NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 17 December 2019 at 14:30 in the Seminar Room, David Anderson Building

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

IN ATTENDANCE
Ms Rachel Lahat, First Year Medical Student, observer.
Dr Prakash Abraham, Consultant Endocrinology and Diabetes, Clinical Lead Endocrinology, for item 8.1.
Ms Caitlin Wilkinson, Formulary Team administrator.

Note some items were taken outwith the agenda running order.

ITEM	SUBJECT	ACTION
	The Chairman welcomed members, opened the meeting and noted that a quorum was present. The Chairman reminded members that to assist preparation of the meeting note and ensure decisions are accurately recorded the meeting would be recorded digitally. As soon as the minute is "approved" the relevant MP3 file will be deleted. Members consented to recording the meeting.	
1.	**APOLOGIES** Apologies for absence were requested and noted.	
2.	**DRAFT MINUTE OF THE MEETING HELD 19 NOVEMBER 2019** The Chairman apologised that the draft minute of the November meeting was not available for the meeting. The draft minute will be submitted at the January meeting.	**FD**
4.	**MATTERS ARISING**	
4.1.	**ACTION LOG** Ms Doney apologised for the action log not being available for the meeting.	**FD**
4.2.	**HEALTH AND SPORT COMMITTEE** The Chairman highlighted the submission from NHS Grampian Area Drug and Therapeutics Committee (GADTC) to the Health and Sports Committee inquiry to consider the supply and demand for medicines in Scotland. Ms Doney confirmed that the submission was discussed at the Grampian Area Drug and Therapeutics Committee (GADTC) meeting held in November. The Group was unclear of the objectives of the Health and Sport Committee's inquiry, and members requested clarification of the local consultation process to ensure interested parties are involved in responses. The Chairman will take forward the queries with the Chair of the GADTC.	**JMcL/FD**

ITEM	SUBJECT	ACTION

3. PRESENTATION - CINACALCET IN PRIMARY HYPERPARATHYROIDISM

The Chairman welcomed Dr Prakash Abraham, Consultant Endocrinologist, to the meeting to discuss the potential formulary inclusion of cinacalcet for the reduction of hypercalcaemia in adult patients with primary hyperparathyroidism (HPT).

Dr Abraham reported that:

- cinacalcet:
  - is a calcimimetic that increases sensitivity of the calcium sensing receptor on the parathyroid gland
  - is administered orally, and the recommended starting dose is 30mg twice daily, titrated through sequential doses every two to four weeks to a maximum dose of 90mg four times daily
  - was licensed in 2008, and a NICE guideline (covering diagnosis, assessment and management of primary hyperparathyroidism) was released in May 2019
  - has been used in NHS Grampian on an individual patient request basis
  - the preferred route of prescribing would be Primary Care based on the advice of Endocrinology
  - monitoring [of cinacalcet in primary HPT] is not onerous
- patients with untreated hypercalcaemia are at a higher risk of hypercalcaemic crisis, and hypercalcaemic crisis requires urgent hospital admission

In response to questions Dr Abraham confirmed that:

- there is some long-term data for the use of cinacalcet
- parathyroid hormone (PTH) levels can be requested in Primary Care, however the request must be discussed with Endocrinology and the sample must arrive the same day
- the request is only for proven primary HPT, hypercalcaemia from other causes must be excluded, i.e. exclude malignancy
- the request for cinacalcet is not for use in the emergency setting
- surgery remains the first-choice for patients and previously the pathway was managed by surgeons [it is now managed by Endocrinology]
- currently, for patients unsuitable for surgery, discharge letters advise that clinicians should contact Endocrinology for advice/to discuss medical management if a calcium level is 3.1mmol/litre or above
- there is no reason to expect that the treatment effect of cinacalcet will wain with time
- cinacalcet would be considered for patients who have had unsuccessful surgery for primary HPT

The Chairman thanked Dr Abraham for attending the meeting, and Dr Abraham left the meeting before decision-making.

8.1 FG1 400/17(2) - CINACALCET (REDUCTION OF HYPERCALCAEMIA IN ADULT PATIENTS WITH PRIMARY HYPERPARATHYROIDISM)

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

The Group noted that:

- in 2008, cinacalcet was not recommended by the Scottish Medicines Consortium (SMC) [for this indication] on the grounds of non-submission
- the NICE Clinical Guideline (CG) documents have no standing/statutory authority in NHS Scotland. Additionally, the CG does not provide a full technology appraisal, and the clinical evidence summary [page 8] for cinacalcet showed that the quality of evidence is rated as low or very low.
- there is a local process for clinicians to request cinacalcet for individual patients, however it can be challenging to arrange IPTRs

