NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 18 February 2020 at 14:30 in the Seminar Room, David Anderson Building

PRESENT	APOLOGIES	APPROVED
Dr D Culligan	Ms M Galvin	
Ms A Davie	Mr C Rore	
Ms F Doney	Mr R Sivewright	
Dr L Elliot	Dr A Sun	
Dr J Fitton		
Professor J McLay (Chairman)		
Mrs L Montgomery		
Mr M Paterson		

IN ATTENDANCE
Ms Caitlin Wilkinson, Formulary Team administrator

OBSERVER
Ms Anna Shimbulu, Senior Medicines Information and Safety Pharmacist, Namibia Medicine Regulatory Council, Ministry of Health and Social Services

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The Chairman welcomed members, opened the meeting and noted that a quorum was present.

THANK YOU AND GOODBYE

The Chairman reported that Dr Moore and Dr MacDonald have resigned from the Formulary Group. Professor McLay led members in thanking Dr MacDonald and Dr Moore for the considerable contribution they have both given in support of medicines/medicines management work-streams locally and nationally, specifically their contribution to the Formulary Group.

1. APOLOGIES

Apologies for absence were requested and noted.

2. DRAFT MINUTE OF THE MEETING HELD 21 JANUARY 2020

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 approval. **FD**

3. PRESENTATION

Ms Doney informed the Group that the scheduled presentation would be re-arranged for a future meeting.

4. MATTERS ARISING

4.1. ACTION LOG

The Action log was noted.

4.2. CLINITAS® SINGLE USE – INCLUSION IN DRY EYE GUIDANCE

Ms Doney reported that following a request for review, Clinitas® single-use eye drops (sodium hyaluronate 0.4%) is now included in the dry eye guidance as a second-line treatment option for severe dry eyes. The formulary webpage has been updated and an updated guidance document will be issued within the next few weeks.

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5. FORMULARY GROUP DECISIONS JANUARY 2020 – PUBLISHED – 3 FEBRUARY 2020

5.1. FORMULARY GROUP DECISIONS JANUARY 2020

Members ratified the decisions of the January 2020 meeting as published. **FTeam**

6. NETFORMULARY/FORMULARY REVIEW

6.1. ULTRA-ORPHAN SBAR

The Chairman discussed the SBAR prepared by the Formulary Team and colleagues in Tayside and Highland.

The Chairman highlighted the recommendations in the SBAR and the proposal to create a new decision classification *"Non-formulary - Not routinely available in NHS Grampian however if local need is identified:.. "*.

Ms Doney confirmed that a new classification will make it easier to separate medicines that are 'not recommended for use' from those that are 'not routinely available' - because they are available from specialist centres, e.g. pulmonary arterial hypertension medicines, medicines available via the Scottish Government ultra-orphan (UO) medicines pathway.

The Group supported the recommendations, and requested that the new 'non-formulary' classification is implemented with immediate effect. **FTeam**

Ms Doney will submit an updated SBAR to the next meeting of the Grampian Area Drug and Therapeutics Committee (GADTC) for ratification. **FD**

6.2. CARBIMAZOLE AND LEVOTHYROXINE

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

CARBIMAZOLE

Ms Doney confirmed that:

- two additional strengths of carbimazole tablet are being marketed, 10mg and 15mg
- neither strength is included on the Scottish Drug Tariff (SDT), and on a cost per milligram basis they are not as cost-effective as the current SDT preparations [5mg and 20mg]
- currently there are too few manufacturers for the new strengths to be considered for inclusion in the SDT
- the SDT provides information regarding the reimbursement [prescribing and dispensing] of medicines prescribed in Primary Care

The Group agreed that:

- prescribing by generic name and use of the SDT supports cost-effective prescribing
- SDT preparations are preferred and carbimazole as the 10mg and 15mg strength tablets should be recorded as non-formulary.

Carbimazole 10mg, 15mg tablets is not routinely available in NHS Grampian.
Indications under review: in adults and children in all conditions where reduction of thyroid function is required:

- **hyperthyroidism**
- **preparation for thyroidectomy in hyperthyroidism**
- **preparation for, and as concomitant therapy with, radio-iodine treatment**

Carbimazole should only be administered if hyperthyroidism has been confirmed by laboratory tests.
Not recommended for use within NHS Grampian. **FTeam**

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LEVOTHYROXINE

Ms Doney confirmed that:

- levothyroxine is included on the SDT as 25microgram, 50microgram and 100microgram strength tablets
- two other strengths are available - 12.5microgram and 75microgram
- currently levothyroxine 12.5microgram tablet is noted as 'non-formulary'; because it previously cost £15.00 for 28 tablets. However, the cost has dropped significantly since first marketed.
- the local guidance for combination levothyroxine and liothyronine therapy currently includes mention of levothyroxine 12.5microgram, however it is not known if there is a clinical need for the low strength tablet or if patients can be managed with the current SDT levothyroxine strengths
- information will be available for the March meeting **FTeam**

