NHS GRAMPIAN
Minute of Formulary Group Meeting held on Tuesday 19th April 2016 in the Aspen Room, Forest Grove House

PRESENT	APOLOGIES	APPROVED
Dr David Counter	Mrs J Jordan	
Dr Dominic Culligan (from item 8.3)	Dr T McGoldrick	
Ms A Davie	Mr M Paterson	
Ms F Doney		
Dr L Elliot		
Dr Janet Fitton		
Mrs L Harper		
Dr C Hind		
Dr A MacDonald		
Professor J McLay (Chairman)		
Mrs L Montgomery		
Dr W Moore (from item 7.3)		
Mr C Rore		
Mr R Sivewright		
Dr A Sun (from item 7.3)		

IN ATTENDANCE
Ms Kate Robertson, Secretary Formulary Team.

OBSERVER
Ms Kirsty Reegan, Pre-registration Pharmacist, Aberdeen Royal Infirmary.

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	The Chairman opened the meeting, noted that a quorum was present and welcomed members and observers to the meeting.	
	WELCOME TO NEW MEMBER Dr Janet Fitton joins the Group as a General Practitioner representative for Aberdeenshire Health and Social Care Partnership.	
1.	**APOLOGIES**	
	Apologies for absence were requested and noted.	**FD**
2.	**DRAFT MINUTE OF THE MEETING HELD ON THE 16TH MARCH 2016**	
	The Group accepted the draft note of the meeting held on the 16th March 2016 as an accurate record of the meeting subject to correction of item 9 where the first paragraph should read "If published next month the negative SMC recommendations, for eculizumab (Soliris®) SMC 1130/16 and ataluren (Translarna®) ▼ SMC 1131/16, will not be included on the Grampian Joint Formulary for the indications in question."	**FD**
	The corrected approved minute will be in the public domain within 21 days.	**FTeam**
3.	**PRESENTATION – NONE**	
4.	**MATTERS ARISING**	
	4.1. FRONT-LINE TREATMENT OF MULTIPLE MYELOMA/CLOSURE OF MYELOMA CLINICAL TRIAL	
	The Secondary Care Pharmacy representative was not available to provide an update for the meeting. It was confirmed that: • other areas/cancer networks are not currently using lenalidomide plus bortezomib plus dexamethasone for the front-line treatment of multiple myeloma • a submission for lenalidomide plus dexamethasone as per SMC 1096/15 (for previously untreated multiple myeloma who are not eligible for transplant and unsuitable for thalidomide-containing regimens) is currently in process • the clinical trial Myeloma XI has closed and there are currently no other front-line clinical trials open to recruitment locally	

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- lenalidomide plus bortezomib plus dexamethasone for the front-line treatment of multiple myeloma is an unlicensed regime and if the service wishes the Group to consider this regime for formulary inclusion robust clinical- and cost-effectiveness data would be required

5. FORMULARY GROUP DECISIONS MARCH 2016 – PUBLISHED 29/03/2016

The Group ratified the advice as published.

6. CMO(2012)1 REPORTING FOR SCOTTISH MEDICINES CONSORTIUM (SMC) ADVICE – 2015/16

It was confirmed that for the SMC accepted medicines published April 2015 to March 2016 the Formulary Group (FG) audit standard for CMO(2012)1 reporting was achieved for the following criteria:

- Local decision on SMC accepted medicine published within 90 days: 87 of 87 - 100%
- FG decision published within 14 days of the decision being reached: 87 of 87 - 100%

As part of the proposed changes to the presentation of decisions regarding new medicines, moving to exception reporting coupled with annual/bi-annual reporting will be considered. An update or proposal will be provided for the June meeting. **FD**

7. OTHER BUSINESS

7.1. NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE (NICE) (MULTIPLE) TECHNOLOGY APPRAISAL GUIDANCE - NONE

7.2. AREA DRUGS AND THERAPEUTICS COLLABORATIVE (ADTC) NEWSLETTER MARCH 2016

The Group noted the content of the March ADTC Collaborative Newsletter. As a result of feedback the Collaborative changed the way it communicates by preparing a regular bimonthly communication and keeping ad hoc emails to a minimum. The Collaborative has requested feedback on the latest edition of the newsletter and on the changes made to how it communicates. Members to feedback comments to Ms Doney or directly to the Collaborative (hcis.adtc-collaborative@nhs.net). **All**

7.3. FORMULARY REVIEW

7.3.1. EXTENSION TO THE USE OF ZOLEDRONIC ACID INFUSION (IN CANCER)

The Group considered the request from colleagues in the oncology department to extend the use of zoledronic acid 4mg.

