NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 16 March 2021 at 14:30 via Microsoft Teams

PRESENT	APOLOGIES	APPROVED
Ms A Davie	Ms M Galvin	
Ms F Doney	Dr M Metcalfe	
Dr L Elliot	Dr Angela Sun	
Dr J Fitton		
Professor J McLay (Chairman)		
Mrs L Montgomery		
Mrs K Neave		
Mr M Paterson		
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 16 FEBRUARY 2021**	
	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
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.	FTEAM
4.2.	**PRIADEL® 200MG AND 400MG TABLET FINANCIAL IMPACT**	
	The Group noted the content of the SBAR estimating the financial impact created by the increase in the NHS list price of Priadel® 200mg and 400mg tablets.	
	Ms Doney confirmed that using eDispensed data for the three months August to October 2020, it is projected that the price change will result in an estimated additional annual spend of approximately £20,000.	
5.	**FORMULARY GROUP DECISIONS FEBRUARY 2021 – PUBLISHED – 01/03/2021**	
5.1.	**FORMULARY GROUP DECISIONS FEBRUARY 2021**	
	Members ratified the decisions of the February 2021 meeting as published.	FTEAM
6.	**netFORMULARY/FORMULARY REVIEW**	
6.1.	**PAEDIATRIC LICENCE EXTENSIONS**	
	There were no declarations of interest recorded in relation to the medicines and Marketing Authorisation Holders (MAHs).	

ITEM	SUBJECT	ACTION

The Group considered the Formulary Team's proposed recommendations for some of the paediatric licence extensions.

DABIGATRAN 75MG, 110MG, 150MG CAPSULES; 20MG, 30MG, 40MG, 50MG, 110MG, 150MG COATED GRANULES; 6.25MG/ML POWDER AND SOLVENT FOR ORAL SOLUTION (PRADAXA®)

The Chairman confirmed that dabigatran is not currently licensed and marketed in the UK, for the treatment of venous thromboembolism (VTE) and prevention of recurrent VTE in paediatric patients [from birth to less than 18 years of age].

The Group agreed to defer decision-making until medicines are licensed and marketed in the UK for the relevant paediatric licence extension(s).

The Formulary Team will keep a watching brief on the paediatric licensing of dabigatran. **FTEAM**

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

Ms Doney confirmed that insulin glargine as 100units/mL is included on the formulary but the high strength 300units/mL is non-formulary. September 2015, the 300units/mL preparation was not included on the formulary because of bioequivalence difference between the different strengths, and the risk of dosing errors.

Due to the potential for medication error, and in line with the current positon for adults, the Group did not support formulary inclusion for insulin glargine 300units/mL.

Insulin glargine 300units/mL solution for injection in a pre-filled pen (Toujeo®) is not routinely available in NHS Grampian.
Indication under review: for the treatment of diabetes mellitus in adolescents and children from the age of the 6 years to <18 years.
Not recommended for use in NHS Grampian. **FTEAM**

SODIUM OXYBATE 500MG/ML ORAL SOLUTION

Ms Doney confirmed that:
- September 2007, following a resubmission sodium oxybate (as the reference brand Xyrem®) was not recommended for use within NHS Scotland for the treatment of cataplexy in adult patients with narcolepsy
- the licence has been extended to include adolescents and children from the age of 7 years to <18 years

In line with the current positon for adults, the Group did not support formulary inclusion for sodium oxybate 500mg/mL oral solution for the treatment of narcolepsy with cataplexy in adolescents and children from the age of 7 years to <18 years.

Sodium oxybate 500mg/mL oral solution (Xyrem®) is not routinely available in NHS Grampian.
Indication under review: for the treatment of narcolepsy with cataplexy in adolescents and children from the age of 7 years (to <18 years).
Not recommended for use in NHS Grampian **FTEAM**

SUCROFERRIC OXYHYDROXIDE 125MG ORAL POWDER IN SACHET, 500MG CHEWABLE TABLETS (VELPHORO®)

Ms Doney confirmed that:
- Velphoro®, as the 500mg chewable tablet:
  - was accepted for use in NHS Scotland (April 2015)

ITEM	SUBJECT	ACTION

- is currently noted as non-formulary '*because clinical experts have not requested formulary inclusion*', a position that was reiterated in 2018
- the licence has been extended to include paediatric patients from 2 years and older
- there is a new formulation available, 125mg oral powder in sachet

In line with the current positon for adults, the Group did not support formulary inclusion for sucroferric oxyhydroxide (Velphoro®) as licensed for paediatric patients from 2 years and older.

