NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 20 December 2022 at 14:30 via Microsoft Teams

PRESENT	APOLOGIES	APPROVED
Dr V Chieng	Dr D Culligan	
Ms F Doney (Vice-Chair)	Ms L Cameron	
Dr E Elias	Ms A Davie	
Dr L Elliot (Chair)	Mrs G McKerron	
Ms M Galvin		
Dr M Metcalfe (Vice-Chair)		
Mrs K Neave		
Dr J Newmark		
Mrs S O'Beirne		
Mr M Paterson		
Mr R Sivewright		

IN ATTENDANCE
Ms. Cynthia Santiago, Associate Specialist/Retina Lead and Deputy Clinical Lead for Ophthalmology, for item 3.

Note some items were taken outwith agenda order.

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	WELCOME The Chair welcomed members, opened the meeting and noted that a quorum was present.	
1.	**APOLOGIES** Apologies for absence were requested and noted.	
2.	**DRAFT MINUTE OF THE MEETING HELD 15 NOVEMBER 2022** The Group 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**
4.	**MATTERS ARISING**	
	4.1. Action Log The action log was noted. No additional items were identified that should have been included on the agenda.	
	4.2. North Cancer Alliance (NCA) update Ms Doney reported that the North Cancer Alliance (NCA) suspended work during the pandemic but work has now resumed. The NCA is planning to develop a regional process for the review and introduction of cancer medicines into clinical practice. Initial discussions regarding processes have begun, with the NCA planning to pilot a review of one or two SMC accepted medicines from the provisional advice issued in January 2023. Review of local implications (service and/or financial) related to introduction will remain the responsibility of Health Boards.	

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4.3. SMC 2368 - Olaparib (availability of genomic instability testing)

Mr Paterson declared a personal, non-specific interest in AstraZeneca UK Limited and took part in decision-making.

Last month the Group noted the lack of benefit in homologous recombination deficiency (HRD)-negative patients when olaparib [in combination with bevacizumab] was used for the maintenance treatment of ovarian cancer, SMC 2368.
The Group requested confirmation that a validated genomic instability test was available locally.

Ms Galvin confirmed that a test for genomic instability is not yet available, however it is expected in the near future. She requested extension of the formulary approval pending availability of the test.

Mindful of the lack of benefit in HRD-negative patients but noting the potential that testing would be available in the near future, the Group accepted the restricted local need for olaparib in combination with bevacizumab, in line with SMC 2368, for adults whose cancer is associated with HRD-positive status including those with genomic instability determined using a validated test. Formulary acceptance is subject to availability of a validated test to confirm genomic instability.

SMC 2368 - Olaparib 100mg, 150mg film-coated tablets (Lynparza®) is routinely available in line with local guidance.
Indication under review: in combination with bevacizumab for the maintenance treatment of adults with advanced (FIGO stages III and IV) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy in combination with bevacizumab and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either a BRCA1/2 mutation and/or genomic instability.
Restriction: adults with confirmation of genomic instability determined using a validated test.
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 olaparib should be initiated and supervised by a physician experienced in the use of anticancer medicinal products. FTEAM

4.4. SMC 2446 - Sacituzumab govitecan (clinical practice guideline for mTNBC)

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

Last month the Group was minded to accept sacituzumab govitecan to formulary, but considered that additional information related to the treatment options and pathway/clinical practice guideline for metastatic triple-negative breast cancer (mTNBC) was needed to support decision-making.

Ms Galvin consulted with Dr Urquhart and he confirmed that:
- the regional clinical management guideline for breast cancer (including mTNBC) is under review, an update should be available soon and will be shared when available
- it has been very difficult to mandate lines of therapy in mTNBC because there are many influences - individual patients wishes, patient's fitness, prior drug exposure etc.

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Ms Galvin requested formulary approval of sacituzumab pending availability of the regional guidance.