The Formulary Group considered the comprehensive review undertaken by the West of Scotland Cancer Network (WoSCAN) and revised economic analyses underpinning the new WoSCAN Guideline for Prevention of Skeletal Related Events in Cancer Patients.

The Group accepted the recommendations of the review undertaken by HIS on behalf of WoSCAN. It noted that that generic zoledronic acid is now a cost-effective treatment option in other solid tumours, in addition to breast cancer and myeloma, and supported the proposals to widen the guideline to include access to zoledronic acid in other solid tumour types. **FTeam**

The Group supported the proposal to revise the current local guidelines in line with the WoSCAN guidance for the prevention of skeletal related events. **JJ**

8. NEW PRODUCT REQUESTS

8.1. FG1 SMC 615/10 - GEFITINIB (NON-SMALL CELL LUNG CANCER)

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

The Group noted that:

- gefitinib:
  - is an epidermal growth factor receptor tyrosine kinase (EGFR-TK) inhibitor licensed for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating mutations of EGFR-TK. The submitting company has requested that the SMC only consider use as a first-line therapy.
  - is taken orally at a dose of one 250mg tablet once a day, and adverse events are

managed by dose interruption not dose reduction
  - meets SMC end of life criteria and the SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of gefitinib
  - is the third tyrosine kinase inhibitor considered for first-line use for this patient group and will compete directly with afatinib and erlotinib
  - demonstrated an improvement in the progression-free survival and tumour response rates compared with platinum-doublet chemotherapy, but there was no overall survival benefit demonstrated
- there are no head-to-head data for gefitinib versus afatinib and/or erlotinib
- the SMC advice restricts use of gefitinib to first-line use which is consistent with TA374 - erlotinib and gefitinib for treating non-small cell lung cancer that has progressed after prior chemotherapy
- the request is essentially cost-neutral, as first-line use of gefitinib will replace first-line use of erlotinib or afatinib

A member queried if the costings for gefitinib included VAT, the information will be checked. **MH**

The Group accepted the restricted local need for the first-line use of gefitinib as outlined in SMC 615/10.

SMC 615/10 - Gefitinib 250mg film-coated tablets (Iressa®) is included on the Grampian Joint Formulary for the indication in question; restricted use.
Indication under review: the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with activating mutations of epidermal growth factor receptor tyrosine kinase (EGFR-TK).
Restriction: in patients with previously untreated locally advanced or metastatic NSCLC with activating EGFR-TK mutations i.e. as a first-line therapy.
In patients with EGFR mutation-positive, advanced NSCLC, randomised controlled studies demonstrated an improvement in the progression-free survival and tumour response rates for those treated with gefitinib compared with platinum-doublet chemotherapy. There was no overall survival benefit demonstrated.
This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of gefitinib and is contingent upon the continuing availability of the patient access scheme 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 physician experienced in the use of anticancer therapies. **FTeam**

8.2. FG1 SMC 1066/15 - ENZALUTAMIDE (METASTATIC CASTRATION-RESISTANT PROSTATE CANCER)

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

The Group considered the submission for enzalutamide for the treatment of adult men with metastatic castration-resistant prostate cancer (mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated.

The Group noted:
- enzalutamide:
  - for this indication was accepted for use in NHS Scotland following the output from the PACE process, and after application of the appropriate modifiers, and following an Independent Review Panel
  - meets SMC end of life and orphan equivalent criteria.
  - is already included on the formulary for the treatment of adult men with metastatic castration-resistant prostate cancer whose disease has progressed on or after docetaxel therapy
  - has a different side-effect profile to and will provide an alternative to abiraterone for this patient group. Sequencing is not anticipated due to cross-resistance, but patients may be changed from one agent to the other in the event of unacceptably toxicity with the first agent.
- the median treatment duration for enzalutamide was ~16 months

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- medical castration with a luteinising hormone-releasing hormone (LHRH) analogue should be continued during treatment of patients not surgically castrated
- the SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of enzalutamide, and the PAS is available in Primary Care
- that a shared care arrangement is not currently in place for abirateone or enzalutamide but if prescribing in Primary Care was requested there is a need for co-ordinated care between Secondary and Primary Care

The Group accepted the restricted local need for enzalutamide as outlined in SMC 1066/15 for the treatment of metastatic castration-resistant prostate cancer.