Sucroferric oxyhydroxide 125mg oral powder in sachet, 500mg chewable tablets (Velphoro®) is not routinely available as the ADTC is waiting for further advice from local clinical experts.
Indication under review: for the control of serum phosphorus levels in paediatric patients from 2 years and older with CKD stages 4-5 (defined by a glomerular filtration rate <30mL/min/1.73m²) or with CKD on dialysis. Not routinely available as the ADTC is waiting for further advice from local clinical experts. **FTEAM**

ZAVICEFTA® 2G/0.5G POWDER FOR CONCENTRATE FOR SOLUTION FOR INFUSION

Ms Doney confirmed that:
- January 2018, Zavicefta® (ceftazidime/avibactam) 2g/0.5g powder for concentrate for solution for infusion was not recommended for use within NHS Scotland; due to non-submission from the holder of the Marketing Authorisation
- the licence has been extended to include adolescents and children aged 3 months to <18 years

In line with the current positon for adults, the Group did not support formulary inclusion for Zavicefta® as licensed for paediatric patients aged 3 months to <18 years.

Zavicefta® 2g/0.5g powder for concentrate for solution for infusion (ceftazidime/avibactam) is not routinely available in NHS Grampian.
Indication under review: adolescents and children aged 3 months to <18 years for the treatment of the following infections:
- **complicated intra-abdominal infection (cIAI)**
- **complicated urinary tract infection (cUTI), including pyelonephritis**
- **hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP)**
- **infections due to aerobic Gram-negative organisms in paediatric patients with limited treatment options only after consultation with a physician with appropriate experience in the management of infectious diseases (see Summary of Product Characteristics (SmPC) section 4.4).**

Not recommended for use in NHS Grampian. **FTEAM**

PERAMPANEL TABLETS AND ORAL SUSPENSION (FYCOMPA®)

Ms Doney confirmed that:
- perampanel:
  - is licensed for the adjunctive treatment of:
    1) primary generalised tonic-clonic seizures in patients from 7 years of age and older with idiopathic generalised epilepsy
    2) partial-onset seizures with or without secondarily generalised seizures in patients from 4 years of age and older
  - is not included on the formulary for the adjunctive treatment of primary generalised tonic-clonic seizures. This is based on a non-submission to SMC (adults and adolescents from age 12; SMC 1200/16 and SMC 2218).
  - tablets and oral suspension are currently included on the formulary as a second-

ITEM	SUBJECT	ACTION

line adjunctive treatment for adults and adolescents from age 12 years with refractory partial onset epilepsy (SMC 819/12, SMC 2172)
  - tablets are all flat-priced and subject to a Patient Access Scheme (PAS)
- the current SMC advice for the 500micrograms/mL oral suspension applies to adolescents and adults over 12 years, does not include a PAS and notes that the use of the oral suspension should be restricted to those who are unable to swallow perampanel tablets (SMC 2172). The oral suspension is available in a 340mL bottle costing £127.50 (excluding VAT), and its in-use shelf-life is 90 days.

The Group accepted that perampanel is prescribed in Primary Care on the advice of a specialist, and the oral solution is a cost-effective option for lower daily doses and for lower weight children.
The Group agreed that for children from 4 years to <12 years physicians should prescribe the most appropriate formulation and strength according to weight and dose.

In line with the current positon for adults, the Group did not support formulary inclusion for the adjunctive treatment of primary generalised tonic-clonic seizures, but did support inclusion for refractory partial onset epilepsy for paediatric patients from 4 to <12 years.

