NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 19 January 2021 at 14:30 via Microsoft Teams

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

IN ATTENDANCE
Ms Caitlin Wilkinson, Formulary Team administrator
Ms Christine Hay, Formulary and Medicines Management Pharmacist

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.	
2.	**DRAFT MINUTE OF THE MEETING HELD 15 DECEMBER 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**
	ITEM 4.1 FG1SMC 2288 - SODIUM ZIRCONIUM CYCLOSILICATE (HYPERKALAEMIA)	
	Dr Metcalfe queried if the Cardiologists had expressed an intention to use sodium zirconium cyclosilicate to keep potassium levels down when introducing an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker. Ms Doney will confirm if the Cardiology service plans to use sodium zirconium cyclosilicate.	**FD**
3.	**PRESENTATION**	
	None	
4.	**MATTERS ARISING**	
	4.1. ACTION LOG	
	The action log was noted. No additional items were identified that should have been included in the agenda.	
5.	**FORMULARY GROUP DECISIONS DECEMBER 2020 – PUBLISHED – 29/12/2020**	
	5.1. FORMULARY GROUP DECISIONS DECEMBER 2020	
	Members ratified the decisions of the December 2020 meeting, as published.	**FTEAM**
6.	**NETFORMULARY/FORMULARY REVIEW**	
	6.1. LOFEXIDINE 200MICROGRAM TABLETS	
	The Group considered the '*Discontinuations and changes to formulations of drugs*	

ITEM	SUBJECT	ACTION

included on the formulary' document, that was issued the day before the meeting.

Discontinued products:
- lofexidine 200microgram tablets (BritLofex®)
- Migril® (ergotamine tartrate/cyclizine hydrochloride/caffeine hydrate)
- misoprostol (Mysodelle®)
- necitumumab (Portrazza®)

Formulation change:
- ceritinib 150mg tablet has replaced the hard capsule formulation
- enzalutamide 40mg film-coated tablet has replaced the soft-capsule formulation. Enzalutamide (Xtandi®) 40mg and 80mg tablets have been approved by the European Medicines Agency (EMA) for registration. However, the 80mg tablet is not marketed and is not available in any European country.
- palbociclib 75mg, 100mg, 125mg tablets (Ibrance®) have replaced the hard capsule formulation

Ms Doney confirmed that, where appropriate, the formulary would be updated or amended. **FTEAM**

The Chairman highlighted the discontinuation of lofexidine 200microgram tablets (BritLofex®).

Ms Doney confirmed that:
- lofexidine is included in the NHS Grampian Drug and Alcohol Services Formulary, and there is a local prescribing guidance document '*Guidance for the use of lofexidine in the symptomatic management of opioid withdrawal by clinicians working within NHS Grampian*'.
- the Substance Misuse pharmacists have been informed about the withdrawal of lofexidine so that the local Drug and Alcohol Services Formulary is updated
- a request to withdraw the local prescribing guidance has been sent to the Medicines Guidelines and Policies Group (MGPG)

7. OTHER BUSINESS - NONE

8. NEW PRODUCT REQUESTS

8.1. FG1SMC 2257 - PEMBROLIZUMAB (HEAD AND NECK SQUAMOUS CELL CARCINOMA)

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

The Group considered the request for pembrolizumab as monotherapy or in combination with platinum and fluorouracil chemotherapy, for the first-line treatment of metastatic or unresectable recurrent head and neck squamous cell carcinoma (HNSCC) in adults whose tumours express programmed cell death ligand-1 (PD-L1) with a combined positive score (CP)≥1.

The Group noted:
- pembrolizumab:
  - was accepted for restricted use as monotherapy or in combination with platinum and fluorouracil chemotherapy, for the first-line treatment of metastatic or unresectable recurrent HNSCC in adults whose tumours express PD-L1 with a CPS≥1
  - [for this indication] was assessed under the SMC end of life process, and accepted for restricted use in NHS Scotland following the output from the PACE process, and application of the appropriate SMC modifiers
  - monotherapy as first-line treatment of metastatic or unresectable recurrent HNSCC **regardless of PD-L1 expression** status, is currently supported by the COVID-19 National Cancer Medicines Advisory Group

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- HNSCC are an anatomically heterogeneous group of cancers including tumours originating in the lip, oral cavity, hypopharynx, oropharynx, nasopharynx or larynx
- patients with metastatic or unresectable recurrent HNSCC have a poor prognosis and median overall survival is likely to be less than 1 year
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of pembrolizumab
- the SMC restricted treatment with pembrolizumab to a two-year clinical stopping rule
- patient numbers are expected to be small, fitness and performance status will be a factor in patient selection. Previously, PD-L1 status would not have been tested, and there is no historic data to support estimation of patient numbers.
- it is difficult to predict patient numbers which makes the estimation of the financial impact of treatment problematic

Ms Doney will highlight the difficulty estimating patient numbers and so potential cost range with finance. **FD**

Mr Rore questioned how the two-year stopping rule would work in practice. If a patient successfully reaches two years on treatment, in a disease with a median survival of one year or less they are doing well, would treatment be stopped?
Ms Galvin confirmed that, in this instance the PACS Tier 2 system would be available to consider access to extended treatment.

