NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 16 August 2022 at 14:30 via Microsoft Teams

PRESENT	APOLOGIES	APPROVED
Ms L Cameron	Ms A Davie	
Dr V Chieng	Dr J Newmark	
Dr D Culligan		
Ms F Doney (Vice-Chair)		
Dr E Elias		
Dr L Elliot (Chair)		
Ms M Galvin		
Mrs G McKerron		
Dr M Metcalfe (Vice-Chair)		
Mrs L Montgomery (technical issues prevented access to the meeting)		
Mrs K Neave		
Mrs S O'Beirne		
Mr M Paterson		
Mr R Sivewright		

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	The Chair welcomed members, opened the meeting and noted that a quorum was present.	
1.	**APOLOGIES**	
	Apologies for absence were requested and noted. The Chair led introductions to two new members, Dr Vui Yung Chieng a General Practitioner (GP) in Links Medical Practice, and Dr Erwan Elias a GP in Kemnay Medical Practice. Dr Chieng and Dr Elias are joining the Group as GP representatives.	
2.	**DRAFT MINUTE OF THE MEETING HELD 21 JUNE 2022**	
	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 on the agenda. Items 4.2 and 4.3 were taken together.	
	4.2. SMC 2398 - TUCATINIB (BREAST CANCER)	
	4.3. SMC 2388 - TRASTUZUMAB DERUXTECAN (BREAST CANCER)	
	There were no declarations of interest recorded in relation to these products. Ms Doney summarised the status of the formulary requests for tucatinib [in combination with trastuzumab and capecitabine] and trastuzumab deruxtecan [monotherapy] for the	

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treatment of adults with HER2-positive locally advanced or metastatic breast cancer who have received at least two prior anti-HER2-based regimens.

It was confirmed that:

- decision-making for both agents was deferred with a request that a breast cancer specialist attend a meeting to discuss the submissions and the breast cancer pathway(s)
- since discussed in May:
  - the PAS for tucatinib has been reviewed
  - NICE has revised its advice to include subcutaneous trastuzumab
  - colleagues in finance have confirmed how the costs of 'new medicines fund (NMF)' drugs and any new drugs approved by the Formulary Group are managed
  - a Scottish Cancer Network (SCN) has been introduced that will develop and operate a national system for the production and review of clinical management pathways. Breast and lung will be the first two pathways piloted.
- the breast cancer service remains very busy, additionally mutual aid is being provided to another Health Board
- colleagues from the SCN could attend a meeting to discuss the work of the national group and the development of the national cancer pathways

Members supported inviting colleagues from the SCN to a future meeting, and pending their attendance, the Group accepted the restricted local need for trastuzumab deruxtecan and tucatinib for the treatment of adults with unresectable or metastatic HER2-positive breast cancer, as outlined in SMC 2388 and SMC 2398 respectively.

SMC 2388 - Trastuzumab deruxtecan 100mg powder for concentrate for solution for infusion (Enhertu®) ▼ is routinely available in line with national guidance (SMC 2388).
Indication under review: as monotherapy for the treatment of adults with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer who have received two or more prior anti-HER2-based regimens.
In an open-label single-arm phase II study trastuzumab deruxtecan was associated with clinically relevant overall response rates in adults with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens.
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. Trastuzumab deruxtecan should be prescribed by a physician and administered under the supervision of a healthcare professional experienced in the use of anticancer medicinal products.
In order to prevent medicinal product errors, it is important to check the vial labels to ensure that the medicinal product being prepared and administered is Enhertu® (trastuzumab deruxtecan) and not trastuzumab or trastuzumab emtansine. **FTEAM**

SMC 2398 - Tucatinib 50mg, 150mg film-coated tablets (Tukysa®) ▼ is routinely available in line with national guidance (SMC 2398).
Indication under review: in combination with trastuzumab and capecitabine for the treatment of adults with HER2-positive locally advanced or metastatic breast cancer who have received at least two prior anti-HER2 treatment regimens.
In a phase II study the addition of tucatinib to trastuzumab plus capecitabine was associated with a statistically significant improvement in progression-free survival.

