics and triptans, use should be restricted to 8 to10 days per month (~2 per week) to prevent the development of medication overuse headache
- introduction will not affect patient numbers, i.e., not a new group of patients identified for treatment

The Group accepted the restricted local need for a lower strength sumatriptan injection for the acute relief of migraine attacks in adults who respond to treatment but are intolerant of the side-effects from the 6mg dose.

SBAR - Sumatriptan 3mg/0.5mL solution for injection in pre-filled pen is routinely available in line with local guidance.
Indication under review: in adults for the acute relief of migraine attacks, with or without aura.
Sumatriptan should only be used where there is a clear diagnosis of migraine.
It was classified 1a - available for general use and 8e - treatment may be initiated in either Primary or Secondary care.
Sumatriptan should not be used prophylactically.
The efficacy of sumatriptan is independent of the duration of the attack when starting treatment. Administration during a migraine aura prior to other symptoms occurring may not prevent the development of a headache. **FTEAM**

ELETRIPTAN TABLETS

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

Members noted the local 2021 and 2022 Primary Care triptan prescribing data, and that the Scottish Drug Tariff (SDT) triptan prices have been variable recently.

The Group discussed triptan efficacy and cost-effectiveness and supported the Headache Service's proposed changes to the current oral triptan choices, including eletriptan and removing oral zolmitriptan.

Eletriptan 20mg, 40mg film-coated tablets is routinely available in line with local guidance.
Indication under review: in adults for the acute treatment of the headache phase of migraine attacks, with or without aura.
Restriction: third-line oral triptan.
It was classified 1a - available for general use and 8e - treatment may be initiated in either Primary or Secondary care.
Eletriptan tablets should be taken as early as possible after the onset of migraine headache but they are also effective if taken at a later stage during a migraine attack.
Eletriptan, if taken during the aura phase, has not been demonstrated to prevent migraine headache and therefore eletriptan should only be taken during the headache phase of migraine.
Eletriptan tablets should not be used prophylactically. **FTEAM**

ITEM	SUBJECT	ACTION

Zolmitriptan 2.5mg, 5mg film-coated tablets, orodispersible tablets is not routinely available as there is a local preference for alternative medicines.
Indication under review: in adults for the acute treatment of migraine headache with or without aura.
Not routinely available as there is a local preference for alternative medicines. **FTEAM**
People currently established on zolmitriptan for acute migraine may continue to receive treatment until they and their clinician consider it appropriate to stop.

FLUNARIZINE

Members touched on the possibility of moving the prescribing of unlicensed flunarizine to Primary Care. Whilst accepting that there may be advantages to this change, members agreed that this was not the correct forum to open this discussion. Ms Doney will highlight the need for discussion at different groups, including the Grampian Area Drug and Therapeutics Committee (GADTC) meeting. **FD**

2. DRAFT MINUTE OF THE MEETING HELD 17 OCTOBER 2023

Ms Doney confirmed that in October publication of the vutrisiran decision was deferred because vutrisiran was only agreed for inclusion in the National Services Scotland (NSS) Ultra-orphan medicines financial risk-share arrangements in November (not October as originally expected).

In line with the previous discussion the Group agreed to include the local decision for vutrisiran in the November decisions document.

SMC 2596 - Vutrisiran sodium 25mg solution for injection in pre-filled syringe (Amvuttra®)▼ is routinely available in line with national guidance (SMC 2596).
Indication under review: for the treatment of hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) in adults with stage 1 or stage 2 polyneuropathy.
Vutrisiran offers an additional treatment choice of double-stranded small interfering ribonucleic acid (siRNA) for this indication.
Another double-stranded siRNA, patisiran, has been accepted via the ultra-orphan medicine process for this indication.
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.
It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only. Therapy should be initiated under the supervision of a physician knowledgeable in the management of amyloidosis.
Treatment should be started as early as possible in the disease course to prevent the accumulation of disability. **FTEAM**

Members agreed the wording of the rivaroxaban decision, noting that it will only be published when prescribing guidance is available. **FTEAM**

The Group accepted the draft note of the meeting subject to removal of the vutrisiran and rivaroxaban decisions and minor typographical changes. **FD**

The corrected final approved minute will be in the public domain within 21 days of final approval. **FD**

ITEM	SUBJECT	ACTION

4. MATTERS ARISING

4.1. ACTION LOG

The action log was noted.