7. OTHER BUSINESS

7.1. HEALTHCARE IMPROVEMENT SCOTLAND – NATIONAL REVIEW PANEL FOR PACS TIER 2 MEMBERSHIP

The Chairman highlighted the letter from Healthcare Improvement Scotland (HIS) regarding National Review Panels for PACS Tier 2 Membership. HIS is requesting volunteers for the panels and those interested in volunteering should contact the Director of Pharmacy. **All**

7.2. EMA MEASURES TO MINIMISE RISK OF SERIOUS SIDE EFFECTS OF MULTIPLE SCLEROSIS MEDICINE LEMTRADA® (ALEMTUZUMAB)

The Chairman highlighted the article from the European Medicines Agency (EMA). The article recommends the restricted use of the multiple sclerosis medicine Lemtrada® ▼ (alemtuzumab) due to reports of rare but serious side effects.

8. NEW PRODUCT REQUESTS

Items 8.1 and 8.2 were taken together.

8.1. FG1SMC 2166 - VENETOCLAX IN COMBINATION WITH RITUXIMAB (CHRONIC LYMPHOCYTIC LEUKAEMIA (CLL)) AND

8.2. FG1SMC 1249/17 - VENETOCLAX (CHRONIC LYMPHOCYTIC LEUKAEMIA (CLL))

Dr Culligan declared a personal, non-specific interest in AbbVie Ltd and took part in the discussion and decision-making.

The Group considered the requests for venetoclax, used in combination with rituximab or as monotherapy, for the treatment of relapsed or refractory chronic lymphocytic leukaemia (CLL).

The Group noted:

- venetoclax:
  - is the third novel therapy to be marketed for CLL (after the B cell receptor pathway inhibitors ibrutinib and idelalisib)
  - is a first-in-class antineoplastic agent [Bcl-2 inhibitor] and is an oral treatment option
  - is requested for use in two positions; 1) in combination with rituximab early in the treatment pathway after one prior therapy, and 2) as monotherapy as an advanced stage treatment option for i) patients with particular genetic changes or ii) patients who do not have these genetic changes after treatments with chemo-immunotherapy and a B cell receptor pathway inhibitor have both failed
  - [for these indications] was accepted for use in NHS Scotland following the output from the PACE process, and application of the appropriate SMC modifiers

  - can cause rapid reduction in tumour burden, and poses a risk for tumour lysis syndrome in the initial 5-week dose-titration phase
  - when used in combination with rituximab [6 cycles only] has a fixed treatment period of two years which may be advantageous for patients
  - would be attractive for patients on anticoagulants and those with cardiac arrhythmias
  - is an expensive treatment option but cost offset will be available, e.g. the cost of alternative medicines (ibrutinib)
- that a significant minority of CLL patients do not require treatment
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of venetoclax [both indications]
- there is a potential for retreatment [with venetoclax]
- the introduction of venetoclax will impact on clinic/staff time due to the monitoring required during titration; and the aseptic unit (for preparation of rituximab)

The Group accepted the restricted local need for venetoclax for the treatment of CLL as outlined in SMC 2166 and SMC 1249/17.

SMC 2166 and SMC 1249/17 – Venetoclax 10mg, 50mg, and 100mg film-coated tablets (Venclyxto®) ▼ is routinely available in line with national guidance (SMC 2166 and SMC 1249/17).
Indication under review:
1. **in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy.**
2. **as monotherapy for the treatment of CLL:**
   - **in the presence of 17p deletion or TP53 mutation in adult patients who are unsuitable for or have failed a B-cell receptor pathway inhibitor, or**
   - **in the absence of 17p deletion or TP53 mutation in adult patients who have failed both chemo-immunotherapy and a B-cell receptor pathway inhibitor.**

It was classified 1b – available for restricted use under specialist supervision and 8b – recommended for hospital use only.
Treatment with venetoclax should be initiated and supervised by a physician experienced in the use of anticancer medicinal products. **FTeam**

8.3. FG1SMC 2180 - DARATUMUMAB (MULTIPLE MYELOMA)

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

The Group considered the request for daratumumab in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma (MM) who have received one prior therapy only.

