NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 15 January 2019 at 14:30 in the Seminar Room, David Anderson Building

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

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 18 DECEMBER 2018**	
	The Group accepted the draft note of the meeting subject to correction of typographical changes, and minor clarification to one bullet point in item 3.	
	The corrected final approved minute will be in the public domain within 21 days of approval.	**FD**
3.	**PRESENTATION – NONE**	
4.	**MATTERS ARISING**	
	4.1. ACTION LOG	
	4.1.1. SCRIPTSWITCH CAN IT HIGHLIGHT MULTIPLE DAILY DOSING?	
	Ms Davie confirmed that ScriptSwitch messages trigger for multiple daily dosing requests. The Group agreed that messages should be set up for sildenafil multiple daily dose prescriptions.	**AD/FD**
	4.1.2. HYDROCHLOROTHIAZIDE PRESCRIBING FIGURES	
	The Chairman reminded members of the recent Drug Safety Update article (November 2018) advising that hydrochlorothiazide, particularly in long-term use, is linked with an increased risk of non-melanoma skin cancer.	
	The Chairman confirmed that: • hydrochlorothiazide is only available in combination products • local use is not significant but there are people in Grampian receiving hydrochlorothiazide-containing products, and it is possible that they may have been on treatment for a long time	
	Dr Moore highlighted that non-melanoma skin cancer is common but not generally captured in cancer registry statistics.	
	The Group agreed that: • the Drug Safety Update article should be highlighted to prescribers • patients should be reviewed and consideration given to switching to another diuretic • a ScriptSwitch message should be set up to trigger for acute prescription requests for hydrochlorothiazide-containing products	

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	The Chairman agreed to draft information for prescribers to include suggestions for possible alternatives.	**JMcL**
	Ms Doney will provide a list of the current hydrochlorothiazide-containing products and arrange for the prescribing data to be shared with the Lead Pharmacists for the Health and Social Care Partnerships (H&SCPs).	**FD**
	Ms Davie will draft a ScriptSwitch message for acute prescriptions.	**AD**

ITEMS ON THE ACTION LOG NOT INCLUDED ON THE AGENDA

The Chairman reviewed the meeting Action log with the Group to clarify the status of items that were not included on the agenda.

STATINS

This item remains open and information should be submitted for the next meeting. **FD**

CILEST

Ms Doney queried if information regarding the discontinuation of Cilest® had been shared with the three H&SCPs. Information will be shared with the Lead Pharmacists for Aberdeenshire and Moray. **AD**

Item closed.

FEBUXOSTAT

Ms Doney confirmed that febuxostat should have been included on the Action log from the December meeting. There was a request for clarification of the measures the service will take to manage the cardiovascular risk profile of febuxostat. The Summary of Product Characteristics (SmPC) notes that "*Patients undergoing chemotherapy for haematologic malignancies at intermediate to high risk of Tumor Lysis Syndrome treated with ADENURIC should be under cardiac monitoring as clinically appropriate*".

The service confirmed that an individual risk-benefit assessment would be undertaken with review of patient's cardiovascular status prior to prescribing. Only if the benefits outweigh the risks would a patient with ischemic heart disease or congestive heart failure receive febuxostat, and in discussion with the consultant.

Item closed.

5. FORMULARY GROUP DECISIONS DECEMBER 2018 - PUBLISHED 01/01/2019

5.1. FORMULARY GROUP DECISIONS DECEMBER 2018

The Group ratified the decisions of the December 2018 meeting as published.

5.2. DRAFT NETFORMULARY UPDATE FOR NOVEMBER AND DECEMBER 2018 FORMULARY GROUP DECISIONS

Ms Doney confirmed that due to workload issues, the netFormulary update was not available for the meeting but an email update will be issued within seven working days. **FD**

6. NETFORMULARY/FORMULARY REVIEW

6.1. ZOVIRAX® (ACICLOVIR) 3% W/W EYE OINTMENT DISCONTINUED

The Group reviewed the notification from GlaxoSmithKline advising that manufacture of Zovirax® (aciclovir) eye ointment 3% w/w ceased December 2018. The discontinuation is a commercial decision and, subject to demand, stock is anticipated to last until June 2019.

Ms Doney confirmed that aciclovir 3% eye ointment is included in local empirical guidance and advice is awaited from the Antimicrobial Management Team and Ophthalmology.

The Group requested that the Eye Health Network is included in the review. **FD**

6.2. HIV MEDICINES LIST

It was confirmed that the formulary HIV medicines list has been updated and published in line with the decisions of the November formulary Group meeting.