No additional items were identified for discussion at the meeting.

4.2. FORMULARY GROUP SURVEY RESULTS

Mrs Standen presented the results of the survey of the format, content and presentation of the information provided for Formulary Group reviews.

5. FORMULARY GROUP DECISIONS OCTOBER 2023 - PUBLISHED 30/10/2023

Members ratified the decisions of the October 2023 meeting as published.

6. FORMULARY REVIEW

6.1. FORMULARY UPDATES

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

The Group reviewed the Formulary Team's summary document highlighting two suggested updates.

It was confirmed that for:

- SMC 2570 voclosporin:
  - October 2023, following a full submission reviewed by the SMC executive, voclosporin in combination with mycophenolate mofetil for the treatment of adults with active class III, IV or V (including mixed class III/V and IV/V) lupus nephritis [SMC 2570] was accepted for use in NHS Scotland
  - the Service confirmed that it does not wish to apply for formulary inclusion at this time, as the preferred treatment for this indication is tacrolimus
- SMC 2286 cerliponase alfa:
  - is an ultra-orphan medicines assessment report (UMAR):
  - medicines undergoing an initial assessment of evidence (i.e., UMAR) by the SMC are considered outwith remit for the Formulary Group; these medicines will ultimately be accessed via the Scottish Government ultra-orphan pathway
  - October 2020, the SMC issued an UMAR for cerliponase alfa [SMC 2286] for the treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease, and the same month it was added to Formulary as '*Not routinely available in NHS Grampian. If local need identified contact the Pharmacist Team Leader/Principal Pharmacist – Supply (ARI)*'
  - the Scottish Government confirmed that from 2 November 2023, cerliponase alfa (Brineura®) can be prescribed within the ultra-orphan pathway while further evidence on its effectiveness is generated. After 3 years the company will provide an updated submission for reassessment to allow a decision on its routine use in NHS Scotland.

The Formulary Group supported the Service's position and recorded voclosporin as 'Not routinely available as there is a local preference for alternative medicines'.

SMC 2570 - Voclosporin 7.9mg soft capsules (Lupkynis®)▼ is not routinely available as there is a local preference for alternative medicines.
Indication under review: in combination with mycophenolate mofetil for the treatment of adults with active class III, IV or V (including mixed class III/V and IV/V) lupus nephritis.

ITEM	SUBJECT	ACTION

Addition of voclosporin to mycophenolate mofetil significantly improved renal response rate in adults with active class III, IV or V (including mixed class III/V and IV/V) lupus nephritis.
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.
Not routinely available as there is a local preference for alternative medicines. **FTEAM**

In line with local formulary processes the Group supported updating the decision for SMC 2286 to 'If local need identified treatment is available through the National Services Scotland Ultra orphan medicines Risk Share Scheme'.

SMC 2286 - Cerliponase alfa 150mg solution for infusion (Brineura®)▼ is not routinely available in NHS Grampian.
Indication under review: for the treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency.
Not routinely available in NHS Grampian. If local need identified treatment is available through the National Services Scotland Ultra orphan medicines Risk Share Scheme.
Cerliponase alfa must only be administered by a trained healthcare professional knowledgeable in intracerebroventricular administration in a healthcare setting. **FTEAM**

6.2. CHANGE OF NAME FOR SOMATULINE® AUTOGEL® (LANREOTIDE) SOLUTION FOR INJECTION IN A PREFILLED SYRINGE

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

Ms Doney conformed that:
- Ipsen will be changing the name of Somatuline® Autogel® (lanreotide) to Lanreotide Ipsen
- there will be no change to the medicine inside the pre-filled syringe nor to the pre-filled syringe itself
- the formulary entry will be updated **FTEAM**

6.3. NATIONAL HEADACHE PATHWAY PUBLISHED

Discussed under item 3 and 8.1, members noted publication of the national headache pathways.

7. OTHER BUSINESS

Items 7.1 and 7.2 were taken together.