The Group noted:
- daratumumab:
  - is an immunoglobulin G1 kappa (IgG1K) human monoclonal antibody
  - as monotherapy, is already included on the formulary as a fourth line treatment option in adult patients with relapsed and refractory MM [SMC 1205/17]
  - [for this indication] meets SMC orphan criteria, and was accepted for use in NHS Scotland following the output from the PACE process and application of the appropriate SMC modifiers
  - is given as an intravenous infusion, and the initiation schedule moves from weekly infusions to infusions every 4 weeks over a 25-week period
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of daratumumab
- patients will move through all treatment options with time
- the significant service burden (clinic and aseptic unit) with the introduction of

daratumumab
- infusion-related reactions are common, and daratumumab interferes with blood compatibility tests, (including antibody screening and crossmatching)

The Group accepted the restricted local need for daratumumab in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received one prior therapy only, as outlined in SMC 2180.

SMC 2180 – Daratumumab 20mg/mL concentrate for solution for infusion (Darzalex®) ▼ is routinely available in line with national guidance (SMC 2180). Indication under review: in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received one prior therapy only.
Progression-free survival was significantly longer in patients who received daratumumab in combination with bortezomib and dexamethasone compared with those who received bortezomib and dexamethasone in a phase III study in patients with multiple myeloma who had received at least one prior therapy.
This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of daratumumab and is contingent upon the continuing availability of the PAS in NHS Scotland or a 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. Daratumumab should be administered by a healthcare professional, in an environment where resuscitation facilities are available. **FTeam**

8.4. FG1SMC 2225 - TEDUGLUTIDE (SHORT BOWEL SYNDROME (SBS) IN ADULTS)

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

The Group considered the information regarding teduglutide for the treatment of adults with short bowel syndrome (SBS).

The Group noted:
- teduglutide:
  - is a glucagon-like-peptide-2 analogue, that is licensed for the treatment of patients aged 1 year and above with Short Bowel Syndrome (SBS)
  - SBS is a rare condition and patient numbers are expected to be very small, and currently there are no adult patients waiting for treatment
  - is already included on the formulary for the treatment of paediatric patients aged 1 to 17 years [SMC 1139/16]
  - [for this indication] meets SMC orphan medicine criteria and is an expensive treatment
  - was accepted for use in NHS Scotland following the output from the PACE process and application of the appropriate SMC modifiers
  - is supplied via a Homecare arrangement for paediatric patients and there is an expectation this would be extended to include adult patients
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of teduglutide

The Group accepted the restricted local need for teduglutide for the treatment of adult patients with short bowel syndrome (SBS) without the need for a full submission.

SMC 2225 – Teduglutide 5mg vial of powder and solvent for solution for injection (Revestive®) ▼ is routinely available in line with national guidance (SMC 2225). Indication under review: for the treatment of adult patients with short bowel

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syndrome (SBS). Patients should be stable following a period of intestinal adaptation after surgery. In a phase III randomised study in adults, significantly more patients achieved at least a 20% reduction in parenteral support volume at weeks 20 and 24 when treated with teduglutide compared with placebo.
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 under the supervision of a medical professional with experience in the treatment of SBS. **FTeam**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE – FEBRUARY 2020

The Group noted the SMC provisional advice issued February 2020.

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

10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS – FEBRUARY 2020

The Group noted the SMC advice published February 2020.

Following publication of the negative SMC recommendation for sodium zirconium cyclosilicate (Lokelma®)▼ SMC 2233, and the non-submission statements, for apalutamide (Erleada®)▼ SMC 2268, daratumumab (Darzalex®)▼ SMC 2269 and ranibizumab (Lucentis®) SMC 2270, these medicines will not be included on the Grampian Joint Formulary for the indications in question. **FTeam**

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

- SMC 2216 cemiplimab (Libtayo®)▼(submission expected)
- SMC 2238 encorafenib (Braftovi®)▼

Local advice for these medicines and indications will be included in the February 2020 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts.' **FTeam**

ULTRA-ORPHAN MEDICINES ASSESSMENT REPORTS

The Chairman highlighted the SMC initial assessment reports published for burosumab and voretigene.

Burosumab and voretigene are medicines for very rare diseases, the medicines have been validated as 'ultra-orphan' (UO) and will be made available through the NHS in Scotland for up to three years [for the indications in question] while evidence on their effectiveness is generated – the Scottish Government (SG) ultra-orphan pathway.

Medicines accessed via the SG ultra-orphan pathway are considered outwith remit for the Group, and will be classified as 'non-formulary' as agreed under item 6.1.

SMC 2240 - Burosumab solution for injection (Crysvita®)▼ is not routinely available in NHS Grampian.
Indication under review: treatment of X-linked hypophosphataemia with radiographic evidence of bone disease in children 1 year of age and older and adolescents with growing skeletons.