Perampanel 2mg, 4mg, 6mg, 8mg, 10mg 12mg film-coated tablets, 500micrograms/mL oral suspension (Fycompa®) is not routinely available in NHS Grampian.
Indication under review: for the adjunctive treatment of primary generalised tonic-clonic seizures in patients from 7 to <12 years of age with idiopathic generalised epilepsy.
Not recommended for use in NHS Grampian. **FTEAM**

Perampanel 2mg, 4mg, 6mg, 8mg, 10mg 12mg film-coated tablets (Fycompa®) is routinely available in line with local guidance.
Indication under review: as a second-line adjunctive treatment in children (aged from 4 to <12 years) with refractory partial onset epilepsy.
Restriction: only on advice from specialists (paediatric neurologists or paediatricians with an expertise in epilepsy).
This advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of perampanel and is contingent upon the continuing availability of the patient access scheme 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 the community on the recommendation of a consultant/specialist. Treatment should be initiated only by physicians who have appropriate experience in the treatment of epilepsy. **FTEAM**

Perampanel 500micrograms/mL oral suspension (Fycompa®) is routinely available in line with local guidance.
Indication under review: as a second-line adjunctive treatment in children (aged from 4 to <12 years) with refractory partial onset epilepsy.
Restriction: only on advice from specialists (paediatric neurologists or paediatricians with an expertise in epilepsy). The physician should prescribe the most appropriate formulation and strength according to weight and dose.
It was classified 1b - available for restricted use under specialist supervision and 8d – treatment may be initiated in the community on the recommendation of a consultant/specialist. Treatment should be initiated only by physicians who have appropriate experience in the treatment of epilepsy. **FTEAM**

6.2. TRIMETAZIDINE PRESCRIBING INFORMATION

At the March 2020 meeting, trimetazidine was accepted to formulary for restricted use as

ITEM	SUBJECT	ACTION

add-on therapy for the symptomatic treatment of adult patients with stable angina pectoris who are inadequately controlled by or intolerant to first-line antianginal therapies. Prescribing in Primary Care was subject to provision of supporting information.
It was noted that trimetazidine is an unlicensed product and although it may be prescribed in Primary Care, after initiation in hospital, it was felt that prescribing information should be made available.

Ms Doney requested the Group review the proposed prescribing information and feedback comments to the Formulary Team within one week. **ALL**

Ms Davie will check if the unlicensed product is available for selection in prescribing systems, and feedback for inclusion in the information document. **AD**

7. OTHER BUSINESS - NONE

8. NEW PRODUCT REQUESTS

8.1. FG1SMC 2280 - ROMOSOZUMAB (SEVERE OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN)

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

The Group considered the request for romosozumab for the treatment of severe osteoporosis in postmenopausal women at high risk of fracture. The MAH requested that the SMC considered romosozumab when positioned for use in patients who have experienced a fragility fracture and are at imminent risk of another fragility fracture (within 24 months).

The Group noted:

- romosozumab:
  - is a monoclonal antibody that increases bone formation and decreases bone resorption by binding to and inhibiting sclerostin. This anabolic therapy has a novel mechanism of action that differs from teriparatide, a human parathyroid hormone.
  - [November 2020] was accepted for use within NHS Scotland following a full submission
  - is administered by subcutaneous injection at a recommended dose of 210mg (given as two subcutaneous injections of 105mg each at different injection sites)
  - is given monthly for 12 months, and patients should be adequately supplemented with calcium and vitamin D
  - is contraindicated in patients with a history of myocardial infarction or stroke and hypocalcaemia, and should be discontinued if a patient experiences a myocardial infarction or stroke during treatment
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of romosozumab
- teriparatide, another formulary anabolic therapy, requires daily injection for two years. Teriparatide is available as biosimilar products and the contract is currently up for review so the cost-base may change.
- the service plans to use romosozumab as an alternative to teriparatide - as a second-line agent when a patient with significant osteoporosis suffers a low trauma vertebral or hip fracture despite having been on a bisphosphonate for an appropriate length of time; or when someone with severe osteoporosis has a further low trauma fracture after appropriate length of first-line therapy.
- romosozumab will be available for patients where teriparatide is contraindicated (i.e. malignancy or radiotherapy history), and as such there will be minimal cost offset
- the SIGN guidance, updated January 2021, also suggests romosozumab as a first-line agent for patients with severe spine osteoporosis [and high risk of hip or non-vertebral fracture]
- the Rheumatology service plans to supply romosozumab via Homecare

ITEM	SUBJECT	ACTION

- patient numbers are expected to be small, but will potentially increase with time

The Group accepted the restricted local need for romosozumab for the treatment of severe osteoporosis in postmenopausal women at high risk of fracture, as outlined in SIGN 142 (revised January 2021).