7.1. YELLOW CARD CENTRE SCOTLAND ANNUAL REPORT 2022 – 2023 AND 7.2. #MEDSAFETYWEEK 2023 (6-12 NOVEMBER)

Mrs Cameron confirmed that #MedSafetyWeek was held on the 6th to the 12th November. It is an annual social media campaign from the Medicines and Healthcare products Regulatory Agency (MHRA) which aims to raise awareness of how adverse drug reactions (ADRs) can be reported through its Yellow Card reporting scheme.

As part of #MedSafetyWeek the trainee pharmacists based in Aberdeen Royal Infirmary (ARI) wrote a MedWatch newsletter about ADRs, who can report ADRs, what is an ADR, and how to report an ADR.

Linked in to the MedWatch article is the most recent Yellow Card Centre Scotland annual report (April 2022 to March 2023).
This year the COVID vaccines are included in the total number, so it does look different to

ITEM	SUBJECT	ACTION

previous years. Patient groups remain the highest group reporting.
NHS Grampian sits just below the national average in terms of number of reports per 100,000 population.

A breakdown of the local data is expected and will be shared with the Group when available. **LC**

7.3. WAAW 18TH - 24TH NOVEMBER

The Chair confirmed that the World Health Organization (WHO) has renamed World Antimicrobial Awareness Week to World Antimicrobial Resistance Awareness Week (WAAW or World AMR Awareness Week).
WAAW aims to increase awareness of global antimicrobial resistance (AMR) and to encourage best practices for using antimicrobials responsibly among the general public, health workers and policy makers, to avoid the further emergence and spread of drug-resistant infections.
The theme for WAAW 2023 will remain "Preventing antimicrobial resistance together", as in 2022. AMR is a threat to humans, animals, plants and the environment.

7.4. ANASTROZOLE FOR THE PREVENTION OF BREAST CANCER

Ms Doney confirmed the arrangements [in NHS Scotland] for review of a generic medicine, anastrozole, which was recently licensed for the prevention of breast cancer in post-menopausal women at moderate or high risk of developing the disease.

It was confirmed that:
- on 6 November 2023 authorisation for this new indication was granted to Accord Healthcare Ltd
- the licensing work was undertaken by Accord Healthcare on a not-for-profit basis. The Medicines Repurposing Programme will now work with the Medicines and Healthcare products Regulatory Agency (MHRA) and the British Generic Manufacturers Association to ensure other companies that make anastrozole adopt the new licensed indication.
- anastrozole is a generic medicine and is considered outwith remit for SMC
- although outwith remit, the National Cancer Medicines Advisory Group (NCMAG) has scheduled a proposal for review at the NCMAG Council meeting on Thursday 21 March 2024, with the advice to be published in late April 2024
- three medicines will be considered for chemoprevention of breast cancer (anastrozole, tamoxifen, raloxifene)
- if supported there will be challenges with the implementation of these proposals

8. NEW PRODUCT REQUESTS

8.2. FG1 458/23 - TOBRAMYCIN POWDER [UNLICENSED] (INFECTED NON UNIONS OR HIGH RISK OF INFECTION FRACTURES)

The Group considered the request for unlicensed tobramycin as a local antibiotic treatment of patients with infected non-unions or high-risk of infection fractures to coat intramedullary nails with antibiotic loaded calcium sulfate.

The Group noted that:
- tobramycin 40mg/mL solution for injection is available as a licensed product in the UK, however use for this indication would be off-label use
- the service has stated that when the solution is mixed with the calcium sulfate it sets too quickly to allow application to the intramedullary nail. If the powder is used they would expect slightly longer setting times.
- the Antimicrobial Management Team (AMT) has no concerns with this application, and the Chair noted it gives orthopaedics a wider array of agents they can use, which is