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	Not routinely available in NHS Grampian. If local need identified treatment is available through the Scottish Government Ultra-orphan pathway.	**FTeam**
	SMC 2228 - Voretigene neparvovec 5 x 10^{12} vector genomes/mL concentrate and solvent for solution for injection (Luxturna®) ▼ is not routinely available in NHS Grampian. **Indication under review: for the treatment of adult and paediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells.** **Not routinely available in NHS Grampian. If local need identified treatment may be available through the Scottish Government Ultra-orphan pathway.**	**FTeam**
	SMC 2249 PLERIXAFOR (MOZOBIL®) (STEM CELL MOBILISATION, PAEDIATRICS) There were no declarations of interest recorded in relation to this product. The Group discussed the information submitted regarding the use of plerixafor, in combination with granulocyte-colony stimulating factor (G-CSF), to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in children aged 1 year to <18 years with lymphoma or solid malignant tumours. Ms Doney confirmed that: • plerixafor is included on the formulary for adult patients [SMC 594/09] • NHS Grampian does not undertake stem cell harvesting in children as paediatric patients are treated in a specialist centre in another Health Board. There is an expectation that the specialist centre would supply and administer plerixafor prior to the patients having the procedure. • plerixafor [for this indication] would be consider 'non-formulary' as agreed under item 6.1 The Group agreed that plerixafor for children and adolescents as outlined in SMC 2249 should be recorded as non-formulary, routinely available from a specialist centre in another health board. **SMC 2249 - Plerixafor 20mg/mL solution for injection (Mozobil®) is routinely available from a specialist centre in another Health Board.** **Indication under review: in combination with granulocyte-colony stimulating factor (G-CSF) to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in children aged 1 year to <18 years with lymphoma or solid malignant tumours, either:** • **pre-emptively, when circulating stem cell count on the predicted day of collection after adequate mobilisation with G-CSF (with or without chemotherapy) is expected to be insufficient with regards to desired hematopoietic stem cells yield, or** • **who previously failed to collect sufficient haematopoietic stem cells.** **SMC has previously accepted plerixafor for use in adults, in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in patients with lymphoma and multiple myeloma whose cells mobilise poorly (SMC No. 594/09).** **Treatment is routinely available from a specialist centre in another Health Board.**	**FTeam**
11.	**GENERAL INFORMATION FROM SCOTTISH MEDICINES CONSORTIUM – FEBRUARY 2020** None	

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12. DOCUMENTS FOR INFORMATION

Items 12.1 (Drug Safety Update January 2020), 12.2 (MedWatch November 2019) and 12.3 (Antimicrobial Management Team minute November 2019) were noted.

13. AOCB

NEXPLANON®

Ms Doney confirmed that:

- guidance regarding the recommended Nexplanon® insertion site has been updated to reduce the risk of neurovascular injury and implant migration
- the Sexual and Reproductive Health Service issued advice to General Practices last week
- the formulary entry has been updated to include the new advice, and the Patient Group Directions were checked but no changes are required

RIVAROXABAN 2.5MG TABLETS

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

Ms Doney confirmed that the Cardiology Service has decided not to proceed with a submission for rivaroxaban 2.5mg tablets, when used in combination with aspirin for the prevention of atherothrombotic events in adult patients at high risk of ischaemic events with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD).

The Group reiterated its previous concern regarding the increased risk of bleeding shown in the study, and the availability of a lower dose tablet posed a risk of confusion with the licensed doses used for the treatment of non-valvular atrial fibrillation, deep vein thrombosis and pulmonary embolism.

SMC 2128 - Rivaroxaban 2.5mg film-coated tablet (Xarelto®) ▼ is not routinely available as local clinical experts do not wish to add the medicine to the formulary at this time.
Indication under review: co-administered with acetylsalicylic acid for the prevention of atherothrombotic events in adult patients with:
- coronary artery disease, or
- symptomatic peripheral artery disease at high risk of ischaemic events.
SMC restriction: use in patients with stable coronary artery disease that does not require dual antiplatelet therapy.
Addition of rivaroxaban to low-dose aspirin (acetylsalicylic acid) reduced the incidence of a composite outcome that included stroke, cardiovascular death and myocardial infarction, mainly due to reductions in stroke and cardiovascular death. It also increased the incidence of major bleeding.
Not routinely available as local clinical experts do not wish to add the medicine to the formulary at this time. **FTeam**

SINGLE NATIONAL FORMULARY (SNF)

Ms Doney confirmed a formal update is expected within the next few months however, current understanding is that the SNF will take on a regional dimension with the East region [NHS Lothian, Fife and Borders] testing the 'SNF platform' to give 'real world' feedback on the platform. **FTeam**

NORTH CANCER ALLIANCE (NCA)
The Chairman requested an update on the status of the North Cancer Alliance. **FTeam**

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	DATE OF NEXT MEETING Tuesday 17 March 2020 starting at 14.30 in the Seminar Room, David Anderson Building.	

CHAIRMAN'S SIGNATURE **DATE** **17 MARCH 2020**