SMC 2280 - Romosozumab 105mg solution for injection in pre-filled pen (Evenity®) ▼ is routinely available in line with national guidance (SIGN 142 - Management of osteoporosis and the prevention of fragility fracture).
Indication under review: for the treatment of severe osteoporosis in postmenopausal women who have experienced a fragility fracture and are at imminent risk of another fragility fracture (within 24 months).
In a phase III study in post-menopausal women with osteoporosis who were at high risk of fracture, romosozumab for 12 months followed by an oral bisphosphonate reduced the risk of fractures compared with an oral bisphosphonate alone.
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 initiated and supervised by specialist physicians experienced in the management of osteoporosis. **FTEAM**

8.2. FG1SMC 2265 - SIPONIMOD (SECONDARY PROGRESSIVE MULTIPLE SCLEROSIS)

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

The Group considered the request for siponimod for the treatment of adults with secondary progressive multiple sclerosis (SPMS) with active disease evidenced by relapses or imaging features of inflammatory activity.

The Group noted:

- siponimod:
  - [October 2020] was accepted for use in NHS Scotland following a full submission
  - treatment is initiated with a 5-day titration pack, and treatment must be re-titrated if the patient misses four or more consecutive days of treatment
- SPMS occurs when there is a gradual accumulation of disability with or without superimposed relapses
- the only other treatment licensed for use in SPMS with active disease is interferon beta-1b, however due to dubious efficacy, it is only used in a small number of patients
- genotype testing is required prior to commencing treatment with siponimod. Initially Novartis Pharmaceuticals UK Ltd will carry out testing, however with time this will move to the local genetics department.
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of siponimod
- the service plans to supply siponimod via Homecare
- this will be a new medicine cost to the service, with minimal offset available
- additional costs expected include CYP2C9 genotyping, regular ongoing monitoring [full blood count, liver function tests and screening for macular oedema and cutaneous neoplasms], MRI scans, ECG monitoring and monitoring of adverse effects
- although there is no long-term data, siponimod is potentially a long-term treatment option. Treatment will be stopped if it is not tolerated, the patient reaches an Expanded Disability Status Scale (EDSS) ≥7 or suffers continued relapses while on treatment.
- the SmPC states that patients with certain pre-existing cardiac conditions should be observed for 6 hours after their first dose and observation may require to be continued overnight. In this case, patients would be admitted as a day case; this arrangement is

in place already for patients commencing treatment with fingolimod.
- initially a large number of patients will need to be assessed [prevalent population], with a small number of new patients identified for treatment [incident population]

The Group accepted the restricted local need for siponimod for the treatment of adult patients with SPMS with active disease evidenced by relapses or imaging features of inflammatory activity, in line with SMC 2265.

SMC 2265 - Siponimod 250microgram, 2mg film coated tablets (Mayzent®) ▼ is routinely available in line with national guidance (SMC 2265).
Indication under review: treatment of adult patients with secondary progressive multiple sclerosis (SPMS) with active disease evidenced by relapses or imaging features of inflammatory activity.
In a randomised, double blind, placebo-controlled phase III study, siponimod was associated with a reduction in disability progression confirmed after 3 months in patients with SPMS.
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.
It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only. Treatment with siponimod should be initiated and supervised by a physician experienced in the management of multiple sclerosis. **FTEAM**

8.3. FG1SMC 2293 - VENETOCLAX (CHRONIC LYMPHOCYTIC LEUKAEMIA)

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

The Group considered the request for venetoclax in combination with obinutuzumab for previously untreated chronic lymphocytic leukaemia (CLL) in adults as outlined in SMC 2293.

