NHS GRAMPIAN
Minute of Formulary Group Meeting held on Tuesday 15th September 2015
in the Aspen Room, Forest Grove House

PRESENT	**APOLOGIES**	**APPROVED**
Ms A Davie	Dr D Counter	
Ms F Doney	Dr D Culligan	
Mr A Duncan	Mrs L Harper	
Dr C Hind	Dr W Moore	
Dr A MacDonald	Mr C Rore	
Professor J McLay (Chairman)	Mr R Sivewright	
Mrs L Montgomery		
Mr M Paterson		

ITEM	**SUBJECT**	**ACTION**
	The Chairman opened the meeting and welcomed members to the September Formulary Group Meeting.	
1.	**APOLOGIES**	
	Apologies for absence were requested and noted.	
2.	**DRAFT MINUTE OF THE MEETING HELD ON THE 18TH AUGUST 2015**	
	The Group accepted the draft note of the meeting held on the 18th August 2015 as an accurate record of the meeting subject to minor typographical changes.	**FD**
	The final approved minute will be published within 21 days.	**FTeam**
3.	**PRESENTATION - NONE**	
4.	**MATTERS ARISING**	
	4.1. MEDICINES RELATED TO VALPROATE - UPDATE	
	The Group noted the letter dated October 2014 that was sent to the Medicines and Healthcare Products Regulatory Agency (MHRA) from the British Paediatric Epilepsy Group (a special interest group of the British Paediatric Neurology Association), and that an official response is awaited. It was confirmed that after the August meeting the MHRA advice was highlighted with the Mental Health Service and sent to the Chairman of the Grampian Medicines Management Group (GMMG) for action and noting.	
	The Chairman will send a letter to colleagues in NHS Grampian highlighting the strengthening of the MHRA advice and the need to tighten current processes, including providing patient information leaflets and the recording of advice given to females of childbearing age.	**JMcL**
	4.2. INTEGRATED JOINT BOARD REPRESENTATION ON FORMULARY GROUP – UPDATE	
	The Chairman reported that General Practitioner/Integrated Joint Board representation for the Group is being progressed by the Grampian Medicines Management Group (GMMG).	
5.	**FORMULARY GROUP DECISIONS AUGUST 2015 – PUBLISHED 31/08/2015**	
	The Group ratified the advice as published.	
6.	**CMO(2012)1 REPORTING FOR SCOTTISH MEDICINES CONSORTIUM (SMC) ADVICE 2015/16 – AT 31/08/2015**	
	It was confirmed that for the SMC accepted medicines published April to August 2015 the Formulary Group audit standard for CMO(2012)1 reporting was achieved for the following criteria: ▪ Local decision on SMC accepted medicine published within 90 days: 36 of 36 - 100% ▪ FG decision published within 14 days of the decision being reached: 36 of 36 - 100%	

7. OTHER BUSINESS

7.1. NICE MULTIPLE TECHNOLOGY APPRAISALS – NONE

7.2. AREA DRUG AND THERAPEUTICS COMMITTEE (ADTC) COLLABORATIVE – UPDATE

The Group noted the content of the ADTC Collaborative flash report (July 2015).

It was confirmed that:
- review of the categorisations of Health Board formulary decisions is underway
- Ms Doney will participate in the ADTC public and patient involvement interviews
- Dr Hind and Ms Doney will attend the National ADTC event on the 17th November

SCOTTISH PALLIATIVE CARE GUIDELINES SBAR

The Group considered the content of the Scottish Palliative Care Guidelines SBAR dated 2nd July 2015 outlining a framework for the proposed governance arrangements and update of the Scottish Palliative Care Guidelines.

The Group noted that, based on the information in the SBAR, "ADTCs are asked to:
- note the progress with this initiative
- note the proposed multidisciplinary governance arrangements
- note the proposed process for communication of updates described within the governance arrangements
- advise Healthcare Improvement Scotland ADTC Collaborative if support the proposed approach"

The Group felt that the SBAR did not provided enough detail to allow constructive comment. It is not clear if the Healthcare Improvement Scotland review will take account of clinical- and cost-effectiveness, and how the review will link with any new evidence or advice, e.g. SMC advice, and how Boards should approach the introduction of new medicines licensed for use in palliative care.
The Group noted the proposed points for communication of updates, and requested clarity in the form of a communication plan that would include the information distribution arrangements, where/if a 'catalogue' of updates would be housed, and how urgent issues would be highlighted to Boards, would the communication include suggestions for alternate formulary options for items in short supply?