SMC 1066/15 – Enzalutamide 40mg soft capsules (Xtandi®) ▼ is included on the Grampian Joint Formulary for the indication in question; restricted use.
Indication under review: Treatment of adult men with metastatic castration-resistant prostate cancer (mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated.
In a randomised, double-blind phase III study of adult men with chemotherapy naive mCRPC treatment with enzalutamide was associated with a statistically significant extended overall survival and radiographic progression free survival compared to placebo.
This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost effectiveness of enzalutamide 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. **FTeam**

8.3. FG1 SMC 1123/16 - Guanfacine (ADHD children and adolescents)

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

The Group considered the submission from the Child and Adolescent Mental Health Service for guanfacine, as outlined in SMC 1123/16, for the treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents 6 to 17 years old.

The Group noted:

- guanfacine is a selective alpha$_{2A}$-adrenergic receptor agonist that would provide a licensed alternative to off-label use of clonidine, and an alternative non-stimulant preparation to atomoxetine
- the need for careful dose titration, initial and ongoing monitoring
- that the dosage is age and weight dependent
- blood pressure and pulse may increase following discontinuation of guanfacine; individuals may have larger increases - blood pressure and pulse should be monitored in all patients during dose downward titration (decrements of no more than 1mg every 3 to 7 days) and following discontinuation of guanfacine
- if two or more consecutive doses are missed, re-titration is recommended based on the patient's tolerability to guanfacine
- during dose titration, weekly monitoring for signs and symptoms of somnolence and sedation, hypotension and bradycardia should be performed
- during the first year of treatment, the patient should be assessed at least every 3 months for 1) signs and symptoms of somnolence and sedation, hypotension, bradycardia; 2) weight increase/risk of obesity. It is recommended clinical judgement be exercised during this period. 6 monthly monitoring should follow thereafter, with more frequent monitoring following any dose adjustments.
- the requestor confirmed that atomoxetine and guanfacine would be available when stimulants are not suitable, not tolerated or have been shown to be ineffective. The choice of agent may depend on comorbidities, guanfacine may be preferred for ADHD patients with tics, weight loss or insomnia.

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- that licensed medicines are preferred to off-label use of medicines. The use of clonidine will likely reduce but the Service requested that clonidine remains on formulary until prescribers have more experience of the use of guanfacine.

The Group considered that the introduction of an alternative licensed non-stimulant preparation with a different mechanism of action to current licensed treatments is advantageous for prescribers and patients. However due to concerns regarding initial dose titration and monitoring, and the risk of patients missing doses and requiring re-titration, treatment is subject to update of the local ADHD child and adolescent prescribing policy, and patients must be stable before transfer to Primary Care.

The Group accepted the restricted local need for guanfacine prolonged-release tablets as outlined in SMC 1123/16, use is subject to inclusion in the local ADHD prescribing guidance for children and adolescents. Patients should be on a stable dose of guanfacine before transfer to Primary Care.

SMC 1123/16 - Guanfacine 1mg, 2mg, 3mg, 4mg prolonged-release tablets (Intuniv®) ▼ is not included on the Grampian Joint Formulary for the indication in question, pending protocol.
Indication under review: treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents 6 to 17 years old for whom stimulants are not suitable, not tolerated or have been shown to be ineffective. Treatment must be used as part of a comprehensive ADHD treatment programme, typically including psychological, educational and social measures.
Two phase III studies in children and adolescents aged 6 to 17 years with ADHD demonstrated that guanfacine improved the symptoms of ADHD compared with placebo. It was classified 1b – available for restricted use under specialist supervision and 8c – treatment to be initiated in hospital prior to handover. Treatment must be initiated under the supervision of an appropriate specialist in childhood and/or adolescent behavioural disorders. Use is subject to inclusion in the ADHD prescribing guidance. **FTeam**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE – ISSUED APRIL 2016

The Group noted the SMC provisional advice issued April 2016.