important in the context of more multidrug resistant gram-negative bone and joint infections
- Quality Assurance has carried out a risk assessment on the unlicensed product and assigned the level of risk as low
- Stimulan® is an absorbable, calcium sulfate antibiotic carrier that is specifically designed to support the proactive management of dead space and surgical site infection.
- the alternative to using calcium sulfate as an antibiotic carrier is to use an antibiotic cement coated nail. The service has stated that the disadvantages of this method are that you have to ream high above the diameter of the nail due to the space occupied by the cement which can lead to increased blood loss, and the cement does not dissolve, leaving a foreign body for bacterial growth.
- a study reported on their recent experience with antibiotic-loaded calcium sulfate-coated interlocking intramedullary nails (CS-IMN) for infection prevention and they compared the efficacy of CS-IMN versus antibiotic-loaded polymethylmethacrylate-coated intermedullary nails (PMMA-IMN) for infection eradication.
  - when used for infection prophylaxis there was a:
    - 100% (24/24 patients) prevention of infection rate
    - 95.5% union rate (21/22 patients)
    - 100% (24/24 patients) limb salvage rate
  - when used for infection eradiation:
    - the infection was eradicated in 7/9 patients (77.8%) in the CS-IMN group versus 21/26 patients (80%) in the PMMA-IMN group
    - bone union/fusion was achieved in 8/9 patients (88.9%) in the CS-IMN group versus 21/24 patients (87.5%) in the PMMA-IMN group
    - the limb salvage rate in the CS-IMN group was 100% (9/9 patients) versus 89% (25/28 patients) in the PMMA-IMN group.
  - The conclusion was that CS-IMN are very effective at infection prophylaxis in high-risk cases where infection is suspected and that early analysis suggests that CS-IMN are non-inferior to PMMA-IMN for infection eradication
- patient numbers are expected to be small. However, there may also be patients from other Health Boards as ARI is the Major Trauma Centre for the North of Scotland.

The Group accepted the restricted local need for unlicensed tobramycin powder as a local antibiotic treatment of patients with infected non unions or high risk of infection fractures to coat intramedullary nails with antibiotic loaded calcium sulfate.

FG1 458/23 - Tobramycin 1.2g powder [unlicensed] is routinely available in line with local guidance.
Indication under review: [unlicensed product] for local antibiotic treatment of patients with infected non-union or high-risk of infection fractures to coat intramedullary nail with antibiotic loaded calcium sulfate.
It was classified 3a – unlicensed product [available for restricted use under specialist supervision] and 8b - recommended for hospital use only. FTEAM

8.3. SMC 2543 - IBRUTINIB (ADULTS WITH PREVIOUSLY UNTREATED CHRONIC LYMPHOCYTIC LEUKAEMIA (CLL))

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

The Group considered the request for use of ibrutinib in combination with venetoclax for the treatment of adults with previously untreated chronic lymphocytic leukaemia (CLL).

The Group noted that:
- ibrutinib is given as 420mg once daily as a single agent for three cycles (1 cycle is 28 days), followed by 12 cycles of ibrutinib plus venetoclax. Venetoclax is administered at a starting dose of 20mg daily for 7 days then gradually increased over a period of 5

weeks up to 400mg once daily.
- in the CAPTIVATE study (non-comparative), the complete response was 58% for patients without a del17p mutation (n=136) and 56% for patients with a del17p and/or TP53 mutation (n=27)
- in the GLOW study, after a median follow-up of 34.1 months the median progression-free survival (PFS) was 23.7 months for chlorambucil plus obinutuzumab and it was not reached for ibrutinib plus venetoclax. The Kaplan-Meier estimated progression-free survival (PFS) at 36 months was 28% versus 79% for chlorambucil plus obinutuzumab and ibrutinib plus venetoclax respectively.
- the Marketing Authorisation Holder (MAH) presented an indirect treatment comparison to SMC which concluded ibrutinib plus venetoclax had similar efficacy to venetoclax plus obinutuzumab
- in the CAPTIVATE study, the most common grade ≥3 adverse events were neutropenia (33%) and hypertension (6%)
- the Service highlighted that there is a slight increase in cardiac risk with ibrutinib compared to venetoclax plus obinutuzumab. The Service will not consider patients with a cardiac history or significant risk factors for ibrutinib plus venetoclax.
- patient numbers are expected to be very small, and ibrutinib plus venetoclax will be used as an alternative to venetoclax plus obinutuzumab in those with un-mutated IGHV status, so cost offset is available
- ibrutinib and venetoclax are both oral tablets whereas obinutuzumab is an intravenous (IV) infusion which requires more nurse/chair time

The Group accepted the restricted local need for ibrutinib in combination with venetoclax for the treatment of adults with previously untreated CLL, in line with SMC 2543.