The comments will be sent to the Chairman of the GMMG. **FD**

8. NEW PRODUCT REQUESTS

8.1. FG1 SMC 1012/14 – CETUXIMAB - *RAS* WILD-TYPE METASTATIC COLORECTAL CANCER

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

The Group considered the submission from the oncology department for cetuximab for patients with *RAS* wild-type metastatic colorectal cancer (mCRC). It noted that the submission requested first-line use in combination with chemotherapy as per SMC 1012/14 and third-line use as a single agent if a patient has not received first-line cetuximab. It was confirmed that single agent use is a licensed indication [as a single agent in patients who have failed oxaliplatin- and irinotecan-based therapy and who are intolerant to irinotecan] but the Group was unable to consider third-line use because no clinical evidence was submitted to support the request.

The Group noted that:
- the indication for cetuximab was refined from *KRAS* wild-type mCRC to *RAS* wild-type mCRC - patients must demonstrate both wild-type *KRAS* and wild-type *NRAS* to be eligible for treatment. Evidence of wild-type *RAS* (*KRAS* and *NRAS*) status is required before initiating treatment.
- cetuximab:
  - is a chimeric monoclonal IgG1 antibody that binds to the epidermal growth factor receptor
  - meets SMC end of life criteria for this indication [first-line in combination with chemotherapy] and was accepted for use within NHS Scotland in the context of SMC

decision modifiers and the output of the Patient and Clinician Engagement meeting
  - will become the first-line choice for wild-type mCRC replacing XELOX (oxaliplatin and capecitabine)
  - is given as an infusion, licensed for administration once a week (initial dose 400mg/m^2 then subsequent doses 250mg/m^2 body surface area). Although in clinical studies doses up to 700mg/m^2 given every 2 weeks have been used, and the safety profile was consistent with the weekly dosing schedule.
  - severe infusion-related reactions, including anaphylactic reactions, may occur and close monitoring is required during the infusion and for at least one hour after the end of the infusion
- patients must receive premedication with an antihistamine and a corticosteroid at least 1 hour before administration of cetuximab, and the concomitantly used chemotherapy must not be administered earlier than 1 hour after the end of the cetuximab infusion
- treatment is continued until progression of the underlying disease
- the SMC advice takes account of the benefits of a Patient Access Scheme that improves the cost-effectiveness of cetuximab
- XELOX is administered as a day case, cetuximab plus chemotherapy moves treatment to an in-patient setting and significantly increases the patient's length of stay
- cetuximab plus FOLFOX would require a minimum of 3 medicines to be prepared aseptically per patient; cetuximab plus FOLFIRI would require 5 medicines to be prepared aseptically per patient
- the introduction of cetuximab plus chemotherapy will have significant implications for service delivery and the aseptic preparation unit (capacity)

The Group considered that the introduction of cetuximab plus chemotherapy for mCRC would have significant service implications for the oncology department/team and the pharmacy aseptic unit. From the submission, it was not clear, if the operational issues have been fully discussed and if the effect that the introduction of cetuximab will have on the other service areas have been fully considered and addressed.

The Group accepted the restricted local need for cetuximab as outlined in SMC 1012/14 but due to the significant service implications the case will be referred to Acute Sector Management. To allow the introduction of cetuximab plus chemotherapy the Group requested an implementation plan that addresses the operational issues and impact on other service areas. **FD** **FD**

The Group noted the anticipated budget impact and will highlight this to the GMMG and Finance as the impact is outwith the financial resource available to the Formulary Group. **FD**

SMC 1012/14 - Cetuximab 100mg/20mL and 500mg/100mL solution for infusion (Erbitux®) is included on the Grampian Joint Formulary for the indication in question; restricted use.
Indication under review: Treatment of patients with epidermal growth factor receptor (EGFR)-expressing, *RAS* wild-type metastatic colorectal cancer:
- **in combination with irinotecan-based chemotherapy**
- **in first-line in combination with FOLFOX**

Restriction: for use in patients with *RAS* wild-type metastatic colorectal cancer, in combination with irinotecan or oxaliplatin-based chemotherapy, in patients who have not previously received chemotherapy for their metastatic disease (first-line treatment).
Efficacy data for the *RAS* wild-type population come from post hoc subgroup analyses of two studies that compared cetuximab plus chemotherapy with chemotherapy alone. In the *RAS* wild-type population, response rates (complete and partial responses) were significantly higher in both studies and overall survival was significantly longer in one study for cetuximab plus chemotherapy than chemotherapy alone.
This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of cetuximab 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. Cetuximab must be administered under the supervision of a physician experienced in the use of

antineoplastic medicinal products. Close monitoring is required during the infusion and for at least one hour after the end of the infusion. Availability of resuscitation equipment must be ensured. **FTeam**

8.2. FG1 SMC 1027/15 – NINTEDANIB ▼ - NON-SMALL CELL LUNG CANCER

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

The Group considered the submission from the Oncology department for nintedanib in combination with docetaxel for the treatment of adult patients with locally advanced, metastatic or locally recurrent non-small cell lung cancer (NSCLC) of adenocarcinoma tumour histology after first-line chemotherapy.