The Group noted:
- venetoclax:
  - [for this indication] was accepted for use in NHS Scotland following the output from the PACE process, and application of the appropriate SMC modifiers
  - [December 2020] was accepted for restricted use following a full submission under the orphan equivalent process
  - is already included on the formulary [for the treatment of CLL] as monotherapy (SMC 1249/17) and in combination with rituximab (SMC 2166)
  - is an oral treatment taken for 12 cycles - the first six cycles taken in combination with obinutuzumab, with the next six cycles of venetoclax as monotherapy
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of treatment
- cost offset will be available as treatment will replace oral chlorambucil plus obinutuzumab or bendamustine plus rituximab in patients without a TP53 mutation, or ibrutinib monotherapy in patients with a TP53 mutation
- additional costs include blood and radiographic monitoring, supportive medicines and management of adverse reactions. Additional costs will also include aseptic preparation, chair time and nursing staff when venetoclax is given in combination with intravenous obinutuzumab.
- for patients with a TP53 mutation, ibrutinib will remain a first-line option as some patients will choose an oral-only regimen (particularly if based far from Aberdeen Royal Infirmary (ARI))
- the new combination may be preferred as it is a time-limited treatment option, or where cardiac history, baseline ECG/echo abnormalities or the need for anticoagulation preclude the use of ibruntinb

ITEM	SUBJECT	ACTION

The Group accepted the restricted local need for venetoclax in combination with obinutuzumab for previously untreated CLL in adults as outlined in the SMC advice (SMC 2293).

SMC 2293 - Venetoclax 10mg, 50mg, 100mg film-coated tablets (Venclyxto®) ▼ is routinely available in line with national guidance (SMC 2293).
Indication under review: in combination with obinutuzumab for the treatment of adults with previously untreated chronic lymphocytic leukaemia (CLL):
- with del (17p)/T53 mutation, or
- without del (17p)/T53 mutation who are not fit to receive FCR (fludarabine, cyclophosphamide and rituximab) chemotherapy.
Venetoclax-obinutuzumab, compared with chlorambucil-obinutuzumab, significantly improved progression-free survival in adults with CLL and co-morbidities.
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.
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 venetoclax should be initiated and supervised by a physician experienced in the use of anticancer medicinal products. **FTEAM**

8.4. FG1SMC 2296 - AVATROMBOPAG AND SMC 2227 – LUSUTROMBOPAG (SEVERE THROMBOCYTOPENIA)

There were no declarations of interest recorded in relation to these products.

The Group considered the request for avatrombopag for the treatment of severe thrombocytopenia in adults with chronic liver disease who are scheduled to undergo an invasive procedure.

The Group noted:

- avatrombopag:
  - is a thrombopoietin (TPO) receptor agonist that increases platelet production through stimulation of proliferation and differentiation of megakaryocytes from bone marrow progenitor cells
  - meets SMC orphan equivalent criteria and was accepted for use in NHS Scotland following a full submission reviewed by the SMC executive [December 2020]
  - is also licensed for the treatment of primary chronic immune thrombocytopenia in adult patients who are refractory to other treatments [SMC advice is due to be published later this year].
  - [for this indication] is given as a 5-day treatment course, the recommended daily dose is based on the patient's platelet count. The patient should undergo their procedure five to eight days after the last dose of avatrombopag.
- lusutrombopag is another TPO-receptor agonist that is accepted for use in NHS Scotland for the treatment of severe thrombocytopenia in adult patients with chronic liver disease undergoing invasive procedures (SMC 2227)
- lusutrombopag is currently not included on the formulary. The requestor has confirmed that only one TPO-receptor agonist is required on formulary and the preference is for avatrombopag.
- patient numbers are expected to be very small
- no direct drug cost offset is available, however treatment aims to avoid platelet transfusions and the need for hospital admission
- the SmPC states '*avatrombopag should be initiated by and remain under the supervision of a physician who is experienced in the treatment of haematological*

ITEM	SUBJECT	ACTION

diseases'. The requesting Haematologist believes prescribing will be mainly by the liver team, and if the liver team discusses potential cases with Haematology, advice on the prescribing of avatrombopag can be provided.

The Group noted the statement in the SmPC, and agreed that a pragmatic decision is needed but that the note in the SmPC should be included in the decision and highlighted to the Haematology and liver teams. **FTEAM**

The Group accepted the restricted local need for avatrombopag for the treatment of severe thrombocytopenia in adults with chronic liver disease who are scheduled to undergo an invasive procedure, as outlined in SMC 2296.