Members acknowledged that these are challenging situations, and accepted the restricted local need for sacituzumab govitecan for the treatment of adults with unresectable locally advanced or mTNBC, as outlined in SMC 2446. Acceptance is subject to provision of the clinical management guideline for breast cancer when it is available. **GU/MG**

SMC 2446 - Sacituzumab govitecan 180mg powder for concentrate for solution for infusion (Trodelvy®) ▼ is routinely available in line with national guidance (SMC 2446).
Indication under review: treatment of adults with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior lines of systemic therapies, at least one of them given for unresectable locally advanced or metastatic disease.
Sacituzumab govitecan, compared with a range of single-agent chemotherapies, significantly improved progression free survival and overall survival in adults with mTNBC, without brain metastases, who had received at least two prior chemotherapy regimens including a taxane.
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 must only be prescribed and administered to patients by healthcare professionals experienced in the use of anti-cancer therapies and should be administered in an environment where resuscitation facilities are available. **FTEAM**

5. FORMULARY GROUP DECISIONS NOVEMBER 2022 - PUBLISHED 28/11/2022

Members ratified the decisions of the November 2022 meeting as published. **FTEAM**

6. NETFORMULARY/FORMULARY REVIEW

6.1. Formulary updates December 2022

Mr Paterson declared a personal, non-specific interest in AstraZeneca UK Limited and took part in decision-making. There were no other declarations of interest recorded in relation to these products.

The Group reviewed the Formulary Team's proposed decisions and actions for a newly licensed medicine and some discontinued medicines.

ATGAM® 50MG/ML CONCENTRATE FOR SOLUTION FOR INFUSION (HORSE ANTI-HUMAN T LYMPHOCYTE IMMUNOGLOBULIN (EATG))

Ms Doney reported that:

- the unlicensed product anti-thymocyte globulin [equine] (ATGAM®) is currently included on the formulary. June 2016 it was accepted for restricted use as a treatment option for aplastic anaemia in adults and children.
- immunosupressive therapy with equine anti-thymocyte globin (ATG), usually with ciclosporin, has been the standard first-line treatment for patients with aplastic anaemia who are not eligible for haematopoietic stem cell transplant for decades
- the MHRA recommends that an unlicensed medicine should only be used when a patient has special requirements that cannot be met by the use of a licensed medicine

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- September 2022, Pfizer launched a licensed version of Atgam® and colleagues in the Haematology Service confirmed that use will switch to the licensed product when the current stocks of the unlicensed product have been exhausted
- the change to a licensed preparation is potentially cost minimising

The Group accepted the restricted local need for the licensed product Atgam®, replacing the unlicensed product, without the need for a submission. The indication and classification remain in line with the current formulary position.

SBAR - Atgam® 50mg/mL concentrate for solution for infusion (horse anti-human T lymphocyte immunoglobulin (eATG)) is routinely available in line with local guidance.
Indication under review: for use in adults and in children aged 2 years and older for the treatment of acquired moderate to severe aplastic anaemia of known or suspected immunologic aetiology as part of standard immunosuppressive therapy in patients who are unsuitable for haematopoietic stem cell transplantation (HSCT) or for whom a suitable HSC donor is not available.
Restriction: prescribing is limited to Consultant Haematologists in line with national guidance.
It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only. Only physicians experienced in immunosuppressive therapy should use Atgam®. Facilities equipped and staffed with adequate laboratory and supportive inpatient medical resources should be used. **FTEAM**

KOMBOGLYZE® 2.5/850MG TABLETS AND PARATHYROID HORMONE (RDNA) (NATPAR®)

Ms Doney reported that:
- Komboglyze®:
  - is a fixed dose combination tablet containing saxagliptin hydrochloride plus metformin hydrochloride, available in two strengths - 2.5/850mg and 2.5/1000mg film-coated tablets
  - the MAH, AstraZeneca UK Limited, discontinued Komboglyze® 2.5/850mg film-coated tablets on 31st May 2022 and there is no longer stock available. As the higher strength tablet remains available it is assumed this is a commercial decision.
  - the Formulary Team proposed amending the formulary entry to note the withdrawal of the lower strength tablet
- parathyroid hormone (rDNA) (Natpar®):
  - is not recommended for use within NHS Scotland due to non-submission [SMC 1334/18, April 2018]
  - the MAH, Takeda UK Limited, published a Direct Healthcare Professional Communication (DHPC) confirming the discontinuation of all strengths of Natpar® by the end of 2024 due to manufacturing challenges
  - the Formulary Team proposed amending the formulary entry to note the withdrawal