- it is not clear if the request is being made for patients that have a calcium level of ≥ 3.1mmol/L or for patients that fulfil the NICE CG criteria
- [for this indication] there are no other pharmacological options licensed for managing primary HPT and this would be a 'last-line' treatment option
- [for this indication] there are no economic evidence and only low quality clinical review evidence
- cinacalcet is an expensive treatment option and the cost-effectiveness [of cinacalcet for this indication] is highly uncertain
- cinacalcet:
  - has a recognised mechanism of action and evidence of benefit will be shown by the calcium level dropping to an acceptable level
  - is not a first-line choice, it is a symptomatic treatment option unlike surgery which provides the opportunity for cure
  - could be of benefit to a restricted group of patients with primary HPT
  - is also licensed (and included on the formulary) for the treatment of secondary hyperparathyroidism in adults with end-stage renal disease (ESRD) on maintenance dialysis therapy. The dose recommendations for ESRD are different to use in primary HPT.
- a PTH level is very difficult to arrange in General Practice
- the patent is due to expire in 2020 and at least one generic preparation is in the process of licensing. However, a significant drop in drug cost cannot be assumed, generics may be priced very similarly to the reference product.
- the cost of pharmacological management will depend on the dose required to return the calcium level to an acceptable level; annual costs range from ~£3,300 to over £18,000 (ex VAT)

The Group accepted that:

- the Formulary Group is the correct forum for discussion of the potential for a group of patients to access a non-SMC accepted medicine
- cinacalcet is licensed for "*the reduction of hypercalcaemia in adult patients with primary HPT for whom parathyroidectomy would be indicated on the basis of serum calcium levels (as defined by relevant treatment guidelines), but in whom parathyroidectomy is not clinically appropriate or is contraindicated*." Patients that refuse surgery are outwith the licensed indication, as are patients that have failed surgery.
- management of patients unfit for surgery can be difficult. The patients may not be fit for aggressive treatment, are generally the frail elderly and potentially less able to look after themselves.
- patients unfit for surgery would not include patients that refused surgery
- the symptoms of hypercalcaemia are insidious and if effective in reducing calcium levels cinacalcet may provide the opportunity to prevent hospital admission
- there is a lack of high quality studies/evidence, and for this indication the Marketing Authorisation Holder (MAH) did not submit to the SMC
- there is a lack of economic evidence, and NICE conducted a simple estimate of cost-effectiveness. The NICE estimate, even at low dose, was above generally accepted cost-effectiveness thresholds. However, it was unclear if the data was limited to a sub-cohort of patients with high calcium levels **and** unsuitable for surgery.
- there are no other licensed treatments available and there may be a potential for the prevention of harm in a group of individuals who are unfit for surgery and have a creeping increasing calcium level

The Group was minded to consider cinacalcet for inclusion on the formulary, only for patients with proven primary HPT in whom parathyroidectomy is not clinically appropriate or is contraindicated, and for patients who have had unsuccessful surgery for primary HPT.

ITEM	SUBJECT	ACTION

The Group felt it was reasonable to suppose that cost-effectiveness would improve if treatment avoided hospital admission. However at this time, the Group did not feel there was sufficient information to make a decision and requested that the service:

- more clearly defines the indication/patient group cinacalcet has the potential to benefit (including any restrictions, level of hypercalcaemia to consider starting/stopping treatment, if treatment would be restricted to initiation only on the advice of certain specialists, e.g. only on the advice of Endocrinology)
- confirms the number of IPTRs [for cinacalcet], and provide a summary of the IPTRs including their outcomes. Did every patient's calcium level reduce to acceptable levels, and what was the maintenance dose required? **Endo**

The Group unanimously agreed to bring this item to a future meeting for further discussion. **FTeam**

Ms Doney will review PRISMs data. **FD**

5. FORMULARY GROUP DECISIONS NOVEMBER 2019 – PUBLISHED – 03/12/2019

5.1. FORMULARY GROUP DECISIONS NOVEMBER 2019

Members ratified the decisions of the November 2019 meeting as published. **FTeam**

6. NETFORMULARY/FORMULARY REVIEW

6.1. MHRA: MEDICINES RECALL – EMERADE®

The Chairman informed the Group that Emerade®, an injectable adrenaline, has been recalled due to an issue with the injector device. Dr Richard Herriot, Consultant Immunologist will attend a future meeting to discuss the use of adrenaline auto-injectors and national shortages.

6.2. TERIPARATIDE BIOSIMILAR: TERROSA®▼

The Chairman highlighted the information regarding the introduction of biosimilar teriparatide injection.