The Group noted that:

- nintedanib ▼
  - meets SMC orphan equivalent and end of life criteria in this treatment setting
  - was accepted for use within NHS Scotland in the context of SMC decision modifiers and the output of the Patient and Clinician Engagement meeting
  - is an oral medication taken twice daily on days 2 to 21 of a standard 21 day docetaxel treatment cycle, i.e. it must not be taken on the day of docetaxel chemotherapy administration
- the poor prognosis for NSCLC patients relapsing after first-line chemotherapy
- the lack of second-line treatments for unselected adenocarcinoma patients
- nintedanib in combination with docetaxel offers a median overall survival improvement of 2.3 months (10.3 versus 12.6 months)
- treatment should be limited to very fit patients (Eastern Cooperative Oncology Group performance status of 0 or 1) as per the eligibility criteria within the LUME-Lung 1 study
- the SMC advice takes account of the benefits of a Patient Access Scheme that improves the cost-effectiveness of nintedanib

The Group accepted the restricted local need for nintedanib (Vargatef®) ▼ in combination with docetaxel for the treatment of adult patients with locally advanced, metastatic or locally recurrent non-small cell lung cancer (NSCLC) of adenocarcinoma tumour histology after first-line chemotherapy as outlined in SMC 1027/15.

SMC 1027/15 - Nintedanib 100mg and 150mg soft capsules (Vargatef®) ▼ is included on the Grampian Joint Formulary for the indication in question, restricted use. Indication under review: in combination with docetaxel for the treatment of adult patients with locally advanced, metastatic or locally recurrent non-small cell lung cancer (NSCLC) of adenocarcinoma tumour histology after first-line chemotherapy. Addition of nintedanib to second-line treatment of stage IIIb/IV NSCLC with docetaxel significantly increased overall survival in the subgroup patients with adenocarcinoma tumour histology. This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost effectiveness of nintedanib 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. Treatment should be initiated and supervised by a physician experienced in the use of anticancer therapies. **FTeam**

The Group agreed an estimate of £50,000 to allow the introduction of nintedanib capsules as Vargatef® ▼ for NSCLC as per SMC 1027/15, and this will be highlighted with finance. **RS**

8.3. FGA SMC 1084/15 – HARVONI® ▼ - CHRONIC HEPATITIS C (GENOTYPE 3)

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

The Group considered the abbreviated submission from the Hepatology department requesting the use of Harvoni® ▼ for the treatment of genotype 3 chronic hepatitis C (CHC) in adults as licensed – patients with cirrhosis and/or prior treatment failure and accepted by SMC.

The Group noted that:

- the service has experience of the use of Harvoni® ▼ for the treatment of CHC

- the service will follow the National Clinical Guidelines for the Treatment of HVC in Adults
- the treatment of chronic hepatic C virus is a rapidly changing field and guidelines will be changing as more evidence becomes available
- the most cost-effective regimen amongst the recommended options should be chosen to maximise the number of patients who can be treated

The Group accepted the restricted local need for Harvoni® ▼ for the treatment of genotype 3 chronic hepatitis C as licensed and outlined in SMC 1084/15, noting that prescribing should be in line with the National Clinical Guidelines and the most cost-effective regimen amongst the recommended options should be chosen to maximise the number of patients who can be treated.

SMC 1084/15 - Ledipasvir/sofosbuvir (Harvoni®) ▼ is included on the Grampian Joint Formulary for the indication in question, restricted use.
Indication under review: Treatment of genotype 3 chronic hepatitis C (CHC) in adults.
Restriction: patients who are ineligible for or unable to tolerate interferon.
Efficacy data are limited to a phase II open-label study. The addition of ledipasvir to sofosbuvir plus ribavirin is expected to increase antiviral activity, although the magnitude of this effect is not well characterised. It was classified 1b - available for restricted use under specialist supervision and 8b - treatment recommended for hospital use only. Treatment should be initiated and monitored by a physician experienced in the management of patients with CHC. **FTeam**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE – ISSUED SEPTEMBER 2015

The Group noted the SMC provisional advice issued September 2015.