The Group supported the changes proposed by the Formulary Team. **FTEAM**

CALFOVIT D3® 1200MG/ 800I.U. POWDER FOR ORAL SUSPENSION (CALCIUM PHOSPHATE/COLECALCIFEROL)

Ms Doney reported that:
- Calfovit D3® sachet is a once-a-day preparation that is included on formulary for people with swallowing difficulties
- colleagues in Medicines Information are investigating potential cost-effective alternatives for people with swallowing difficulties
- pending advice from colleagues regarding possible alternatives, the Formulary Team

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proposed amending the formulary entry to note the product withdrawal

The Group supported the changes proposed by the Formulary Team.

SBAR - Calfovit D3® 1200mg/800I.U. powder for oral suspension (calcium phosphate/colecalciferol) is now withdrawn from use/discontinued.
Indication under review: in adults and elderly:
- **for the correction of calcium and Vitamin D deficiency.**
- **as an adjunct to specific therapy for osteoporosis, in patients with either established vitamin D and calcium combined deficiencies or in those patients at high risk of needing such therapeutic supplements.**

This medicine is now withdrawn from use/discontinued. **FTEAM**

6.2. HIV infection review of formulary choices and webpage

Ms Doney confirmed that the formulary choices and webpage for the treatment of HIV (including recommendations for antivirals used for HIV PrEP (pre-exposure prophylaxis) have been reviewed with the service, and the update sections published.

The Formulary Team plans to restart review of formulary sub-sections in 2023.

7. OTHER BUSINESS

7.1. National Cancer Medicines Advisory Group (NCMAG) advice

Ms Doney reported that the National Cancer Medicines Advisory Group (NCMAG) issued confidential draft advice documents for the off-label use of three medicines.

It was confirmed that:
- the Formulary Team is planning to process the advice in line with the current systems for handling SMC advice
- the Formulary Team is mindful of the overlap with the work of the NCA and development of regional processes
- the provisional advice is available under item 9.2

7.2. NICE draft recommendations on the use of treatments for COVID-19

Dr Elliot confirmed that the National Institute for Health and Care Excellence (NICE) published draft recommendations on the use of treatment for COVID-19 [recommendations currently under consultation].
The Antimicrobial Management Team (AMT) will consider the recommendations when they are finalised. **AMT**

8. NEW PRODUCT REQUESTS

8.4. SMC 2402 - Cannabidiol (seizures associated with tuberous sclerosis complex)

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

The Group considered the request for cannabidiol 100mg/mL oral solution (Epidyolex®) as adjunctive therapy of seizures associated with tuberous sclerosis complex (TSC).

The Group noted that:
- Epidyolex® is currently included on the formulary, for patients 2 years of age and older in conjunction with clobazam, as adjunctive therapy for seizures associated with Lennox-Gastaut syndrome or Dravet syndrome (SMC 2262 and SMC 2263)
- this request extends use to include adjunctive therapy of seizures associated with TSC
- the North of Scotland Child and Adolescent Neurology Network (NeSCANN) guidance

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positions use as adjuvant therapy with clobazam, and after failure of at least two drugs (alone or in combination). It also includes stopping rules.

- the precise mechanisms by which cannabidiol exerts its anticonvulsant effects in humans are unknown
- evidence comes from one randomised, double-blind, phase III study (GWPCARE6):
  - the primary outcome was the change from baseline in the number of TSC-associated seizures during the 16-week treatment period
  - patients with TSC taking Epidyolex® at maximum dose of 25mg/kg/day had a reduction of 49% in the number of seizures compared with 27% in patients receiving a placebo
- Epidyolex®:
  - dosing is by weight, and when doses are below 120mg/day waste will occur due to the 12-week in-use expiry
  - is a Schedule 5 Controlled Drug and 'hospital-only' medicine
  - [for this indication] was accepted for use in NHS Scotland following a full submission assessed under the orphan equivalent medicine process, the output from the PACE process, and application of SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of Epidyolex®
- TSC is a rare and complex genetic condition and epilepsy is the most common neurological feature
- a significant proportion of people with TSC-associated epilepsy do not respond to standard anti-epileptic medicines, cannabidiol would provide an additional therapeutic option that may help to improve seizure control and quality of life
- reducing the number of seizures can decrease the risk of seizure-related injury and death

The Group accepted the restricted local need for cannabidiol 100mg/mL oral solution (Epidyolex®) as adjunctive therapy of seizures associated with TSC, in line with SMC 2402.