Ms Doney confirmed that:

- the local position with regard to biosimilar medicines is that - *As the efficacy and safety of biosimilar medicines is established through the medicines' regulatory processes, biosimilar medicines should be available for prescribing within NHS Grampian without the need for individual formulary submissions if the original reference product is already on formulary. This position is subject to compliance with the relevant monitoring and governance requirements of a biosimilar medicines prescribing framework*.
- there is local agreement to adopt Terrosa®▼ as the preferred biosimilar teriparatide injection
- treatment will be available via a homecare arrangement, and there are currently no prescriptions being issued in Primary Care
- the maximum total duration of treatment with teriparatide is 24 months. New patients will be initiated on Terrosa®▼ with Forsteo® remaining on formulary for patients already established on treatment.

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

The Group supported the restricted local need for biosimilar teriparatide 20micrograms/80microliters solution as a treatment option within treatment pathways for appropriate patients as identified by treating clinicians and subject to compliance with a biosimilar medicines prescribing framework.

Ms Davie will arrange update of the ScriptSwitch profile to note that teriparatide (all

ITEM	SUBJECT	ACTION

preparations) is not prescribed in Primary Care. **AD**

The Group accepted the restricted local need for Terrosa®▼, in line with the current formulary positioning, without the need for a full submission.

Terrosa®▼ 20micrograms/80microliters solution for injection (teriparatide) is routinely available in line with local guidance.
Indications: as licensed in adults.
Restriction: in line with SMC and HealthCare Improvement Scotland advice for the reference product [Forsteo®].
It was classified 1b- available for restricted use under specialist supervision and 8b – recommended for hospital use only.
Patients should receive supplemental calcium and vitamin D supplements if dietary intake is inadequate.
The maximum total duration of treatment with teriparatide should be 24 months.
The 24-month course of teriparatide should not be repeated over a patient's lifetime. **FTeam**

Biological medicines, including biosimlar medicines, should be prescribed by both generic and brand name and the trade name and batch number should be recorded on the patient's prescription, case record or other appropriate clinical system.

6.3. DRY EYE GUIDANCE – UPDATE

Ms Doney informed the Group that the price for Clinitas® (0.4% hyaluronate) eye drops has reduced significantly since 2018 and there is some discussion regarding including this preparation in the current dry eye guidance. The update was not available for the meeting and will be brought to a future meeting. **FTeam**

6.4. OCCUPATIONAL HEALTH SERVICE – CHOICE FOR EMOLLIENT/SOAP SUBSTITUTE HAND WASH

The Chairman informed the Group that Occupational Health (OH) are now recommending QV Wash as a soap substitute for staff. QV Wash does not include an anti-bacterial agent and it foams on use, which is more cosmetically acceptable to users.

7. OTHER BUSINESS

7.1. *N*-NITROSODIMETHYLAMINE

The Chairman highlighted updated information from the European Medicines Agency (EMA) regarding nitrosamine impurities in medicines.

The latest update notes that the EMA is aware that trace amounts of *N*-nitrosodimethylamine (NDMA) have been found in a small number of metformin diabetes medicines outside the European Union (EU).
The levels of NDMA in the affected non-EU metformin medicines are very low and appear to be within or even below the range that people can be exposed to from other sources, including certain foods and water.
At this point, there are no data indicating that EU metformin medicines are affected.
Authorities in the EU are in the process of working with companies to test EU medicines and will provide further updates as more information becomes available.

7.2. ACICLOVIR 3% EYE OINTMENT

Ms Doney reminded the Group that GlaxoSmithKline (GSK) discontinued Zovirax® (aciclovir) 3% Eye Ointment in 2018, with stocks running out mid-2019. A new licensed product has come to market, priced at £45.00/4.5g, which is more than four times the previous cost of Zovirax® 3% Eye Ointment.
Information will be considered at a future meeting. **FTeam**

ITEM	SUBJECT	ACTION

7.3. DISCONTINUATION OF XIAPEX®

Ms Doney informed the Group that the MAH of Xiapex® [collagenase clostridium histolyticum] is in the process of withdrawing the EU Marketing Authorisation. The withdrawal will be effective from 1 March 2020.

Xiapex® injection is licensed for the treatment of Depuytren's contracture and Peyronie's disease, but is only included on the formulary for Depuytren's contracture. The formulary will be updated to reflect the withdrawal. **FTeam**

8. NEW PRODUCT REQUESTS

8.1. FG1 400/17(2) - CINACALCET (REDUCTION OF HYPERCALCAEMIA IN ADULT PATIENTS WITH PRIMARY HYPERPARATHYROIDISM)

This submission was discussed under item 3.

8.2. FG1 405/17 MONOFER® (PRE-OPERATIVE ANAEMIA IN ADULTS)

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

The Group considered the request for Monofer® for the treatment of pre-operative anaemia in adults.