7. OTHER BUSINESS – NONE

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8. NEW PRODUCT REQUESTS

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

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

The Group considered the request for hydrocortisone granules in capsules for opening (Alkindi®).

The Group noted that:
- Alkindi®:
  - is licensed as replacement therapy of adrenal insufficiency in infants, children and adolescents (from birth to <18 years old), it is not licensed for use in adults
  - is available as capsules for opening, the capsule shell should not be swallowed
- the granules are given orally and should not be chewed
- the granules are poured directly onto the child's tongue, into the child's mouth or sprinkled onto a spoonful of soft food
- the granules should not be administered via nasogastric tube as there is a risk of tube blockage
- the cost of the granules is high, and that the cost of 'standard' hydrocortisone tablets has been increasing over the past few years
- the SMC restriction is for use as a first-line treatment of infants and young children with adrenal insufficiency aged from birth to less than six years of age for whom hydrocortisone must otherwise be individually prepared by manipulation such as by compounding (or crushing) or by production of special solutions in order to produce age-appropriate doses, or hydrocortisone given as off-label buccal tablets
- the SMC restriction would limit use to under 6 years of age. Is there an assumption that children would be switched to standard tablets, either at 6 years of age or the age at which the children are able to take the tablets, which may be older than 6 years?
- there is a potential for use outwith the SMC age restriction and off-label, e.g. adults, children and adolescents 6 years and older; adults with swallowing difficulties; unlicensed indications
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of Alkindi®
- the Drug Safety Update article (December 2018) advising that hydrocortisone muco-adhesive buccal tablets should not be used off-label for adrenal insufficiency in children (buccal hydrocortisone tablets provide decreased cortisol release compared with conventional oral tablets)
- the packaging (bottle and outer carton) is marked "do not swallow capsule, risk of choking"

The Group agreed that availability of the hydrocortisone granules would provide a benefit to patients, particularly children (reduced risk of over- or under-dosing), and prescribers/dispensers/parents/carers (no need to crush or compound products). However, the Group has some queries about the safe introduction of the product.

The Group queried:
- how the product was presented in Primary Care Prescribing systems, and if there would be a risk of prescribing error? Recommendations from the specialists may need to be specific to minimise the risk of prescribing error.
- should prescribing by proprietary name be supported?
- when the Paediatric Endocrine Nurse would provide advice on administration. This would need to happen before a request for Primary Care to prescribe Alkindi®. If this does not happen is there a risk of confusion and a patient swallows the capsule?

Ms Davie and Ms Doney will confirm how the product is presented in Primary Care Prescribing systems. **AD/FD**

To facilitate the safe introduction of Alkindi® the Group requested that Dr Sun liaise with paediatric colleagues to clarify what plans the service has regarding:
- education of parents/carers for the correct administration of Alkindi®

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- switching patients. Is there is a plan to switch children under 6 years of age to the granules, and conversely how will older children be changed from the granules to 'standard' tablets? **AS**

The Group supported the restricted local need for hydrocortisone granules in capsules for opening (Alkindi®) for infants and young children with adrenal insufficiency.

SMC 2088 – Hydrocortisone granules in capsules for opening (Alkindi®) is routinely available in line with national guidance (SMC 2088).
Indication under review: replacement therapy of adrenal insufficiency in infants, children and adolescents (from birth to <18 years old).
Restriction: for the first-line treatment of infants and young children with adrenal insufficiency aged from birth to less than six years of age for whom hydrocortisone must otherwise be individually prepared by manipulation such as by compounding (or crushing) or by production of special solutions in order to produce age-appropriate doses, or hydrocortisone given as off-label buccal tablets.
In a single-dose, single-arm, phase III study in children aged <6 years with adrenal insufficiency, Alkindi® significantly increased plasma cortisol levels at 60 minutes compared with baseline.
This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of Alkindi® and is contingent upon the continuing availability of the 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 8d – treatment may be initiated in community on the recommendation of a consultant/specialist. **FTeam**

8.2. FG1SMC 2105 – DINUTUXIMAB BETA (NEUROBLASTOMA)

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

The Group considered the request for dinutuximab beta for the treatment of high-risk neuroblastoma as outlined in SMC 2105.

The Group noted:
- dinutuximab beta:
  - is the only licensed preparation for neuroblastoma
  - is used in combination with isotretinoin, and for relapsed/refractory patients treatment should also include aldesleukin
  - [for these indications] 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
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of dinutuximab beta
- the local estimate of patient numbers is small, but the cost of treatment is high
- the service and aseptic unit have experience in the use of dinutuximab beta

The Group accepted the restricted local need for dinutuximab beta as outlined in SMC 2105, for patients with high-risk neuroblastoma and patients with a history of relapsed or refractory neuroblastoma.