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	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. It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only. Treatment with tucatinib should be initiated and supervised by a physician experienced in the administration of anti-cancer medicinal products.	**FTEAM**

5. FORMULARY GROUP DECISIONS JUNE 2022 – PUBLISHED - 04/07/2022

Members ratified the decisions of the June 2022 meeting as published. **FTEAM**

6. NETFORMULARY/FORMULARY REVIEW

6.1. METOLAZONE 5MG TABLETS (XAQUA®)

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

Ms Doney confirmed that:

- metolazone is a diuretic with actions and uses similar to thiazide diuretics
- in 2012, Sanofi discontinued metolazone 2.5mg and 5mg tablets (Metenix®)
- the unlicensed tablets were included on the formulary because there was a local need for metolazone for the management of oedema
- earlier this year Xaqua®, a 5mg metolazone tablet, was marketed in the UK
- the Medicines and Healthcare products Regulatory Agency (MHRA) advises that an unlicensed medicinal product may only be supplied when a patient has special needs that cannot be met by an equivalent licensed medicinal product
- the availability of a licensed product meant that Community Pharmacies could no longer source unlicensed products and established patients had to be switched to the licensed product
- the Summary of Product Characteristics (SmPC) for Xaqua® includes the note: '*Xaqua tablets bioavailability may be different from other metolazone preparations (see section 5.2). Therefore, the* recommended *doses (expressed in mg) can differ from other metolazone products. A dose adjustment may be necessary and individualised titration based on patient's response and tolerability is advised if switching from Xaqua tablets to another metolazone product, or vice versa.'*
- the Medicines Information department confirmed the bioavailability of Xaqua® and the specialist services (renal and cardiology) provided guidance for colleagues in Primary Care regarding additional monitoring and dosing guidance when switching patients to the licensed product
- patients previously established on unlicensed metolazone have been reviewed and switched to the licensed product, and the formulary needs to reflect the availability of licensed metolazone

The Group acknowledged there was an established local need for metolazone tablets for the management of oedema in a small group of patients. Licensed metolazone tablets were accepted to formulary for the management of oedema without the need for a full submission.

SBAR - Metolazone 5mg tablet (Xaqua®) is routinely available in line with local guidance.
Indication under review: for the treatment of adults with oedema related to:

- **kidney diseases, including the nephrotic syndrome and states of impaired renal function**
- **congestive heart failure**

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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**

Unlicensed metolazone 2.5mg and 5mg tablets will be noted as 'Not routinely available as there is a local preference for alternative medicines'. **FTEAM**

6.2. SBAR - PAEDIATRIC LICENCE EXTENSIONS FOR MEDICINES FOR THE TREATMENT OF HUMAN IMMUNODEFICIENCY VIRUS-1 (HIV-1)

Dr Culligan declared a personal, non-specific interest in Bristol Myers Squibb Pharmaceuticals Limited and took part in decision-making.

The Group considered the Formulary Team's proposed recommendations for the paediatric licence extensions for some medicines indicated for the treatment of human immunodeficiency virus-1 (HIV-1).

Ms Doney reported that:

- the licences for Evotaz® tablets (atazanavir/cobicistat) and doravirine, (as a single agent and as the combination product Delstrigo®), have been extended to include adolescents aged 12 years to <18 years
- prescribing will only be on the advice of specialists in paediatric HIV, with advice from specialists in other Health Boards where appropriate
- patient numbers will be very small, with no patients awaiting treatment
- doravirine, (as a single agent and as the combination product Delstrigo®) is included on the formulary for adults, whereas Evotaz® is non-formulary
- the PASs for doravirine and Delstrigo® have been extended to include adolescents
- including doravirine on the formulary will bring use in line with the adult service and prevent delays in access to treatment should a local need be identified

The Group supported the request to bring the formulary status of doravirine, Delstrigo® and Evotaz® in line with their use in adults.

The Group accepted the restricted local need for doravirine, as a single agent and as the combination product Delstrigo®, as licensed for adolescents aged 12 to <18 years weighing at least 35kg.

SBAR - Doravirine 100mg film-coated tablets (Pifeltro®) ▼ is routinely available in line with local guidance.
Indication under review: in combination with other antiretroviral medicinal products, for the treatment of adolescents aged 12 years to <18 years weighing at least 35kg infected with HIV-1 without past or present evidence of resistance to the non-nucleoside reverse transcriptase inhibitor (NNRTI) class.
Restriction: to be prescribed under the supervision of specialists in paediatric HIV. 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. **FTEAM**

SBAR - Delstrigo® ▼ 100mg/300mg/245mg film-coated tablets (doravirine/lamivudine/tenofovir disoproxil fumarate) is routinely available in line with local guidance.
Indication under review: for the treatment of adolescents aged 12 years to <18 years weighing at least 35kg who are infected with HIV-1 without past or present evidence of resistance to the NNRTI class, lamivudine, or tenofovir and who have experienced toxicities which preclude the use of other regimens that do not

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	contain tenofovir disoproxil. **Restriction: to be prescribed under the supervision of specialists in paediatric HIV. 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.**	**FTEAM**

Note: The classification 'recommended for hospital use only' does not prevent supply of medicines by Primary Care, e.g. use of hospital-based prescription (HBP) stationery.