The Group accepted the restricted local need for pembrolizumab, as monotherapy or in combination with platinum and fluorouracil chemotherapy, for the first-line treatment of metastatic or unresectable recurrent HNSCC in adults whose tumours express PD-L1 with a CP≥1, in line with SMC 2257.

SMC 2257 - Pembrolizumab 25mg/mL concentrate for solution for infusion (Keytruda®) is routinely available in line with national guidance (SMC 2257).
Indication under review: as monotherapy or in combination with platinum and fluorouracil chemotherapy, for the first-line treatment of metastatic or unresectable recurrent head and neck squamous cell carcinoma (HNSCC) in adults whose tumours express programmed cell death ligand-1 (PD-L1) with a combined positive score (CPS)≥1.
Restriction: treatment with pembrolizumab is subject to a two-year clinical stopping rule.
Overall survival was longer in patients who received pembrolizumab as monotherapy or in combination with chemotherapy compared with a monoclonal antibody plus chemotherapy in a phase III study in patients with untreated, locally incurable, recurrent or metastatic HNSCC with PD-L1 CPS≥1.
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 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. Therapy must be initiated and supervised by specialist physicians experienced in the treatment of cancer. **FTEAM**

8.2. FG1SMC 2252 - GILTERITINIB (ACUTE MYELOID LEUKAEMIA)

Ms Galvin declared a personal non-specific interest in Astellas Pharma Ltd and took part in decision-making.

The Group considered the request for gilteritinib as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation.

ITEM	SUBJECT	ACTION

The Group noted:

- gilteritinib:
  - is a protein kinase inhibitor which acts to block FLT3, stopping white blood cell growth and slowing down the development of the cancer
  - is the first agent licensed for the treatment of relapsed or refractory AML in patients with a FLT3 mutation
  - [for this indication] was accepted for use in NHS Scotland following a full submission under the end of life and orphan medicine process, the output from the PACE process, and application of the appropriate SMC modifiers
  - would be a second-line agent that is taken orally as monotherapy
  - is administered until disease progression or unacceptable toxicity
  - is an expensive treatment and patient numbers are expected to be very small
- in the clinical trial, gilteritinib provided an overall response rate of ~68% and a median duration of response of ~11 months
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of gilteritinib

The Group accepted the restricted local need for gilteritinib as monotherapy for the treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation, in line with SMC 2252.

SMC 2252 - Gilteritinib 40mg film-coated tablets (Xospata®) ▼ is routinely available in line with national guidance (SMC 2252).
Indication under review: as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia with a FLT3 mutation.
In an open-label, phase III study, gilteritinib improved overall survival compared with salvage chemotherapy in patients with relapsed or refractory acute myeloid leukaemia with a FLT3 mutation.
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 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 gilteritinib should be initiated and supervised by a physician experienced in the use of anti-cancer therapies. FTEAM

8.3. FG1SMC 2259 - IBRUTINIB (WALDENSTRÖM'S MACROGLOBULINAEMIA)

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

The Group considered the request for ibrutinib used in combination with rituximab for the treatment of adult patients with Waldenström's macroglobulinaemia who have received at least one prior therapy. [Ibrutinib is also licensed as a single agent for the treatment of adults with Waldenström's macroglobulinaemia who have received at least one prior therapy, or in the first line treatment for patients unsuitable for chemo-immunotherapy but these indications are not recommended for use within NHS Scotland due to non-submission (SMC 2245)].

The Group noted:

- the submitting company requested that the SMC considered ibrutinib (plus intravenous rituximab) when positioned for use in patients who have received at least one prior therapy
- ibrutinib:
  - is the first medicine to be licensed specifically for the treatment of Waldenström's macroglobulinaemia
  - [for the requested indication] is used in combination with intravenous rituximab

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- [for the requested indication] was accepted for restricted use in NHS Scotland following a full submission under the end of life and orphan medicine process, the output from the PACE process, and application of the appropriate SMC modifiers
- is an expensive treatment, patient numbers will be very small but will be cumulative with treatment extending for several years

- in the clinical trial (iNNOVATE) ibrutinib plus rituximab compared to placebo plus rituximab improves progression free survival (PFS); the median PFS had not been reached at 34 months and was 20.3 months for placebo plus rituximab
- the SMC advice takes account of the benefits of a complex PAS that improves the cost-effectiveness of ibrutinib
- Waldenström's macroglobulinaemia is a rare incurable B-cell cancer
- the majority of patients included in the iNNOVATE trial had an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1, so the study results may be less generalisable to patients with a worse performance status
- the Haematology service has considerable experience with the use of ibrutinib for other indications

The Group accepted the restricted local need for ibrutinib in combination with rituximab for the treatment of adult patients with Waldenström's macroglobulinaemia who have received at least one prior therapy, in line with SMC 2259.