If published next month the negative SMC recommendations, for everolimus (Afinitor®) SMC 872/13 and budesonide (Cortiment®) SMC 1093/15 will not be included on the Grampian Joint Formulary for the indications in question. **FTeam**

10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS - PUBLISHED SEPTEMBER 2015

The Group noted the SMC advice published September 2015.

Following publication of the negative SMC recommendations for elosulfase alfa (Vimizim®) ▼ SMC 1072/15 and avanafil (Spedra®) ▼ SMC 980/14, and the non-submission statements for ketoconazole (Ketoconazole HRA®) ▼ SMC 1100/15 and tigecycline (Tygacil®) SMC 1101/15, they will not be included on the Grampian Joint Formulary for the indications in question. **FTeam**

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

- SMC 1048/15 pasireotide (as pamoate) (Signifor®) ▼
- SMC 1063/15 bevacizumab (Avastin®)
- SMC 1074/15 aflibercept (Eylea®) ▼
- SMC 1075/15 bortezomib (Velcade®)
- SMC 1079/15 lisdexamfetamine dimesylate (Elvanse® Adult®)
- SMC 1083/15 sitagliptin (Januvia®)
- SMC 1085/15 tafluprost 15 micrograms/mL and timolol 5mg/mL preservative-free eye drops (Taptiqom®)

Local advice for these medicines and indications will be included in the September 2015 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**

SMC 1078/15 - INSULIN GLARGINE 300 UNITS/ML SOLUTION FOR INJECTION IN A PRE-FILLED PEN (TOUJEO®)

The Group noted that:

- insulin glargine 300 units/mL is new high strength insulin product that is not bioequivalent and not interchangeable with any other basal insulin including insulin glargine 100 units/mL, without individualised dose adjustment

- a biosimilar insulin glargine 100 units/mL is licensed and marketed in the UK, and as of May 2015, biosimilar medicines are considered 'out of remit' for SMC
- to allow the safe introduction of insulin glargine 300 units/mL, risk minimisation strategies will be required to minimise the possibility of medication errors such as the wrong insulin dose being administered

Due to the potential for medication error, such as the wrong insulin dose being administered, the Group did not support inclusion on the formulary without clear risk minimisation strategies.

SMC 1078/15 - Insulin glargine 300 units/mL solution for injection in a pre-filled pen (Toujeo®) is not included on the Grampian Joint Formulary – because risk minimisation strategies are required to allow safe introduction.
Indication under review: Treatment of type 1 or type 2 diabetes mellitus in adults aged 18 years and above
Restriction: Its use should be targeted on patients with Type I diabetes who are at risk of or experience unacceptable frequency and/or severity of nocturnal hypoglycaemia on attempting to achieve better hypoglycaemic control during treatment with established insulins. It is also acceptable as a once daily insulin therapy for patients who require carer administration of their insulin. In patients with type 2 diabetes it should be restricted to those who suffer from recurrent episodes of hypoglycaemia or require assistance with their insulin injections.
Insulin glargine 300 units/mL (Toujeo®) has similar efficacy but is not bioequivalent to insulin glargine 100 units/mL and therefore not interchangeable without dose adjustment. At doses that provide comparable glycaemic control, Toujeo® is available at a similar cost to insulin glargine 100 units/mL. It was classified 4 - Not approved for use in NHS Grampian. Not included on the Grampian Joint Formulary – because risk minimisation strategies are required to allow safe introduction. **FTeam**

11. GENERAL INFORMATION FROM SMC SEPTEMBER 2015 – NIL OF NOTE

12. DOCUMENTS FOR INFORMATION

Items 11.1 (Drug Safety Update August 2015), 11.2 (Methadone Flash Report), 11.3 (GMMG minute July 2015) and 11.4 (IMPACT) were noted.

13. AOCB

DECLARATIONS OF INTEREST

The Chairman confirmed that the Health Board has received requests under the Freedom of Information Scotland Act (2004) for details of individual's conflicts of interest. The requests were not in relation to Group members, but members were reminded that conflicts of interest related to agenda items should be made on the day, and members were informed that a refresh of current processes is underway.

DATE OF NEXT MEETING

The date of the next meeting was confirmed as Tuesday 20th October 2015 starting at 14.30 in the Aspen Room Forest Grove House.

CHAIRMAN'S SIGNATURE  **DATE** **20th October 2015**