SMC 2543 - Ibrutinib 140mg, 280mg, 420mg film-coated tablets (Imbruvica®) are routinely available in line with national guidance (SMC 2543).
Indication under review: in combination with venetoclax for the treatment of adults with previously untreated chronic lymphocytic leukaemia (CLL).
In a phase III study, ibrutinib plus venetoclax resulted in a statistically significant improvement in progression-free survival compared with another combination therapy in a defined group of patients with previously untreated CLL.
This advice applies only in the context of approved NHS Scotland Patient Access Scheme (PAS) arrangements delivering the cost-effectiveness results upon which the decision was based, or PAS/list prices that are 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

8.4. SMC 2600 - ZANUBRUTINIB (ADULTS WITH CLL UNSUITABLE FOR CHEMO-IMMUNOTHERAPY)

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

The Group considered the request for the Bruton tyrosine kinase (BTK) inhibitor zanubrutinib for the treatment of adults with CLL in whom chemo-immunotherapy is unsuitable,

The Group noted that:
- zanubrutinib:
  - is taken orally at a recommended total daily dose of 320mg
  - treatment should be continued until disease progression or unacceptable toxicity
- in SEQUOIA (previously untreated CLL), after a median follow-up of 33.5 months, the

median PFS was not reached with zanubrutinib and was 39.2 months for bendamustine plus rituximab
- in ALPINE (relapsed or refractory CLL):
  - the overall survival rate was 78.3% for zanubrutinib and 62.5% for ibrutinib
  - patients previously treated with a BTK inhibitor were excluded from the trial
  - the safety profile of zanubrutinib was better than ibrutinib, with fewer adverse events leading to treatment discontinuation and fewer cardiac events
- the median duration of treatment in the ALPINE trial was 28.4 months, but the service has stated that there will be large variability and as with other BTK inhibitors some patients will remain on therapy for many years
- patient numbers are expected to be small
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of zanubrutinib
- cost avoidance is available as zanubrutinib will be used instead of other BTK inhibitors

The Group accepted the restricted local need for zanubrutinib, as an alternative BTK inhibitor, for the treatment of adults with CLL in whom chemo-immunotherapy is unsuitable, in line with SMC 2600.

SMC 2600 - Zanubrutinib 80mg hard capsules (Brukinsa®)▼ is routinely available in line with national guidance (SMC 2600).
Indication under review: as monotherapy for the treatment of adults with chronic lymphocytic leukaemia in whom chemo-immunotherapy is unsuitable.
Zanubrutinib offers an additional treatment choice in the therapeutic class of Bruton tyrosine kinase inhibitor in this setting.
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.
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 physician experienced in the use of anticancer medicinal products. FTEAM

8.5. SBAR - ATEZOLIZUMAB 1,875MG SOLUTION FOR INJECTION (TECENTRIQ®)

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

The Group considered the request for a new subcutaneous (SC) formulation of atezolizumab.

The Group noted that:
- the new SC formulation is considered outwith remit by the SMC
- SC atezolizumab [1,875mg every three weeks] was non-inferior when compared with IV atezolizumab [1,200mg every three weeks]
- the 1,875mg formulation is licensed for the same indications as the IV formulation
- the cost is equivalent to the 1,200mg dose which is also administered every 3 weeks
- no new or unexpected safety concerns have been identified
- the SC formulation enables patients to receive the medicine over 3 to 8 minutes compared with the IV formulation that requires a 30 to 60 minute infusion
- patients currently receiving atezolizumab IV infusion may transition to atezolizumab SC injection
- the IV formulation is prepared in the Aseptic Unit whereas the SC formulation would be stocked in the Anchor Day Case Unit area
- other centres in Scotland are looking to make the switch to SC atezolizumab, and NHS England has already rolled out the SC injection to patients
- the availability of a ready-made fixed-dose injection, with a shorter administration time, provides the opportunity to release capacity in both the Aseptic Unit and Anchor Day Case Unit

ITEM	SUBJECT	ACTION

- the SC injection is more comfortable than the IV infusion and this coupled with the reduced administration time would significantly improve the patient experience

The Group agreed that the new SC preparation provides the opportunity for significant benefits for patients and the Health Board.