SMC 2402 - Cannabidiol 100mg/mL oral solution (Epidyolex®) ▼ is routinely available in line with national guidance (SMC 2402).
Indication under review: for use as adjunctive therapy of seizures associated with tuberous sclerosis complex (TSC) for patients 2 years of age and older.
Cannabidiol reduced TSC-associated seizure frequency compared with placebo in one randomised, double-blind, phase III study in patients with TSC-associated epilepsy that was inadequately controlled by other anti-epileptic drugs.
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 physicians with experience in the treatment of epilepsy. FTEAM

3. DISCUSSION - ANTI-NEOVASCULARISATION AGENTS

The Chair welcomed Ms. Cynthia Santiago, Associate Specialist/Retina Lead and Deputy Clinical Lead for Ophthalmology, to discuss the requests for faricimab for two indications, 1) the treatment of adults with neovascular (wet) age-related macular degeneration (nAMD), and 2) the treatment of visual impairment due to diabetic macular oedema (DMO).

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Ms. Santiago confirmed that:

- anti-vascular endothelial growth factors (VEGF) are used locally for the treatment of nAMD, and the visual impairment due to DMO
- ranibizumab was the first anti-VEGF agent licensed for use (circa 2007)
- the Ophthalmology Service has 15 years' experience with anti-VEGF agents in nAMD. Previously there were no treatments that improved vision in these patients, but with anti-VEGF agents, at least 90% maintain vision with up to 30% having improved vision.
- with the availability of anti-VEGF agents it is possible to restore vision for the elderly population. If untreated, the natural history of nAMD is that most people lose their sight in one or two years, therefore there is an urgency to start treatment as quickly as possible.
- when first licensed, the need for long-term treatment with anti-VEGF agents was not considered. Some people have been on treatment for 10+ years.
- another agent [potentially fourth] is required because local audit data [for nAMD] shows that only 21% of 'eyes' have an injection frequency of 12 weeks or more, approximately 50% have injection intervals of less than 8 weeks. This results in a significant number of patients attending regularly for repeat injections.
- an agent that shows promise for a less frequent injection schedule is welcome [faricimab studies for DMO and nAMD show the possibility of 70% going to 12 or 16 week intervals]
- fewer injections affect the overall cost of therapy and have lower service implications, so may provide advantages not available with the current agents
- brolucizumab was expected to lengthen the treatment interval, but very soon after introduction it became apparent that the safety of the drug was not sufficient [intraocular inflammation], and local use is very low
- the Medical Retina Team is unlikely to use brolucizumab in the future, particularly if faricimab is available for use and successful in extending the treatment interval
- bevacizumab use is not established. It may be difficult to justify using it as a first-line choice and switching people that are established on existing licensed products, particularly with licensed biosimilar [ranibizumab] products coming to market, and the lack of clarity about the robustness of the supply chain for bevacizumab and biosimilars.
- the Ophthalmology Service is looking to introduce biosimilar ranibizumab (Ongavia® ▼) in 2023. The Service will monitor how 'acceptable' the biosimilar is for patients and their response to treatment, before weighing up if it could be considered a first-line treatment option.