SMC 2296 - Avatrombopag 20mg film-coated tablets (Doptelet®) ▼ is routinely available in line with national guidance (SMC 2296).
Indication under review: treatment of severe thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo an invasive procedure.
In two phase III studies in patients with severe thrombocytopenia with chronic liver disease who were scheduled to undergo an invasive procedure, avatrombopag was superior to placebo for the proportion of patients who did not require a platelet transfusion or any rescue procedure for bleeding after randomisation and up to 7 days following the procedure.
It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only. Treatment should be initiated by and remain under the supervision of a physician who is experienced in the treatment of haematological diseases. **FTEAM**

SMC 2227 – Lusutrombopag 3mg film-coated tablets (Mulpleo®) ▼ is not routinely available as there is a local preference for alternative medicines.
Indication under review: for the treatment of severe thrombocytopenia in adult patients with chronic liver disease undergoing invasive procedures.
In two phase III studies, lusutrombopag was superior to placebo in reducing the need for platelet transfusions in thrombocytopenic patients with chronic liver disease undergoing invasive procedures.
Not routinely available as there is a local preference for alternative medicines. **FTEAM**

8.5. FG1SMC 2247 - PEMBROLIZUMAB IN COMBINATION WITH AXITINIB (ADVANCED RENAL CELL CARCINOMA)

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

The Group considered the request for pembrolizumab in combination with axitinib, for the first-line treatment of advanced renal cell carcinoma in adults.

The Group noted:

- pembrolizumab (in combination with axitinib):
  - [for this indication] was accepted for use in NHS Scotland following the output from the PACE process, and application of the appropriate SMC modifiers. The SMC advice was subject to a full submission assessed under the end of life process, and treatment with pembrolizumab was restricted to a two-year clinical stopping rule.
  - would replace standard first-line treatment with oral tyrosine-kinase inhibitors, such as sunitinib or pazopanib. The service still requires these medicines for patients where immunotherapy is not suitable.
  - [for this indication] is not recommended by NICE due to cost-effective estimates being higher than deemed acceptable
- the recommended dose of pembrolizumab as part of combination therapy is 200mg every 3 weeks administered as an intravenous infusion over 30 minutes
- in clinical trials, the median duration of combination treatment was 10.4 months

ITEM	SUBJECT	ACTION

(versus 7.8 months for sunitinib) however, the requestor feels that the PFS of 15 months would be more representative
- patient numbers are expected to be small
- additional costs expected include additional pressure of clinics, chair time, aseptic preparation and the cost of supportive therapies/care
- sunitinib is due to come off patent in January 2022
- the requestor has confirmed that patients who reach two years of treatment may be considered for continued treatment under the individual patient request processes, e.g. PACS, or may continue with axitinib monotherapy

The Group noted the difficulties of estimating the financial impact of introduction of the combination regimen, and the potential offset costs.

The Group accepted the restricted local need for pembrolizumab in combination with axitinib, for the first-line treatment of advanced renal cell carcinoma in adults with treatment subject to a two-year clinical stopping rule, in line with SMC 2247.

SMC 2247 - Pembrolizumab 25mg/mL concentrate for solution for infusion (Keytruda®) is routinely available in line with national guidance (SMC 2247).
Indication under review: in combination with axitinib, for the first-line treatment of advanced renal cell carcinoma in adults.
Restriction: treatment with pembrolizumab is subject to a two-year clinical stopping rule.
In an open –label, phase III study, first-line treatment with pembrolizumab plus axitinib significantly improved progression-free and overall survival in adults with advanced renal cell carcinoma compared with vascular endothelial growth factor (VEGF)-targeting tyrosine-kinase inhibitor (TKI).
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.
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**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE – MARCH 2021

The Group noted the SMC provisional advice issued March 2021.

SMC 2327 – ATALUREN (TRANSLARNA®) (DUCHENNE MUSCULAR DYSTROPHY)

The Group noted the provisional ultra-orphan medicine assessment report (UMAR) for ataluren, for the treatment of Duchenne muscular dystrophy resulting from a nonsense mutation in the dystrophin gene, in ambulatory patients aged 2 years and older.

The Formulary Team will prepare a summary for the April meeting. **FTEAM**

10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS - MARCH 2021

The Group noted the SMC advice published March 2021.