SMC 2259 - Ibrutinib 140mg, 280mg, 420mg film-coated tablets (Imbruvica®) is routinely available in line with national guidance (SMC 2259).
Indication under review: in combination with rituximab for the treatment of adult patients with Waldenström's macroglobulinaemia in patients who have received at least one prior therapy.
Progression-free survival was longer in patients with Waldenström's macroglobulinaemia who received ibrutinib plus rituximab compared with placebo plus rituximab in a phase III study.
This advice applies only in the context of an approved NHS Scotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.
This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting. It was classified 1b - available for restricted use under specialist supervision and 8b – recommended for hospital use only. Treatment with this medicinal product should be initiated and supervised by a physician experienced in the use of anticancer medicinal products. FTEAM

8.4. FG1SMC 2281 - LENALIDOMIDE (FOLLICULAR LYMPHOMA)

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

The Group considered the request for lenalidomide used in combination with rituximab for the treatment of adult patients with previously treated follicular lymphoma (Grade 1 to 3a).

The Group noted:

- lenalidomide:
  - [for this indication] is used in combination with intravenous rituximab
  - [for this indication] meets SMC orphan medicine criteria and was accepted for use in NHS Scotland following a full submission reviewed by the SMC executive
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of lenalidomide
- the combination of lenalidomide and rituximab increases antibody-dependent cell-mediated cytotoxicity and direct tumour apoptosis in follicular lymphoma cells
- rituximab dosing varies between the Summary of Product Characteristics (SmPCs) for lenalidomide and rituximab. The service has confirmed it will adhere to the dosing in the lenalidomide SmPC.

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- the Haematology service has significant experience with the use of lenalidomide
- patient numbers are expected to be small
- lenalidomide is due to come off patent in June 2022, which will have a significant impact on costs due to its extensive use within the Haematology service

The Group accepted the restricted local need for lenalidomide in combination with rituximab for the treatment of adult patients with previously treated follicular lymphoma (Grade 1 to 3a), in line with SMC 2281.

SMC 2281 - Lenalidomide 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg hard capsules (Revlimid®) ▼ is routinely available in line with national guidance (SMC 2281).
Indication under review: in combination with rituximab (anti-CD20 antibody) for the treatment of adult patients with previously treated follicular lymphoma (Grade 1 to 3a).
In a double-blind phase III study lenalidomide in combination with rituximab, compared with placebo plus rituximab, increased progression-free survival in adults with relapsed or refractory follicular lymphoma (Grade 1 to 3a).
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.
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 anti-cancer therapies. FTEAM

8.5. FG1SMC 2242 - NALDEMEDINE AND SMC 1106/15 NALOXEGOL (OPIOID-INDUCED CONSTIPATION)

Mr Paterson and Dr Fitton declared personal, non-specific interests in AstraZeneca UK Limited and took part in decision-making.
There were no declarations of interest in Kyowa Kirin or Shionogi BV.

The Group considered the request from the Gastroenterology (GI) service for naldemedine and naloxegol, for the treatment of opioid-induced constipation in adult patients who have previously been treated with laxatives.

It was confirmed that:
- the GI service has requested that both agents are added to the formulary because, naldemedine does not require a dose reduction in renal impairment, whereas for moderate and severe renal impairment, the starting dose of naloxegol should be reduced from 25mg to 12.5mg
- naloxegol is licensed to be crushed and administered through a nasogastric tube, which is not included in the licensing for naldemedine
- the review is limited to use for adults with chronic non-cancer pain, the palliative care team will prepare a separate request for use in adults with chronic cancer pain

The Group noted:
- naldemedine:
  - [April 2020] following a full submission, naldemedine was accepted for use in NHS Scotland for the treatment of opioid-induced constipation in adult patients who have previously been treated with a laxative [SMC 2242]
  - does not require a dose reduction in renal impairment
  - can be taken with or without other laxatives, and current laxatives do not need to be stopped when naldemedine treatment is started
- naloxegol:
  - was not included on the formulary when discussed by the Formulary Group in July 2016. The Group requested clarification on the proposed ‘ladder’ of laxative treatment, and naloxegol was categorised as non-formulary pending protocol.