Responding to questions from members Ms. Santiago confirmed that:

- there are no head-to-head data for 'sequencing' agents, all trials are non-inferiority studies
- with the switch from ranibizumab to aflibercept the service has significant experience 'sequencing' anti-VEGF agents. Following the switch, many patients did not have an improved functional performance but showed improved anatomical performance, so the scan and macula were drier than before.
- each injection carries a procedural risk to the eye, e.g., infection, so reducing the number of injections conveys benefits for patients and the service
- faricimab has the potential to reduce the number of injections required - ~70% benefitted from a longer treatment interval (12 weeks or more)
- patients are knowledgeable and are requesting transfer to faricimab because of the potential for a less frequent injection schedule
- there is no evidence that 'sequencing' to faricimab will work, however, there is a group of patients (at least 10%) on 4-weekly injections and providing treatment to this group may be beneficial - if faricimab proves to be safe and provides a longer treatment interval
- in year 1, ranibizumab and aflibercept are given as fixed-dosing regimens with no scanning. The 'treat and extend' regimen is used for both from year 2 onwards.

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- audit data (from year 2 onwards) shows only 21% are on treatment intervals of 12 week or more. Increasing this percentage will provide benefits to the service.
- the service is providing 10,000+ injections per year
- when incorporated into the service and shown to be safe, the service will review the use of faricimab and biosimilar ranibizumab. There is a potential to revisit use and treatment pathways in nine months.

The Chair thanked Ms. Santiago for attending the meeting and clarifying the current and proposed use of anti-VEGF agents in ophthalmology. Ms. Santiago left before decision-making.

Items 8.1 to 8.3 were taken together.

8.1. SMC 2499 - Faricimab (DMO)
8.2. SMC 2512 - Faricimab (nAMD)
8.3. SMC 2508 - Brolucizumab (DMO)

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

The Group discussed the use of anti-VEGF agents in ophthalmology and supported the formulary inclusion of faricimab for use in nAMD and DMO, in line with SMC 2512 and SMC 2499 respectively.

The Group accepted the restricted local need for faricimab as an additional anti-VEGF agent for the management of DMO and nAMD.
Approval is subject to review in nine months to allow the use and safety of biosimilar ranibizumab and faricimab to be evaluated by the service. **FTEAM**

SMC 2499 - Faricimab 120mg/mL solution for injection (Vabysmo®) ▼ is routinely available in line with national guidance (SMC 2499).
Indication under review: for the treatment of visual impairment due to diabetic macular oedema (DMO) in adults with best corrected visual acuity (BCVA) of 75 Early Treatment Diabetic Retinopathy Study (ETDRS) letters or less at baseline.
In two phase III studies faricimab was non-inferior to an anti-vascular endothelial growth factor treatment for change in BCVA from baseline at 1 year.
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 must be administered by a qualified healthcare professional trained in intravitreal injections. **FTEAM**

SMC 2512 - Faricimab 120mg/mL solution for injection (Vabysmo®) ▼ is routinely available in line with national guidance (SMC 2512).
Indication under review: for the treatment of adult patients with neovascular (wet) age-related macular degeneration (nAMD).
Faricimab offers an additional treatment choice in the therapeutic class of antineovascularisation agents 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. Treatment must be administered by a qualified healthcare professional trained in intravitreal injections. **FTEAM**

The Group noted that a safety warning was issued highlighting that the risk of intraocular inflammation and retinal vascular occlusion are increased with short dosing intervals, and

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there is very low use of brolucizumab locally.

Mindful of the safety issues experienced with brolucizumab, that the service has not requested formulary inclusion for DMO, and its use for nAMD is very low, the Group recommended removal of brolucizumab from the formulary. People currently established on brolucizumab for nAMD may continue to receive treatment until they and their clinician consider it appropriate to stop.

SMC 2508 - Brolucizumab 120mg/mL solution for injection in pre-filled syringe (Beovu®) ▼ is not routinely available as there is a local preference for alternative medicines.
Indication under review: for the treatment of visual impairment due to diabetic macular oedema (DMO) in adults with best corrected visual acuity (BCVA) of 75 Early Treatment Diabetic Retinopathy Study (ETDRS) letters or less at baseline.
Not routinely available as there is a local preference for alternative medicines. **FTEAM**

SMC 2272 - Brolucizumab 120mg/mL solution for injection in pre-filled syringe (Beovu®) ▼ is not routinely available as there is a local preference for alternative medicines.
Indication under review: in adults for the treatment of neovascular (wet) age-related macular degeneration (AMD).
Not routinely available as there is a local preference for alternative medicines. **FTEAM**
People currently established on brolucizumab for nAMD may continue to receive treatment until they and their clinician consider it appropriate to stop.