If published next month the negative SMC recommendation for ivacaftor (Kalydeco®) ▼ SMC 1134/16, lumacaftor/ivacaftor (Orkambi®) ▼ SMC 1136/16, ceftolozane/tazobactam (Zerbaxa®) ▼ SMC 1146/16 and the non-submission statements for certolizumab pegol (Cimzia®) SMC 1155/16 and ramucirumab (Cyramza®) ▼ SMC 1156/16, these will not be included on the Grampian Joint Formulary for the indications in question. **FTeam**

10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS - PUBLISHED APRIL 2016

The Group noted the SMC advice published April 2016.

Following publication of the negative SMC recommendations for eculizumab (Soliris®) SMC 1130/16 and ataluren (Translarna®) ▼ SMC 1131/16, these 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 872/13 Everolimus (Afinitor®)
- SMC 1129/16 Isavuconazole (Cresemba®) ▼ – submission in progress
- SMC 1133/16 Camellia sinensis (green tea) leaf extract (Catephen®) – submission in progress

Local advice for these medicines and indications will be included in the April 2016 decisions as '**Not included on the Grampian Joint Formulary because clinicians have not responded to an invitation to apply for formulary inclusion for this medicine for the indication in question**.' **FTeam**

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SMC 1137/16 – ALENDRONIC ACID EFFERVESCENT TABLETS (BINOSTO®)

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

The Group reviewed the abbreviated SMC advice, SMC 1137/16, for alendronic acid effervescent tablets and the cost comparison information collated by the Formulary Team.

The Group noted that:

- the cost of the once-weekly effervescent tablet is comparable to the oral solution but considerably more expensive than standard once-weekly tablets [~£296 per annum for the once-weekly effervescent tablets or solution versus ~£13 per annum for the standard once-weekly tablet]
- the SMC restricted use to patients who are unable to swallow tablets where alendronic acid is the appropriate treatment choice
- like other oral bisphosphonates patient require to stand or sit upright for at least 30 minutes after taking Binosto®
- the oral solution is not currently included on the formulary
- oral bisphosphonates would be avoided in patients with swallowing difficulties
- currently there is no information about the administration of the effervescent tablets via enteral tube

The Medicines information department has confirmed that generally, the administration of bisphosphonates via enteral tubes should be avoided owing to the risk of adverse gastrointestinal effects associated with this class of drugs and consideration should be given to a parenteral bisphosphonate. There is conflicting evidence regarding which preparation of alendronate would be preferred, if administration via enteral tubes is considered essential (a once-weekly preparation as plain tablets dissolved in water or oral solution). Ms Doney will forward the information to members. **FD**

The Chairman requested that prescribers are reminded that calcium and vitamin D levels should be checked and any deficiencies corrected before initiating therapy. **IMPACT**

The Group did not support formulary inclusion for alendronic acid effervescent tablets (Binosto®) and requested the non-formulary status is highlighted on ScriptSwitch. **AD**

SMC 1137/16 - Alendronic acid effervescent tablets (Binosto®) is not included on the Grampian Joint Formulary because the NHS board decision is that the medicine does not represent sufficient added benefit to other comparator medicines to treat the condition in question which are already in the formulary.
Indication under review: treatment of postmenopausal osteoporosis.
Restriction: for use in patients who are unable to swallow tablets where alendronic acid is the appropriate treatment choice.
Alendronic acid 70mg effervescent tablets have demonstrated bioequivalence to alendronic acid 70mg tablets. The effervescent tablet formulation provides an alternative for patients who cannot swallow tablets. It is more expensive than generic alendronic acid tablets but is similar to the cost of existing oral solutions.
It was classified 2a - approved by the SMC but currently not recommended for use in NHS Grampian. Cost effective alternatives are available. **FTeam**

11. GENERAL INFORMATION FROM SMC APRIL 2016 – NIL OF NOTE

12. DOCUMENTS FOR INFORMATION

Items 12.1 (Drug Safety Update March 2016), 12.4 (Minutes of the Grampian Medicines Management Group – January 2016) and 12.5 (Minutes of the Medicine Guidelines and Policies Group – January 2016) were noted.