The Group accepted the restricted local need for SC atezolizumab, in line with the current formulary acceptance for the infusion, without the need for a full submission.

SBAR - Atezolizumab 1,875mg solution for injection (Tecentriq®) is routinely available in line with local guidance.
Indications under review:
In combination with:

- **bevacizumab for the treatment of adults with advanced or unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy – SMC 2349 (July 2021)**
- **paclitaxel albumin for the treatment of adults with unresectable locally advanced or metastatic triple negative breast cancer (TNBC) whose tumours have PD-L1 expression ≥1% and who have not received prior chemotherapy for metastatic disease – SMC 2267 (Nov 2020)**
- **carboplatin and etoposide, is indicated for the first-line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC) - SMC 2279 (Nov 2020)**

Where treatment is subject to a two-year clinical stopping rule:

- **as monotherapy for the treatment of adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy. Patients with EGFR activating mutations or ALK positive tumour mutations should also have received targeted therapy before receiving atezolizumab – SMC 1336/18 (July 2018)**

It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only.
Tecentriq® must be initiated and supervised by physicians experienced in the treatment of cancer.
Tecentriq® subcutaneous formulation is not intended for intravenous administration and should be administered via a subcutaneous injection only.
It is important to check the product labels to ensure that the correct formulation (intravenous or subcutaneous) is being administered to the patient, as prescribed. **FTEAM**

8.6. SBAR - FIDAXOMICIN

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

The Group considered the request from the AMT to extend the use of fidaxomicin to new indications and paediatric patients, and include a new formulation on the formulary.

The Group noted that:

- fidaxomicin, as the tablet formulation, is currently included on the formulary [for adults for recurrence] in line with guidance on *Clostridioides difficile* infection (CDI) published by the Scottish Health Protection Network (SHPN)
- in 2022, the Scottish Antimicrobial Prescribing Group (SAPG) reviewed the NICE guidance [NG199] and noted that the recommendations for first- and second-line treatments differ from current guidance and clinical practice in Scotland, and SAPG recommended Boards review their current recommendations and update guidance locally
- NG199 includes fidaxomicin as:
  - a second-line option for treatment of first episode (patients who fail to improve after 7 days or worsen with oral vancomycin and after discussion with an infection specialist)

ITEM	SUBJECT	ACTION

- treatment of a first recurrence of infection within 12 weeks (relapse) provided the initial treatment was completed
- the availability of fidaxomicin granules for oral suspension provides:
  - an additional licensed formulation for the paediatric population
  - a licensed preparation for those with swallowing difficulties or enteral feeding tubes
- NICE states that '*when prescribing antibiotics for suspected or confirmed CDI in children and young people under 18 years, base the choice of antibiotic on what is recommended for CDI in adults. Take into account licensed indications for children and young people, and what products are available*'.
- the changes will increase the prescribing of fidaxomicin [and vancomycin], but provides the potential for faster resolution of CDI and less risk of recurrence, which will be beneficial for patient care, and ultimately cost-saving
- the treatment course is 10 days, which will cost the same regardless of the formulation used

The Group accepted the recommendation of the local AMT and SAPG to update the local antibiotic choices in line with the recommendations of NICE NG199. Treatment remains restricted to 'on the advice of a Medical Microbiologist or Infection Specialist'.

SBAR - Fidaxomicin 40mg/mL granules for oral suspension is routinely available in line with national guidance (NG199).
Indication under review: for the treatment of *Clostridioides difficile* infections (CDI) also known as *C. difficile*-associated diarrhoea (CDAD) in adults, and paediatric patients from birth to <18 years of age.
Consideration should be given to official guidelines on the appropriate use of antibacterial agents.
Restriction: in line with antibiotic treatment recommendations of NICE guideline NG199, July 2021. Treatment should be started by, or after advice from a Medical Microbiologist or Infection Specialist.
It was classified 1b - available for restricted use under specialist supervision and 8d - treatment may be initiated in community on the recommendation of a consultant/specialist. **FTEAM**