8. 8.5. SMC 2438 - Crizanlizumab (vaso-occlusive crises in sickle cell disease)

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

The Group considered the request for crizanlizumab for the prevention of recurrent vaso-occlusive crises in sickle cell disease patients aged 16 years and older.

The Group noted that:

- crizanlizumab:
  - is a 'hospital-only drug that has a conditional marketing authorisation from the Medicines and Healthcare products Regulatory Agency (MHRA)
  - [for this indication] was accepted for use on an interim basis in NHS Scotland subject to ongoing evaluation and future reassessment following a full submission assessed under the orphan process, the output from the PACE process, and application of SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios
  - is given at a dose of 5mg/kg by intravenous infusion over 30 minutes, at weeks 0 and 2, and every 4 weeks thereafter
  - can be used with or without hydroxyurea/hydroxycarbamide. If treatment is effective and tolerated, costs will be cumulative as treatment may be used long-term.
- treatment options for chronic sickle cell disease include supportive care and prevention of complications, hydroxyurea/hydroxycarbamide, repeat blood infusions, and haematopoietic stem cell transplantation (HSCT)
- HSCT is the only curative treatment for sickle cell disease, but is used infrequently owing to lack of suitable stem cell donors, cost, and risks
- evidence comes from a multicentre, randomised, double-blind, parallel group, phase II study (SUSTAIN) which evaluated the efficacy and safety of crizanlizumab compared with placebo in 198 patients with sickle cell disease
- SUSTAIN:
  - the primary end point was the annual rate of sickle cell-related pain crises (defined

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as acute episodes of pain caused by a vaso-occlusive crises that resulted in a visit to a medical facility and treatment with pain relief medication) with high-dose crizanlizumab versus placebo
    - crizanlizumab was effective at reducing the number of painful crises (average 1.6 crises per year, versus average 3 crises per year for those on placebo)
    - showed that crizanlizumab reduced the yearly number of crises by almost a third in patients already taking hydroxycarbamide (2.4 versus 3.6) and by half in patients not taking hydroxycarbamide (1 versus 2)
    - overall and serious adverse event incidence was comparable across arms
    - is a short-term study (52 weeks) in small patient numbers
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of crizanlizumab
- patient numbers are expected to be small, and crizanlizumab would be a new [medicine] cost to the service
- additional costs would be expected related to preparation, staffing, management of adverse events (including management of infusion-related reactions, pre-medication etc.)
- if effective, crizanlizumab has the potential to reduce the use of painkillers and/or hospital visits for symptom management

Ms Galvin will contact the requestor to obtain answers to the queries posed as part of the Formulary Team's review. **MG**

The Group accepted the restricted local need for crizanlizumab for the prevention of recurrent vaso-occlusive crises in sickle cell disease patients aged 16 years and older, as outlined in SMC 2438.

SMC 2438 - Crizanlizumab 10mg/mL concentrate for solution for infusion (Adakveo®) ▼ is routinely available in line with national guidance on an interim basis subject to ongoing evaluation and future reassessment (SMC 2438).
Indication under review: for the prevention of recurrent vaso-occlusive crises in sickle cell disease patients aged 16 years and older. It can be given as an add-on therapy to hydroxycarbamide or as monotherapy in patients for whom hydroxycarbamide is inappropriate or inadequate.
In a randomised, double-blind, phase II study, crizanlizumab reduced the annual rate of sickle cell-related pain crises requiring medical attention compared with placebo in patients aged ≥16 years who had a history of two to ten such events in the previous year.
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 by physicians experienced in the management of sickle cell disease. **FTEAM**

8.6. SMC 2442 - RYEQO® (UTERINE FIBROIDS)

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

The Group considered the request to include Ryeqo® on the formulary for the treatment of moderate to severe symptoms of uterine fibroids in a group of adult women of reproductive age.

