NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 19 February 2019 at 14:30 in the Seminar Room, David Anderson Building

PRESENT	APOLOGIES	APPROVED
Dr D Culligan	Ms M Galvin	
Ms A Davie	Dr A MacDonald	
Ms F Doney	Mr M Paterson	
Dr L Elliot	Mr R Sivewright	
Dr J Fitton		
Mrs L Harper (from item 3)		
Professor J McLay (Chairman)		
Mrs L Montgomery		
Dr W Moore		
Mr C Rore (from item 3)		
Dr A Sun (from item 3)		

IN ATTENDANCE
Dr Margaret-Ann MacLeod, Consultant Neurologist, Aberdeen Royal Infirmary.

Note some items were taken outwith the order on the agenda.

ITEM **SUBJECT** **ACTION**

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

1. APOLOGIES

Apologies for absence were requested and noted.

3. PRESENTATION

Dr MacLeod provided the Group with a comprehensive update on the use of drug modifying therapies in multiple sclerosis (MS).

8. 8.1. FG1SMC 2121 - OCRELIZUMAB (MULTIPLE SCLEROSIS (MS))

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

The Group considered the request for ocrelizumab as an alternate second-line therapy in the management of relapsing remitting multiple sclerosis (RRMS) in adults with active disease.

The Group noted:
- ocrelizumab:
  - is administered as a day case infusion. The initial 600mg dose is administered as two separate intravenous infusions; first as a 300mg infusion, followed 2 weeks later by a second 300mg infusion. Subsequent doses are given as single 600mg intravenous infusions every six months.
  - would be considered a second-line agent (as per NICE guidance/NHS England algorithm)
  - was accepted for use in NHS Scotland following a resubmission. In the resubmission, the submitting company requested that SMC consider ocrelizumab only for a subgroup of the licence - for the treatment of RRMS in adults with active disease defined by clinical or imaging features who are contra-indicated or otherwise unsuitable for alemtuzumab. This positioning does not include patients with primary progressive MS (PPMS) or relapsing form of secondary progressive MS (SPMS).
- patient numbers would be small
- other second-line options are available, administered orally or as intravenous infusions. However, there is a lack of head-to-head data against these second-line comparators.
- that the lower frequency of administration (infusion every 5 to 6 months) could be advantageous for patients compared to a monthly natalizumab infusion (every 4 weeks) or an annual 5- or 3-day in-patient stay required for alemtuzumab

The Group accepted the restricted local need for ocrelizumab as an alternate second-line agent in the management of RRMS for adults with active disease.

ITEM	SUBJECT	ACTION
	SMC 2121 - Ocrelizumab 300mg concentrate for solution for infusion (Ocrevus®) ▼ is routinely available in line with national guidance (SMC 2121). Indication under review: for the treatment relapsing remitting multiple sclerosis (RRMS) in adults with active disease defined by clinical or imaging features. Restriction: who are contra-indicated or otherwise unsuitable for alemtuzumab. It was classified 1b- available for restricted use under specialist supervision and 8a - licensed for hospital use only. Treatment should be initiated and supervised by specialised physicians experienced in the diagnosis and treatment of neurological conditions and who have access to appropriate medical support to manage severe reactions such as serious infusion-related reactions (IRRs).	**FTeam**

2. DRAFT MINUTE OF THE MEETING HELD 15 JANUARY 2019

Ms Doney confirmed that the confidential Primary Care rebate available on the Flutiform® pMDI device has not been extended to include the k-haler® device. The SMC advice includes the statement that both devices "cost the same" however this only refers to the list price of the inhalers. The discrepancy has been highlighted to the SMC and this statement was not included in the local decision.

The Group accepted the draft note of the meeting subject to correction of minor typographical changes.

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

4. MATTERS ARISING

4.1. ACTION LOG

ITEM NOT ON THE AGENDA - ZOVIRAX® (ACICLOVIR) EYE OINTMENT 3% DISCONTINUATION

Ms Doney confirmed that alternatives to Zovirax® (aciclovir) eye ointment 3% will be considered at the March meeting.

4.1.1. HYDROCHLOROTHIAZIDE DRUG SAFETY

The Group reviewed the draft letter regarding the Drug Safety Update article advising that hydrochlorothiazide, particularly in long-term use, is linked with an increased risk of non-melanoma skin cancer.