SMC 2105 – Dinutuximab beta (Qarziba®) ▼ is routinely available in line with national guidance (SMC 2105).
Indication under review: for the treatment of high-risk neuroblastoma in patients aged 12 months and above, who have previously received induction chemotherapy and achieved at least a partial response, followed by myeloablative therapy and stem cell transplantation, as well as patients with history of relapsed or refractory neuroblastoma, with or without residual disease. Prior to the treatment of relapsed neuroblastoma, any actively progressing disease should be stabilised by other suitable measures.
In patients with a history of relapsed/refractory disease and in patients who have not achieved a complete response after first line therapy, dinutuximab beta should be

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combined with interleukin-2.
Comparisons with historical controls indicate that dinutuximab beta plus isotretinoin with and without aldesleukin (interleukin-2) improved event-free survival and overall survival in patients undergoing first-line treatment for high-risk neuroblastoma and improved overall survival in patients with relapsed neuroblastoma. In patients with relapsed or refractory neuroblastoma dinutuximab beta in combination with isotretinoin and aldesleukin was associated with tumour responses.
This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of dinutuximab beta 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 8a – licensed for hospital use only. Qarziba® ▼ is restricted to hospital-use only and must be administered under the supervision of a physician experienced in the use of oncological therapies. It must be administered by a healthcare professional prepared to manage severe allergic reactions including anaphylaxis in an environment where full resuscitation services are immediately available. **FTeam**

8.3. FGASMC 2016 – FLUTICASONE PROPIONATE/FORMOTEROL FUMARATE (FLUTIFORM® K-HALER®) (ASTHMA – NEW DEVICE)

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

The Group noted:

- flutiform® k-haler®:
  - is licensed, for use in adults and adolescents 12 years and above, in the regular treatment of asthma where the use of a combination product (an inhaled corticosteroid and a long-acting beta2 agonist) is appropriate:
    - for patients not adequately controlled with inhaled corticosteroids and 'as required' inhaled short-acting beta2 agonist, or
    - for patients already adequately controlled on both an inhaled corticosteroid and a long-acting beta2 agonist
  - provides a fixed-dose of fluticasone propionate and formoterol fumarate in a new breath-actuated device. This combination of inhaled corticosteroid and a long-acting beta2 agonist is already included on the formulary as Flutiform® pressurised metered-dose inhaler (pMDI).
- Flutiform® pMDI is included in the Respiratory Managed Clinical Network (MCN) - Principles of Prescribing in Adult Asthma
- there is a rebate available on the Flutiform® pMDI however Napp has not confirmed that the rebate will also apply to the k-haler® device
- the Respiratory MCN is supportive of inclusion of the new device on the formulary

The Group considered that the k-haler® device had the potential to benefit patients that cannot use a pMDI correctly, and accepted the local need for flutiform® k-haler®.

SMC 2016 - Fluticasone propionate/formoterol fumarate 50microgram/5microgram, 125microgram/5microgram pressurised inhalation, suspension (flutiform® k-haler®) is routinely available in line with local guidance.
Indication under review: for the regular treatment of asthma where the use of a combination product [an inhaled corticosteroid (ICS) and a long-acting beta2-agonist (LABA)] is appropriate:

- **For patients not adequately controlled with ICS as 'as required' inhaled short-acting beta2-agonist or**
- **For patients already adequately controlled on both ICS and a LABA**

flutiform k-haler is a breath-actuated inhaler that is bioequivalent to Flutiform® metered-dose inhaler (pMDI). It was classified 1a - available for general use and 8e - treatment may be initiated in either Primary or Secondary care. **FTeam**

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8.4. SBAR – TOCILIZUMAB (ROACTEMRA®) 162MG SOLUTION FOR INJECTION IN PRE-FILLED SYRINGE

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

The Group considered the licence extension for tocilizumab 162mg pre-filled syringe for the treatment of active systemic juvenile idiopathic arthritis (sJIA).

The Group noted:
- tocilizumab:
  - is available as an intravenous infusion and as 162mg solution for injection in a pre-filled syringe or pre-filled pen
  - (all formulations) are included on the formulary for the treatment of sJIA in children from 2 years of age
- the change in licence extends use to children from 1 year of age and only applies to the 162mg pre-filled syringe preparation
- treatment would be in line with national guidance/the recommendations of the Scottish Paediatric and Adolescent Rheumatology Network (SPARN)

The Group accepted the restricted local need for tocilizumab 162mg pre-filled syringe for the management of sJIA in children from 1 to under 2 years of age.