The Group noted that:
- the company requested that SMC considered Ryeqo® when positioned for use in

patients who have failed or are unsuitable for conventional therapies, such as tranexamic acid, hormonal contraceptives and intrauterine delivery systems
- uterine fibroids are hormone-sensitive benign smooth muscle tumours in the uterus, and their prevalence increases with age up to the menopause
- many patients do not have symptoms. Those with symptoms typically have heavy menstrual bleeding, which may lead to iron deficiency anaemia, and they may experience pelvic pain, irregular bleeding or gastrointestinal upset (constipation, bloating or diarrhoea).
- uterine fibroids may be associated with infertility or problems during pregnancy
- initial treatment options for patients with uterine fibroids and heavy menstrual bleeding include tranexamic acid, non-steroidal anti-inflammatory drugs (NSAIDs), levonorgestrel-releasing intra-uterine system and hormonal contraceptives. After these, the progesterone antagonist ulipristal is an option. Subsequent treatment options include uterine artery embolisation or surgeries, such as hysterectomy or myomectomy.
- Ryeqo®:
  - is the first gonadotropin-releasing hormone receptor antagonist (relugolix)/estradiol/norethisterone combination tablet licensed for the treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age
  - provides adequate contraception when taken for at least one month
- evidence:
  - Ryeqo® has been shown to be effective in treating the symptoms linked to uterine fibroids in two studies involving pre-menopausal women aged 18 to 50 with heavy menstrual bleeding. In both studies, around 500 women received either Ryeqo® or placebo for 24 weeks.
  - in the first study, 73% (94 out of 128) of women using Ryeqo® reported monthly menstrual blood loss of fewer than 80mL and at least 50% less blood loss than before the treatment, compared with 19% (24 out of 128) of those taking placebo. In the second study, 71% (89 out of 126) achieved this reduction in the volume of blood lost while using Ryeqo®, compared with 15% (19 out of 129) of those given placebo.
- it is difficult for the service to provide an accurate estimate of patient numbers
- cost-offset would be available from the displacement of other agents
- the Summary of Product Characteristics (SmPC) states that:
  - in patients with risk factors for osteoporosis or bone loss, a dual X-ray absorptiometry (DXA) is recommended prior to starting treatment, and this will form part of the pre-assessment checks conducted by the specialist service
  - a DXA scan is recommended after one year of treatment
- there is a waiting time of several months for DXA scans, and the service confirmed that treatment may need to be stopped if a DXA scan cannot be arranged at one year

Members agreed that Ryeqo® would be a useful treatment option as it:
- provides an oral fixed-dose triple combination tablet, and whilst convenient to take, it does not allow dose adjustment of the individual components
- is an effective non-surgical treatment option that, in contrast to surgical options, preserves the uterus
- does not have a restriction on the duration of treatment, although long-term data is limited

Members raised concerns about:
- the ability of colleagues in Primary Care to arrange a DXA scan at one year
- that stopping treatment whilst waiting a DXA scan would be difficult for women that were currently benefitting from treatment to accept, and would be difficult for colleagues in Primary Care to explain and offer an alternative treatment if required

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Members agreed that hand-over to Primary Care after one year, when the DXA scan was completed and it was appropriate to continue treatment, may be a more suitable alternative.

The Group accepted the restricted local need for Ryeqo® as outlined in SMC 2442. However, as a new agent that colleagues in Primary Care have no knowledge of, members agreed that specialists should initiate and manage treatment. Transfer of prescribing to Primary Care would be possible after one year, when the recommended one-year DXA scan has been undertaken and it was appropriate to continue treatment.

SMC 2442 - Ryeqo® ▼ 40mg/1mg/0.5mg film-coated tablets (relugolix/estradiol/norethisterone acetate) is routinely available in line with national guidance (SMC 2442).
Indication under review: treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age who have failed or are unsuitable for conventional therapies (first-line treatments), such as tranexamic acid, hormonal contraceptives and intrauterine delivery systems.
Relugolix, estradiol, norethisterone acetate tablets (Ryeqo®), compared with placebo, significantly reduced menstrual blood loss volume in patients with uterine fibroids and heavy menstrual bleeding.
It was classified 1b - available for restricted use under specialist supervision and 8c - treatment to be initiated in hospital prior to handover. Treatment to be handed over after one year, subject to confirmation that the recommended 1 year DXA scan has been undertaken and it is appropriate to continue treatment. **FTEAM**

9. PROVISIONAL ADVICE ISSUED DECEMBER 2022

9.1. SMC provisional advice

The Group noted the SMC provisional advice issued December 2022.