The Group agreed that it was not possible to quantify the risk in absolute terms (e.g. numbers needed to treat) and accepted the content of the letter subject to:

- addition of a table that included hydrochlorothiazide-containing products dispensed in the last year
- a complete list of products provided for ScriptSwitch messages **FTeam**

The final letter will be emailed to the Group for review and comment – timescale one week. **FTeam**

Once agreed the information will be linked to the formulary and emailed to the Health and Social Care Partnership (HSCP) Lead Pharmacists. **FTeam**

4.1.2. FG1SMC 2088 - HYDROCORTISONE GRANULES IN CAPSULES FOR OPENING (REPLACEMENT THERAPY OF ADRENAL INSUFFICIENCY (PAEDIATRICS))

At the January meeting, the Group requested clarification on the paediatric service plans regarding education of parents/carers and if children would be switched to or from hydrocortisone granules.

Dr Sun confirmed that:

- all patients/parent/carers will receive training from the endocrine nurse before they receive a prescription from General Practice
- appropriate patients currently on hydrocortisone tablets will be given information in clinic and switched if requested
- the age when a child changes from granules to tablets will be individualised

Item closed. **FTeam**

ITEM	SUBJECT	ACTION

5. FORMULARY GROUP DECISIONS JANUARY 2019 - PUBLISHED 30/01/2019

5.1. FORMULARY GROUP DECISIONS JANUARY 2019

The Group ratified the decisions of the January 2019 meeting as published.

5.2. DRAFT NETFORMULARY UPDATE FOR JANUARY 2019 FORMULARY GROUP DECISIONS

Ms Doney confirmed that due to workload issues, the netFormulary update was not available for the meeting but a summary of the decisions from the last four to six months will be emailed to members within the next 14 working days. **FTeam**

A proposal for publication of the decisions will be presented at the March meeting. **FD**

6. NETFORMULARY/FORMULARY REVIEW

6.1. LEVOSERT®

Ms Doney confirmed that the licence for Levosert®, a levonorgestrel-containing intrauterine system, has been increased from 4 to 5 years.
A review is underway with information planned for the March meeting. **FTeam**

7. OTHER BUSINESS

7.1. GABAPENTIN AND PREGABALIN WILL BECOME SCHEDULE 3 CONTROLLED DRUGS IN APRIL 2019

It was reported that from 1 April 2019 gabapentin and pregabalin will be rescheduled to Schedule 3 Controlled Drugs (CDs), i.e. full prescription requirements but no requirement for safe storage or record keeping in Controlled Drug registers.
The Controlled Drugs Accountable Officers' Network Scotland Executive Group produced a frequently asked questions document.

The link to the Accountable Officers' consensus document will be reissued after the meeting. **FTeam**

7.2. VSL#3 - REVIEW OF ACBS LIST/PART XV OF THE DRUG TARIFF

Ms Doney confirmed that the Advisory Committee on Borderline Substances (ACBS) recently reviewed VSL#3 (and Vivomixx) for continued inclusion in Part XV of the Drug Tariff. The Committee concluded that the evidence did not sufficiently demonstrate that the products are clinically effective and both products have been removed from the ACBS list.

VSL#3 is a probiotic food supplement, it is not a licensed medicine but was previously included in the ACBS list for the maintenance of remission in ileoanal pouchitis induced by antibacterials in adults.

The Group agreed to note VSL#3 as non-formulary on the formulary and in ScriptSwitch and highlight the change to the ACBS list to the Primary Care Prescribing Group. **FD/AD FD**

8. NEW PRODUCT REQUESTS

The Chairman highlighted the overlap in indication for items 8.2 and 8.3.

8.2. FG1SMC 2112 - NIVOLUMAB (ADJUVANT TREATMENT IN MELANOMA AFTER RESECTION)

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

The Group considered the request for nivolumab as adjuvant treatment in melanoma after complete resection.

The Group noted:
- nivolumab:
  - [for this indication] is administered as a 3mg/kg intravenous infusion over 60 minutes every 2 weeks, given for a maximum of 12 months
  - would be available for people with stage III and stage IV melanoma
  - increased the recurrence free survival when compared with another immunotherapy [ipilimumab] but median recurrence free survival was not reached for either drug

ITEM	SUBJECT	ACTION

- ipilimumab would not be the relevant comparator as this does not reflect current practice in NHS Scotland, in the adjuvant setting standard of care would be surveillance
- there are no patients waiting for treatment
- the cost of treatment, and that this would represent a new cost to the Health Board
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of nivolumab

The Group supported the restricted local need for nivolumab for the adjuvant treatment of adults with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection, as outlined in SMC 2112.