SBAR – Tocilizumab (RoActemra®) 162mg solution for injection in pre-filled syringe is routinely available in line with national guidance.
Indication under review: treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients 1 to less than 2 years of age, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids. RoActemra® can be given as monotherapy (in case of intolerance to methotrexate (MTX) or where treatment with MTX is inappropriate) or in combination with MTX.
It was classified 1b- available for restricted use under specialist supervision and 8b – recommended for hospital use only. Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment of sJIA. Patients treated with tocilizumab should be given the Patient Alert Card. **FTeam**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE - ISSUED JANUARY 2019

The Group noted the SMC provisional advice issued January 2019.

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

SMC 2128 - RIVAROXABAN 2.5MG FILM-COATED TABLET (XARELTO®)

The Chairman highlighted the positive recommendation for rivaroxaban 2.5mg tablets 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.

It was noted that:
- the SMC advice restricts use to patients with stable coronary artery disease that does not require dual antiplatelet therapy
- 2.5mg is a lower dose than prescribers are currently acquainted with and it is not clear if there would be a risk of misunderstanding and that the lower dose would be used in people with atrial fibrillation and ischaemic heart disease
- the main concern with rivaroxaban is bleeding

The service leads for Cardiology and Vascular will be contacted for comment. **FD**

SMC 2129 - TISAGENLECLEUCEL

Ms Galvin confirmed that a national group, led by Dr Culligan, is looking at the introduction of tisagenlecleucel and treatment is likely to be provided from one centre in Scotland.
Ms Doney will email Dr Culligan for an update. **FD**

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10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS - PUBLISHED JANUARY 2019

The Group noted the SMC advice published January 2019.

Following publication of the not recommended advice statement for arsenic trioxide (Trisenox®) SMC 2025, this medicine will not be included on the Grampian Joint Formulary for the indication in question. **FTeam**

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

- SMC 2102 - Ertugliflozin 5mg, 15mg film-coated tablet (Steglatro®) ▼
- SMC 2116 - Tofacitinib, 5mg film-coated tablet (Xeljanz®) ▼ (submission expected)
- SMC 2120 - Pertuzumab (Perjeta®) (submission expected)
- SMC 2118 - Tiotropium 2.5 microgram (Spiriva® Respimat®)
- SMC 2092 - Semaglutide (Ozempic®) ▼

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

11. GENERAL INFORMATION FROM SMC JANUARY 2019 - NONE

12. DOCUMENTS FOR INFORMATION

Items 12.1, 12.2 (Drug Safety Update December 2018 and January 2019), and 12.3 (Antimicrobial Management Team Meeting September 2018) were noted.

DRUG SAFETY UPDATE (JANUARY 2019)
The Group noted the article regarding tapentadol and the risk of seizures and reports of serotonin syndrome when co-administered with other medicines.

It was reported that tapentadol is accepted for use in NHS Scotland and pain consultants recommend use but it is non-formulary because local clinicians have not requested formulary inclusions. The pain consultants will be contacted to advise that if there is a local need for tapentadol a formulary submission should be completed. **FTeam**

13. AOCB

STRONTIUM RANELATE ARISTO® ▼ 2G GRANULES FOR ORAL SUSPENSION - OSTEOPOROSIS

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

It was confirmed that:

- in 2014 the European Medicines Agency (EMA) issued a safety warning advising that strontium ranelate should only be used by people for whom there are no other treatments for osteoporosis
- in 2017 strontium ranelate (Protelos®) was discontinued for commercial reasons, patients were reviewed and switched to other products, and strontium ranelate was removed from the formulary
- a new strontium product is being marketed, Strontium ranelate Aristo ▼ 2g granules for oral suspension
- the new product costs significantly more than Protelos® [£49.97 versus £27.08 for 28 sachets]
- it is not known if the Marketing Authorisation Holder will submit to the SMC, confirmation is awaited from the SMC

The Group noted that the EMA safety warning will apply, and deemed strontium ranelate Aristo® ▼ 2g granules non-formulary pending advice from the SMC. **FD**

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Strontium ranelate Aristo® ▼ 2g granules for oral suspension is not routinely available in NHS Grampian.
Indication: treatment of severe osteoporosis:

- **in postmenopausal women;**
- **in adult men;**

at high risk of fracture, for whom treatment with other medicinal products approved for the treatment of osteoporosis is not possible due to, for example, contraindications or intolerance. In postmenopausal women, strontium ranelate reduces the risk of vertebral and hip fractures.
The decision to prescribe strontium ranelate should be based on an assessment of the individual patient's overall risks. Treatment should only be initiated by a physician with experience in the treatment of osteoporosis.
Not routinely available in NHS Grampian. **FTeam**

DATE OF NEXT MEETING

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

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