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

9.2. NCMAG provisional advice

The Group noted the NCMAG provisional advice issued December 2022.

Ms Doney confirmed that NCAMG advice would be published every quarter. A review of the treatment of prostate cancer and off-label use of abiraterone is pencilled in for the February 2023 meeting.

10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS PUBLISHED DECEMBER 2022

The Group noted the SMC advice published December 2022.

Following publication of the negative SMC recommendation for alpelisib (Piqray®) ▼ SMC 2481, 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 2494 - abemaciclib (Verzenios®) ▼ (submission expected)
- SMC 2495 - upadacitinib (Rinvoq®) ▼ (submission expected)

Local advice for these medicines and indications will be included in the December 2022 decisions as 'Not routinely available as the ADTC is waiting for further advice from local

ITEM	SUBJECT	ACTION
	clinical experts'.	FTEAM

SMC 2529 - MICRONISED PROGESTERONE 100MG CAPSULES (UTROGESTAN®)

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

Ms Doney reported that:

- Utrogestan® 100mg oral capsules (micronised progesterone):
  - is licensed for adjunctive use with oestrogen in post-menopausal women with an intact uterus, as hormone replacement therapy (HRT)
  - [for this indication] was assessed by SMC in 2009, and following a full submission it was not recommended for use in NHS Scotland as the manufacturer did not present a sufficiently robust economic analysis to gain acceptance by SMC
  - was accepted to formulary in September 2019 for restricted use as a second-line choice, or alternative for some patient groups
  - was accepted for use in NHS Scotland following an abbreviated submission
- there are limited prescribing options if patients are intolerant of the adverse effects of synthetic progestogens, and micronised progesterone, as Utrogestan® oral capsules, provides an oral treatment option with a potentially beneficial breast cancer risk and lipid profile

The Group ratified the current formulary position for the restricted use of micronised progesterone oral capsules as a second-line or alternative choice progestogen for adjunctive use with oestrogen in post-menopausal women with an intact uterus, as HRT.

SMC 2529 - Micronised progesterone 100mg capsules (Utrogestan®) is routinely available in line with local guidance.
Indication under review: for adjunctive use with oestrogen in post-menopausal women with an intact uterus, as hormone replacement therapy (HRT).
Restriction:

1) **second-line in women who suffer or have suffered moderate or severe progestogenic side-effects when using combined HRT preparations or with other progestogens as part of HRT, contraception or bleeding control**
2) **as an alternative progestogen in women with an increased risk of breast cancer, cardiovascular disease (CVD) or venous thromboembolism (VTE) and do not have an absolute contra-indication to HRT.**

It was classified 1a - available for general use and 8e - treatment may be initiated in either Primary or Secondary care. FTEAM

11. GENERAL INFORMATION FROM SCOTTISH MEDICINES CONSORTIUM - DECEMBER 2022

None.

12. DOCUMENTS FOR INFORMATION

Items 12.1 and 12.2 (Drug Safety Update November and December 2022) were noted.
The December issue highlights that next year changes are expected to the valproate pregnancy prevention programme.
Ms Doney confirmed that the information has been sent to the relevant service areas.

13. AOCB

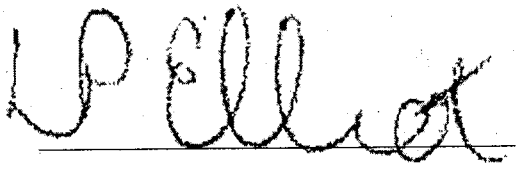
The Chair confirmed this will be Mrs O'Beirne's last meeting for a while and thanked her for her contributions to the Formulary Group.

The Chair wished everyone a very merry Christmas a happy New Year.

ITEM	SUBJECT	ACTION

DATE OF NEXT MEETING

Tuesday 17 January 2023 starting at 14.30 via Microsoft Teams

CHAIR'S SIGNATURE  **DATE 17 JANUARY 2023**