SMC 2112 - Nivolumab 10mg/mL concentrate for solution for infusion (Opdivo®) ▼ is routinely available in line with national guidance (SMC 2112).
Indication under review: as monotherapy for the adjuvant treatment of adults with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection.
Adjuvant treatment with nivolumab improved recurrence free survival compared with another immunotherapy in adults with melanoma with involvement of lymph nodes or metastatic disease who had undergone complete resection.
This advice takes account of the benefit of Patient Access Schemes (PAS) that improve the cost effectiveness of nivolumab and is contingent upon the continuing availability of this PAS in NHS Scotland or a 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 initiated and supervised by physicians experienced in the treatment of cancer. **FTeam**

8.3. FG1SMC 2131 DABRAFENIB PLUS TRAMETINIB (ADJUVANT TREATMENT IN STAGE III MELANOMA AFTER RESECTION IN PATIENT WITH BRAFV600 MUTATION)

Dr Culligan declared a personal, non-specific interest in Novartis and took part in decision-making.

The Group considered the request for dabrafenib used in combination with trametinib as adjuvant treatment for adults with stage III melanoma as outlined in SMC 2131.

The Group noted:
- dabrafenib:
  - [for this indication] is used in combination with trametinib
  - meets SMC ultra-orphan criteria, and was accepted for use in NHS Scotland following the output from the PACE process and application of SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios
- treatment is for a maximum of 12 months [unless there is disease recurrence or unacceptable toxicity]
- the SMC advice takes account of the benefits of PASs that improve the cost-effectiveness of dabrafenib and trametinib
- patient numbers are small but the cost of treatment is high
- there is overlap with the nivolumab submission [item 8.2], and patients with a positive BRAF V600 mutation would be offered the choice of either immunotherapy or targeted therapy

The Group accepted the restricted local need for dabrafenib used in combination with trametinib for the adjuvant treatment of adult patients with Stage III melanoma with a BRAF V600 mutation following complete resection.

SMC 2131 - Dabrafenib 50mg, 75mg hard capsules (Tafinlar®) is routinely available in line with national guidance (SMC 2131).
Indication under review: in combination with trametinib for the adjuvant treatment of adult patients with Stage III melanoma with a BRAF V600 mutation, following complete resection.
Relapse-free survival was significantly longer in the dabrafenib plus trametinib group compared with placebo in a phase III study of patients with completely resected, stage III melanoma with BRAF V600E or V600K mutations.

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This advice takes account of the benefits of Patient Access Schemes (PAS) that improve the cost-effectiveness of dabrafenib and trametinib, and is contingent upon the continuing availability of the PASs in NHS Scotland or a 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 qualified physician experienced in the use of anticancer medicinal products **FTeam**

8.4. FG1SMC 1335/18 - TIVOZANIB (ADVANCED RENAL CELL CARCINOMA)

Mrs Harper declared a non-personal, non-specific interest in Napp Pharmaceuticals Limited and took part in decision-making.

The Group noted:

- tivozanib:
  - is a tyrosine kinase inhibitor (TKI) licensed for the first line treatment of adult patients with advanced renal cell carcinoma (RCC) **and** for adult patients who are vascular endothelial growth factor receptor (VEGFR) and mechanistic Target of Rapamycin (mTOR) pathway inhibitor-naïve following disease progression after one prior treatment with cytokine therapy for advanced RCC
  - for first-line treatment in adults with advanced RCC meets SMC end of life criteria
- the submitting company requested that SMC only considered a sub-group of the licensed indication (for use as a first-line treatment of adult patients with advanced RCC). For this sub-group of the licence, tivozanib was accepted for restricted use in NHS Scotland after consideration of the available evidence and the output from the PACE process.
- preferred first-line TKIs for advanced RCC would be pazopanib or sunitinib, and there is no direct comparative data versus the preferred TKIs
- tivozanib has a different adverse event profile [to pazopanib and sunitinib] and may offer a useful option particularly for patients unable to tolerate existing first-line TKIs
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of tivozanib

The Group considered that tivozanib would provide a possible alternate first-line option for a small number of patients, and accepted the restricted local need for tivozanib as outlined in SMC 1335/18.