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- can be crushed and administered through a nasogastric tube
- the risk of perforation with either agent
- only naloxegol recommends stopping all laxatives before initiating treatment to allow assessment of treatment

The Group agreed that:
- refractory opioid-induced constipation is a common problem that is managed by General Practice and other services, e.g. the Pain Service, so limiting use to 'only on the advice of specialists' may be too restrictive
- patient numbers are likely to rise progressively with time, and naldemedine and naloxegol are more expensive than other laxatives

Mindful of waiting lists, the Group supported prescribing in General Practice if backed by a robust prescribing protocol, to include starting and stopping criteria. The Group requested that the service develop a clear, robust protocol for use that should be authorised by the Medicines Guidelines and Policies Group.

The Group accepted the restricted local need for naldemedine and naloxegol in the management of opioid-induced constipation in adults with chronic non-cancer pain. Acceptance is subject to provision of a prescribing protocol that is approved by the MGPG, and could be used by other services, e.g. Pain Service.

Until the local prescribing protocol is published by the MGPG, prescribing should remain within the managed service.

SMC 2242 - Naldemedine 200micrograms film-coated tablets (Rizmoic®) ▼ is routinely available in line with local guidance.
Indication under review: for the treatment of opioid-induced constipation in adults who have previously been treated with a laxative.
Restriction: for the treatment of refractory opioid-induced constipation in adults with chronic non-cancer pain whose constipation has not adequately responded to at least two laxatives.
It was classified 1a - available for general use and 8e - treatment may be initiated in either Primary or Secondary care. **FTEAM**

SMC 1106/15 - Naloxegol 12.5mg, 25mg film-coated tablets (Moventiq®) is routinely available in line with local guidance.
Indication under review: for the treatment of opioid-induced constipation in adults who have had an inadequate response to laxative(s).
Restriction: for the treatment of refractory opioid-induced constipation in adults with chronic non-cancer pain whose constipation has not adequately responded to at least two laxatives.
It was classified 1a - available for general use and 8e - treatment may be initiated in either Primary or Secondary care. **FTEAM**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE – JANUARY 2021

The Group noted the SMC provisional advice issued January 2021.

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.

SMC 2305 - RAVULIZUMAB 300MG CONCENTRATE FOR SOLUTION FOR INFUSION (ULTOMIRIS®) ▼

The Group noted the provisional advice for ravulizumab for the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH):
- in patients with haemolysis with clinical symptom(s) indicative of high disease activity

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- in patients who are clinically stable after having been treated with eculizumab for at least the past 6 months

As recommendations to prescribe ravulizumab will only be under the advice of the national PNH service the Group felt there was little benefit requesting a full submission from the local specialities.

The Formulary Team will prepare a summary, to include cost estimates for ravulizumab and eculizumab, for discussion at the February meeting. FTEAM

10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS – JANUARY 2021

The Group noted the SMC advice published January 2021.

Following publication of the negative SMC recommendation for melatonin (Slenyto®) SMC 2306 and the non-submission statements apalutamide (Erleada®) ▼ SMC 2323, dupilumab (Dupixent®) ▼ SMC 2324 and talazoparib (Talzenna®) ▼ SMC 2325 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 2294 entrectinib (Rozlytrek®) ▼
- SMC 2300 fostamatinib (Tavlesse®) ▼(submission expected)
- SMC 2302 daratumumab (Darzalex®) ▼(submission expected)
- SMC 2308 secukinumab (Cosentyx®) (submission expected)
- SMC 2310 brentuximab vedotin (Adcetris®) ▼(submission expected)
- SMC 2314 brigatinib (Alunbrig®) ▼
- SMC 2326 daratumumab subcutaneous injection (Darzalex®) ▼(submission expected)

Local advice for these medicines and indications will be included in the January 2021 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 – JANUARY 2021 - NONE

12. DOCUMENTS FOR INFORMATION

ITEMS 12.1 AND 12.2 (DRUG SAFETY UPDATE DECEMBER 2020 AND JANUARY 2021)
Ms Doney confirmed the relevant articles have been shared with the Antimicrobial Management Team.
Item 12.3 (MedWatch newsletter December 2020) was noted.

13. AOCB

THANK YOU AND GOODBYE

The Chairman reported that this is Mr Rore's last Formulary Group meeting as he is leaving NHS Grampian in February 2021. Professor McLay led members in thanking Mr Rore for all of his work as part of the Medicines Information service and the contribution he has given in support of the Formulary Group.

DATE OF NEXT MEETING

Tuesday 16 February 2021 starting at 14.30 via Microsoft Teams.

CHAIRMAN'S SIGNATURE **DATE 16 FEBRUARY 2021**