It was confirmed that:

- Monofer®:
  - was removed from the formulary several years ago. At that time Monofer® was contraindicated in atopic patients [now a caution], and the Maternity unit had witnessed adverse reactions to Monofer® in different patients.
  - allows a higher dose of iron to be given in a single infusion (dose not limited to 1g per infusion)
- the current submission is for the management of anaemia identified in the pre-operative setting

The Group requested clarity of the processes to ensure treatment could not be given to patients without evidence of iron deficiency anaemia. **FTeam**

The Group unanimously agreed to approach the Haematologists for advice. **FTeam**

Medicines Information will update the previous Monofer® review. **MI/CR**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE – ISSUED DECEMBER 2019

The Group noted the SMC provisional advice issued December 2019.

10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS – PUBLISHED DECEMBER 2019

The Group noted the SMC advice published December 2019.

Following publication of the negative SMC recommendation for trabectedin (Yondelis®) SMC 2210, and the non-submission statements, for atezolizumab (Tecentriq®)▼ SMC 2254, prasterone (Intrarosa®)▼ SMC 2255 and ceftolozane/tazobactam (Zerbaxa®)▼ SMC 2256, these medicines will not be included on the Grampian Joint Formulary for the indications in question. **FTeam**

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

- SMC 2206 lanadelumab (Takhzyro®)▼ (submission received)
- SMC 2209 olaparib (Lynparza®) (submission expected)
- SMC 2213 ruxolitinib (Jakavi®) (submission received)
- SMC 2227 lusumtrombopag (Mulpleo®)▼

ITEM	SUBJECT	ACTION

Local advice for these medicines and indications will be included in the December 2019 decisions as 'Not routinely available as local implementation plans are being developed or the ADTC is waiting for further advice from local clinical experts.' **FTeam**

FG1SMC 2204 - ZANAMIVIR (INFLUENZA A OR B VIRUS INFECTION IN ADULT AND PAEDIATRIC PATIENTS

Dr Fitton and Mr Rore declared personal, specific interests in GSK and took no part in decision-making.

It was reported that the adult and paediatric services have confirmed that there is a local need for zanamivir infusion. Previously unlicensed zanamivir [infusion] had been accessed via compassionate use programmes.

The Group accepted the restricted local need for zanamivir infusion, as outlined in SMC 2204, without the need for a full submission.

SMC 2204 - Zanamivir 10mg/mL solution for infusion (Dectova®)▼ is routinely available in line with national guidance (SMC 2204).
Indication under review: for the treatment of complicated and potentially life-threatening influenza A or B virus infection in adult and paediatric patients (aged ≥ 6 months) when:

- **the patient's influenza virus is known or suspected to be resistant to anti-influenza medicinal products other than zanamivir, and/or**
- **other antiviral medicinal products for treatment of influenza, including inhaled zanamivir, are not suitable for the individual patient.**

It was classified 1b – available for restricted use under specialist supervision and 8b – recommended for hospital use only.
Dectova® should be used in accordance with official guidance.
Treatment with Dectova® should commence as soon as possible and usually within 6 days of the onset of symptoms of influenza. **FTeam**

11. GENERAL INFORMATION FROM SCOTTISH MEDICINES CONSORTIUM – DECEMBER 2019

CLADRIBINE 10MG TABLET (MAVENCLAD®)

Ms Doney confirmed that in February 2018, the MHRA issued a statement on the use of gadolinium-containing contrast agents and as a result, the sub-groups within the SMC advice for cladribine [SMC 1300/18] have been redefined. The clinicians are aware of the change and the formulary entry updated to reflect this change.

Cladribine 10mg tablet (Mavenclad®) is routinely available in line with local guidance.
Indication under review: treatment of adult patients with highly active relapsing multiple sclerosis (MS) as defined by clinical or imaging features.
Restriction:

- **patients with rapidly evolving severe relapsing-remitting MS: patients with two or more relapses in the prior year whether on treatment or not, and at least one T1 gadolinium-enhancing lesion at baseline MRI or a significant increase in T2 lesion load compared with a previous MRI**
- **patients with sub-optimal therapy relapsing-remitting MS: patients with one or more relapses in the previous year while on disease modifying therapy, and MRI evidence of disease activity**

It was classified 1b – available for restricted use under specialist supervision and 8b – recommended for hospital use only.
Treatment must be initiated and supervised by a physician experienced in the treatment of MS. **FTeam**

ITEM	SUBJECT	ACTION

12. DOCUMENTS FOR INFORMATION

Items 12.1 (Drug Safety Update November 2019), 12.2 (MGPG minute July 2019) and 12.3 (GPCPG minute September 2019) were noted.

13. AOCB - NONE

CHAIRMAN'S SIGNATURE **DATE** **21 JANUARY 2020**