ITEM 12.2 REVIEW OF ACCESS TO NEW MEDICINES - INDEPENDENT REVIEW BY DR BRIAN MONTGOMERY

The Group noted the scope and approach of the review. A member highlighted the bullet point "How the SMC process should be adapted to include commercial negotiation with the aim of (1) ensuring best value for the NHSS and (2) getting to a pharmaceutical companies'

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best offering on price earlier". This is a significant change to current process as neither the SMC or Patient Access Scheme Assessment Group (PASAG) undertake any negotiation with pharmaceutical companies' around the cost of medicines or patient access schemes that are under review.

ITEM 12.3 PEER APPROVED CLINICAL SYSTEM (PACS) FOR ULTRA-ORPHAN MEDICINES
The Group noted the content of the letter regarding Greater Glasgow and Clyde Health Board's pilot of the Peer Approved Clinical System (PACS) for Ultra-Orphan Medicines that have been reviewed and not recommended for use in NHS Scotland by the SMC. Details of the learning from the pilot have been requested via the Directors of Pharmacy. **CH**

13. AOCB

SMC 1132/16 SACUBITRIL/VALSARTAN (ENTRESTO®) ▼
It was confirmed that a submission for sacubitril/valsartan (Entresto®) ▼ is expected and planned for review at the May meeting.

SMC 114/04 FULVESTRANT (FASLODEX®) ▼
It was confirmed that a submission for fulvestrant has been received.

RECENT SAFETY WARNINGS AND DRUG WITHDRAWALS
The Chairman and Ms Doney highlighted recent safety warnings and drug withdrawals, additional information will be emailed to members. **FD**

THE LATEST (APRIL) DRUG SAFETY UPDATE
The April Drug Safety Update has just been issued and will be forwarded to members for information. **FD**

CORGARD® (NADOLOL) DISCONTINUED
Nadolol has been discontinued for commercial reasons. There is some use locally and patients will have to be reviewed individually. This is being taken forward at General practice level and the information has been highlighted with colleagues in the managed service.

WARNINGS FOR DIABETIC DRUGS
Gliptins - alogliptin and saxagliptin. A U.S. Food and Drug Administration (FDA) safety review has found that type 2 diabetes medicines containing saxagliptin and alogliptin may increase the risk of heart failure, particularly in patients who already have heart or kidney disease. As a result, FDA is adding new warnings to the drug labels about this safety issue.

Canagliflozin - The European Medicines Agency (EMA) has started a review of the diabetes medicine canagliflozin after an increase in amputations, mostly affecting toes, was observed in an ongoing clinical trial [CANVAS]. Cases of lower limb amputation occurred in both the canagliflozin and placebo groups in the trial and the possibility that canagliflozin increases lower limb amputations is currently not confirmed. EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has requested more information from the company to assess whether canagliflozin causes an increase in lower limb amputations and whether any changes are needed in the way this medicine is used in the European Union.
The PRAC will also ask for data on other SGLT2 inhibitors and may decide to extend the scope of the review to cover these medicines.
While the review on canagliflozin is ongoing, healthcare professionals will receive a letter reminding them about the importance of routine foot care to avoid cuts or sores of the feet and to treat them promptly should they occur to prevent infection and ulceration. Patients at increased risk of amputation (such as those who have had a previous amputation) should be carefully monitored. As a precautionary measure, doctors may consider stopping treatment with canagliflozin in patients who develop significant foot complications.
Patients who have any questions should speak to their doctor or pharmacist. It is important that patients with diabetes continue to take their prescribed treatment and do not stop treatment without first consulting a healthcare professional.

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NEW SAFETY MEASURES FOR IDELALISIB (INCLUDED ON FORMULARY FOR CHRONIC LYMPHOCYTIC LEUKAEMIA (CLL) AND FOLLICULAR LYMPHOMA)

All patients treated should receive antibiotics to prevent *Pneumocystis jirovecii* pneumonia. Patients should also be monitored for infection and have regular blood tests for white cell counts because low counts can increase their risk of infection. Idelalisib should not be started in patients with a generalised infection. It should also not be started in previously untreated patients with CLL whose cancer cells have certain genetic mutations (17p deletion or TP53 mutation).

The service is aware and prescribing is in line with the new advice, patients are receiving antibiotic prophylaxis with co-trimoxazole.

DATE OF NEXT MEETING

The date of the next meeting was confirmed as Tuesday 17th May 2016 starting at 14.30 in the Aspen Room Forest Grove House.

CHAIRMAN'S SIGNATURE **DATE** **17th May 2016**