SBAR - Fidaxomicin 200mg film-coated tablets is routinely available in line with national guidance (NG199).
Indication under review: for the treatment of *Clostridioides difficile* infections (CDI) also known as *C. difficile*-associated diarrhoea (CDAD) in adult and paediatric patients with a body weight of at least 12.5kg.
Consideration should be given to official guidelines on the appropriate use of antibacterial agents.
Restriction: in line with the antibiotic treatment recommendations of NICE guideline NG199, July 2021. Treatment should be started by, or after advice from a Medical Microbiologist or Infection Specialist.
It was classified 1b - available for restricted use under specialist supervision and 8d - treatment may be initiated in community on the recommendation of a consultant/specialist. **FTEAM**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE ISSUED NOVEMBER 2023

The Group noted the SMC provisional advice issued November 2023.

If the non-submission statements are published next month, these medicines will not be included on the formulary for the indications in question.

ITEM	SUBJECT	ACTION

10. ADVICE PUBLISHED

10.1. SCOTTISH MEDICINES CONSORTIUM ADVICE PUBLISHED - NOVEMBER 2023

The Group noted the SMC advice published November 2023.

Following publication of the negative SMC recommendations, for efgartigimod alfa (Vyvgart®)▼ SMC 2561, mercaptamine (Procysbi®) SMC 2571 and pegunigalsidase (Elfabrio®)▼ SMC 2591, and the non-submission statement for progesterone vaginal capsules (Utrogestan®) SMC 2630, these medicines will not be included on the Grampian Joint Formulary for the indications in question.

The following SMC accepted medicines have not been processed within a 60-day timescale:
- SMC 2578 avacopan (Tavneos®)▼
- SMC 2605 bimekizumab (Bimzelx®)▼
- SMC 2582 durvalumab (Imfinzi®)▼ (submission received)
- SMC 2534 risankizumab (Skyrizi®)▼ (submission expected)
- SMC 2573 selpercatinib (Retsevmo®)▼
- SMC 2585 tafamidis (Vyndaqel®)▼

Local advice for these medicines and indications will be included in the November 2023 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts'. **FTEAM**

10.2. NCMAG ADVICE PUBLISHED OCTOBER 2023

The Group noted the National Cancer Medicines Advisory Group (NCMAG) advice published October 2023

The following NCMAG supported medicines have not been processed within a 60-day timescale:
- NCMAG 106 nivolumab (Opdivo®) (submission expected)
- NCMAG 107 dabrafenib (Tafinlar®) plus trametinib (Mekinist®) (submission expected)

Local advice for these medicines and indications will be included in the November 2023 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts'. **FTEAM**

11. GENERAL INFORMATION FROM SCOTTISH MEDICINES CONSORTIUM - NOVEMBER 2023

None.

12. DOCUMENTS FOR INFORMATION

ITEMS 12.1 (DRUG SAFETY UPDATE OCTOBER 2023)

The Chair highlighted the Drug Safety Update article outlining new safety measures for the prescribing of isotretinoin, and improved assessment and monitoring of mental health and sexual function issues.
Members discussed the article, and agreed that there is a need to increase awareness of the issues and record that someone is taking isotretinoin, so that a patient presenting with mental health issues is not missed.
Ms Davie will take the issue to the Primary Care Prescribing Group (PCPG). **AD**

Items 12.2 and 12.3 (AMT minute July 2023 and August 2023), 12.4 and 12.5 (Acute and Mental Health Medicines Safety Group minute July and September 2023) and 12.6 (NCMAG Programme Quarterly Update October 2023) were noted.

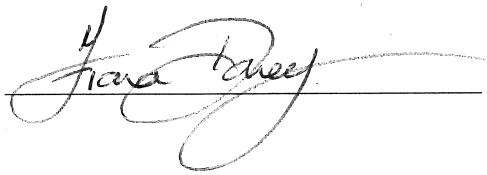
ITEM	SUBJECT	ACTION

13. AOCB

None.

DATE OF NEXT MEETING

Tuesday 19 December 2023 starting at 14.30 via Microsoft Teams

CHAIR'S SIGNATURE  **DATE 19 DECEMBER 2023**