SMC 1335/18 - Tivozanib 890 micrograms, 1,340 micrograms hard capsules (Fotivda®) ▼ is routinely available in line with national guidance (SMC 1335/18).
Indication under review: for the first-line treatment of adult patients with advanced renal cell carcinoma (RCC).
In a phase III, open-label, randomised, controlled study tivozanib increased progression free survival when compared with a multi-kinase inhibitor in patients with advanced RCC.
This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of tivozanib 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 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 supervised by a physician experienced in the use of anticancer therapies. **FTeam**

8.5. FG1SMC 1331/18 - EVEROLIMUS DISPERSIBLE TABLETS (SEIZURES ASSOCIATED WITH TSC)

Dr Culligan declared a personal, non-specific interest in Novartis and took part in decision-making.

The Group considered the request for Votubia® dispersible tablets as outlined in SMC 1331/18.

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The Group noted:

- everolimus:
  - is available as different formulations and as different brands, but only the dispersible tablet as the brand Votubia® is licensed for the indication under consideration
  - [for this indication] was accepted for use in NHS Scotland following the output from the PACE process and application of the appropriate SMC modifiers
- patient numbers would be very small
- calculating the required dose could be quite complex
- there may be some challenges around the practical use of the product as monitoring would be required and it is not clear how easy it is to access trough level monitoring for everolimus

The Group accepted the local need for Votubia® (everolimus) dispersible tablets as an adjunctive treatment in the management of refractory partial-onset seizures associated with tuberous sclerosis complex (TSC), as outlined in SMC 1331/18. Treatment would be limited to the managed service, due to the potential complexity of dose calculation and monitoring.

SMC 1331/18 - Everolimus 2mg, 3mg and 5mg dispersible tablets (Votubia®) is routinely available in line with national guidance (SMC 1331/18).
Indication under review: adjunctive treatment of patients aged 2 years and older whose refractory partial-onset seizures, with or without secondary generalisation, are associated with tuberous sclerosis complex (TSC).
A phase III study identified that everolimus significantly reduced seizure frequency when compared with placebo as adjunctive treatment in patients whose refractory partial-onset seizures, with or without secondary generalisation, are associated with TSC.
This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of everolimus 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 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 a physician experienced in the treatment of patients with TSC and therapeutic drug monitoring. **FTeam**

8.6. FG1SMC 2129 - TISAGENLECLEUCEL (KYMRIAH®) (B-CELL ALL)

Dr Culligan declared a personal, non-specific interest in Novartis and took part in decision-making.

Dr Culligan updated the Group on the current position regarding the availability of cellular modified T cell (CAR-T) treatments in NHS Scotland. Novartis and Gilead currently manufacture CAR-T treatments.

Tisagenlecleucel:

- is an immunocellular therapy containing tisagenlecleucel, autologous T cells genetically modified ex vivo using a lentiviral vector encoding an anti-CD19 chimeric antigen receptor (CAR)
- is indicated for:
  - paediatric and young adults up to 25 years of age with B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse (accepted for use within NHS Scotland, SMC 2129 published 11/02/2019)
  - adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy (not recommended for use within NHS Scotland, provisional SMC 2141 issued February 2019 planned for publication 11/03/2019)
- must be administered in a qualified treatment centre, and should be initiated under the direction of and supervised by a healthcare professional experienced in the treatment of haematological malignancies and trained for administration and management of patients treated with tisagenlecleucel

ITEM	SUBJECT	ACTION

Nationally clinicians are agreeing the pathway for access to tisagenlecleucel, and at this time, treatment will be provided from a specialist centre in another NHS Board.

SMC 2129 - Tisagenlecleucel 1.2 x 10^6 – 6 x 10^8 cells dispersion for infusion (Kymriah®) ▼ is available from a specialist centre in another NHS Board.
Indication under review: treatment of paediatric and young adult patients up to 25 years of age with B-cell acute lymphoblastic leukaemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse.
Tisagenlecleucel was associated with an overall remission rate of 81% within three months of treatment in a single-arm, open-label, phase II study in paediatric and young adult patients with CD19+ relapsed or refractory B-cell ALL.
This advice takes account of the benefit of a Patient Access Scheme (PAS) that improves the cost-effectiveness of tisagenlecleucel 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.
Available from a specialist centre in another NHS Board.
Kymriah® ▼ must be administered in a qualified treatment centre. Therapy should be initiated under the direction of and supervised by a healthcare professional experienced in the treatment of haematological malignancies and trained for administration and management of patients treated with Kymriah® ▼. A minimum of four doses of tocilizumab for use in the event of cytokine release syndrome and emergency equipment must be available prior to infusion.
Kymriah® ▼ is intended for autologous use only. **FTeam**

8.7. SMC 2087 - ESLICARBAZEPINE (EPILEPSY – PAEDIATRICS)

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

The Group considered the abbreviated SMC advice for the paediatric extension of eslicarbazepine to include children aged 6 to <18 years.