The following SMC accepted medicines have not been processed within a 60-day timescale:
- SMC 2295 entrectinib (Rozlytrek®)▼
- SMC 2335 Trimbow® (beclometasone dipropionate/formoterol fumarate dihydrate/glycopyrronium)
- SMC 2332 doravirine (Pifeltro®)▼(submission received)
- SMC 2333 Delstrigo® (doravirine/lamivudine/tenofovir disoproxil fumarate)▼

ITEM	SUBJECT	ACTION

(submission received)
- SMC 2328 trametinib (Mekinist®) (submission expected)

Local advice for these medicines and indications will be included in the March 2021 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts.' **FTEAM**

SMC 2311 – ONASEMNOGENE ABEPARVOVEC (ZOLGENSMA®) (SPINAL MUSCULAR ATROPHY)

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

The Group discussed the SBAR submitted regarding the use of onasemnogene abeparvovec for the treatment of patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA type 1, or patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.

The Group noted:
- onasemnogene abeparvovec:
  - is a very expensive advanced therapy medicinal product that has recently been accepted for restricted use in NHS Scotland (SMC 2311)
  - is a gene therapy and treatment [with onasemnogene abeparvovec] aims to address the genetic cause of SMA and promote the survival and function of transduced motor neurons
  - meets SMC orphan criteria and has a conditional marketing authorisation from the European Medicines Agency (EMA)
  - [for this indication] was accepted for use in NHS Scotland following the output from the PACE process, and application of the appropriate SMC modifiers
- [May 2018] nusinersen was accepted by SMC for restricted use in patients with symptomatic SMA type 1 and is available through the National Services Scotland Ultra-orphan medicines Risk Share Scheme
- onasemnogene abeparvovec will be an alternative treatment option to nusinersen. It is administered as a single intravenous infusion unlike nusinersen which involves repeated lumbar punctures for intrathecal administration every four months.
- SMA is a devastating muscle wasting condition associated with multiple major complications requiring complex medical and supportive care. Care is required 24 hours a day which has a huge impact on parents/carers.
- nationally, the pathway for patients will involve single centre administration (likely NHS Greater Glasgow and Clyde), with local monitoring and selection of patients to strict criteria

The Formulary Team will liaise with Finance to highlight the financial risk of this treatment. **FTEAM**

The Group accepted that onasemnogene abeparvovec would be recorded as non-formulary as it is routinely available from a specialist centre in another health board.

SMC 2311 - Onasemnogene abeparvovec 2 × 10^{13} vector genomes/mL solution for infusion (Zolgensma®) ▼ is routinely available from a Specialist Centre in another Health Board.
Indication under review: for the treatment of patients with 5q spinal muscular atrophy (SMA) with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA type 1, or patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.
Restriction: for the treatment of:
- **patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA type 1, or**

ITEM	SUBJECT	ACTION

- **pre-symptomatic patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene, where patients are expected to develop SMA type 1**

In a phase III study of patients with symptomatic SMA type 1 treated with onasemnogene abeparvovec, survival was significantly better than a historical control cohort. In addition, motor milestones achieved generally exceeded the natural history of SMA type 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 the views from a Patient and Clinician Engagement (PACE) meeting.
Not routinely available in NHS Grampian however if local need identified treatment is available from a Specialist Centre in another Health Board. **FTEAM**

11. GENERAL INFORMATION FROM SCOTTISH MEDICINES CONSORTIUM – MARCH 2021

The Chairman highlighted that the SMC will continue with the interim processes, with some modifications, and will review the processes in Autumn 2021.

12. DOCUMENTS FOR INFORMATION

Items 12.2 (Drug Safety Update February 2021) and 12.2 (Medicines Guidelines and Policies Group minute October 2020) were noted.

13. AOCB

THANK YOU AND GOODBYE

Ms Doney confirmed that Ms Caitlin Wilkinson, the Formulary Team administrator, is moving post to work in the local Pathology Department.
The Group extended its gratitude to Ms Wilkinson for her work within the Formulary Team, and ensuring the smooth running of meetings.

DATE OF NEXT MEETING

Tuesday 20 April 2021 starting at 14.30 via Microsoft Teams.

CHAIRMAN'S SIGNATURE _____ **DATE 20 APRIL 2021**