The Group noted:
- eslicarbazepine:
  - is available for the same indication for adults aged 18 years and older - as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation only in patients with highly refractory epilepsy who have been heavily pre-treated and remain uncontrolled with existing anti-epileptic drugs
  - will be restricted to initiation by or on the advice of physicians experienced in the management of epilepsy
- local use is low

The Group accepted the restricted local need for the paediatric extension [aged 6 years to < 18 years] of eslicarbazepine as outlined in SMC 2087.

SMC 2087 - Eslicarbazepine acetate 200mg, 800mg tablets and oral suspension 50mg/mL (Zebinix®) is routinely available in line with national guidance (SMC 2087).
Indication under review: as adjunctive therapy in adolescents and children aged 6 to < 18 years with partial-onset seizures with or without secondary generalisation.
Restriction: patients with highly refractory epilepsy who have been heavily pre-treated and remain uncontrolled with existing anti-epileptic drugs.
It was classified 1b – available for restricted use under specialist supervision and 8d - treatment may be initiated in the community on recommendation of a consultant/specialist. **FTeam**

8.8. SMC 2126 - ROMIPLOSTIM VIAL (ITP PAEDIATRICS)

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

The Group considered the paediatric licence extension for romiplostim for chronic immune (idiopathic) thrombocytopenic purpura (ITP).

ITEM	SUBJECT	ACTION

The Group noted:
- romiplostim:
  - is available as two preparations 1) vial [125micrograms powder for solution for injection] and 2) reconstitution pack for self-injection
  - both preparations are available for adults with severe symptomatic ITP or with a high risk of bleeding who are refractory to other treatments
- the change in licence extends use to children and adolescents aged from 1 to < 18 years and only applies to the vial presentation
- making romiplostim vial available for paediatrics will bring use in line with the formulary acceptance for adults [aged 18 years and older]

The Group accepted the restricted local need for romiplostim vial for children and adolescents aged 1 to < 18 years as outlined in SMC 2126.

SMC 2126 - Romiplostim 125microgram powder for solution for injection (Nplate®) is routinely available in line with national guidance (SMC 2126).
Indication under review: chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients aged 1 to < 18 years who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).
Restriction: to use in patients with severe symptomatic ITP or patients with a high risk of bleeding.
It was classified 1b- available for restricted use under specialist supervision and 8b – recommended for hospital use only. Treatment should remain under the supervision of a physician who is experienced in the treatment of haematological diseases. **FTeam**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE - ISSUED FEBRUARY 2019

The Group noted the SMC provisional advice issued February 2019.

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. **FTeam**

10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS - PUBLISHED FEBRUARY 2019

The Group noted the SMC advice published February 2019.

Following publication of the negative SMC recommendations, for pembrolizumab (Keytruda®) ▼ SMC 2127, axicabtagene ciloleucel (Yescarta®) ▼ SMC 2114 and cabozantinib (Cabometyx®) ▼ SMC 2136, these medicines will not be included on the Grampian Joint Formulary for the indications in question. **FTeam**

Following publication of non-submission statements, for cabozantinib (Cabometyx®) ▼ SMC 2160, dexmedetomidine (Dexdor®) SMC 2161, doravirine (Pifeltro®) ▼ SMC 2162 and doravirine/lamivudine/tenofovir disoproxil (Delstrigo®) ▼ SMC 2163, 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:
- SMC2128 rivaroxaban 2.5mg tablets (Xarelto®) ▼
- SMC2122 tofacitinib (Xeljanz®) ▼

Local advice for these medicines and indications will be included in the February 2019 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts'. **FTeam**

11. GENERAL INFORMATION FROM SMC FEBRUARY 2019 - NONE

12. DOCUMENTS FOR INFORMATION

Items 12.1 (Medicine Guidelines and Policies Group minute November 2018), and 12.2 (Grampian Medicines Management Group minute September 2018) were noted.

ITEM	SUBJECT	ACTION

13. AOCB - NONE

DATE OF NEXT MEETING

Tuesday 19 March 2019 starting at 14:30 in the Seminar Room, David Anderson Building.

CHAIRMAN'S SIGNATURE _____ **DATE 19 March 2019**