The Group supported extending the 'non-formulary' status of Evotaz® tablets to include its use in adolescents aged 12 to <18 years.

	SBAR - Evotaz® 300mg/150mg film-coated tablets (atazanavir/cobicistat) is not routinely available as there is a local preference for alternative medicines. **Indication under review: in combination with other antiretroviral medicinal products for the treatment of HIV 1 infected adolescents aged 12 years to <18 years weighing at least 35kg without known mutations associated with resistance to atazanavir.** **Not routinely available as there is a local preference for alternative medicines.**	**FTEAM**

6.3. CORRECTION TO FORMULARY ENTRY

Ms Doney reported that an error was published on the formulary website. The strength of the components of a fixed-dose calcium and vitamin D preparation were incorrect, but the dose was correct.
Colleagues in Primary Care reported the error and it was corrected immediately. The update processes have been reviewed to minimise the chance of this happening again.

7. OTHER BUSINESS

7.1. NCMAG - OFF-LABEL USE OF ABIRATERONE IN HIGH-RISK HORMONE-SENSITIVE NON-METASTATIC PROSTATE CANCER

The Group noted that the National Cancer Medicines Advisory Group (NCMAG) does not support the routine off-label use of the originator abiraterone product (in combination with prednisolone and androgen deprivation therapy) for the treatment of high-risk hormone-sensitive non-metastatic prostate cancer.
The proposal will undergo a health economic re-evaluation and prioritised review by NCMAG once generic abiraterone products are available.

8. NEW PRODUCT REQUESTS

8.1. FG1SMC 2408 - CENOBAMATE (FOCAL-ONSET SEIZURES)

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

The Group considered the request for cenobamate for a subgroup of its licence, as a second-line adjunctive treatment for focal-onset seizures with or without secondary generalisation in adults with drug-resistant epilepsy.

The Group noted that:
- epilepsy is usually a life-long condition, uncontrolled or poorly controlled epilepsy is a risk factor for Sudden Unexpected Death in Epilepsy (SUDEP), accidents and injuries
- people with epilepsy have a two to three times higher risk of dying than the general population and persistent seizures have been strongly related to excess mortality
- cenobamate has a dual and complementary mechanism of action which prevents both

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seizure initiation and limits seizure spread
- evidence comes from a short Phase II study (Study C017, n = 437; 6-week titration followed by 12 week maintenance phase), there is no evidence against active comparators/established add-on treatments, and no evidence for the requested placement in the treatment pathway
- drug reaction with eosinophilia and systemic symptoms (DRESS) has been reported in association with cenobamate when started at higher doses and titrated rapidly (weekly or faster titration). When initiated at 12.5mg/day and titrated every two weeks, in an open-label safety study of 1,340 epilepsy patients, no cases of DRESS were reported.
- a dose-dependent shortening of the QTcF interval has been observed with cenobamate
- NICE estimated the cost for the maintenance phase of cenobamate treatment as £206 per person every 28 days (£7.37 per day)
- cenobamate would be an additional adjunctive treatment option, and a degree of cost offset is available from the displacement of alternative formulary options

Members discussed the lack of General Practice experience with cenobamate and the need for patients to be advised of the signs and symptoms of DRESS and monitored closely for skin reactions.
Members agreed that prescribing should be initiated in the managed service before handover to Primary Care.

The Group accepted the restricted local need for cenobamate as a second-line adjunctive treatment of focal-onset seizures with or without secondary generalisation in adults with drug-resistant epilepsy, as outlined in SMC 2408.

SMC 2408 - Cenobamate 12.5mg, 25mg, 50mg, 100mg, 150mg, 200mg film-coated tablets (Ontozry®) ▼ is routinely available in line with national guidance (SMC 2408).
Indication under review: as a second-line adjunctive treatment of focal-onset seizures with or without secondary generalisation in adults with drug-resistant epilepsy who have not been adequately controlled despite previous treatment.
In patients with uncontrolled focal seizures, despite treatment with anti-epileptic medicines, cenobamate was superior to placebo in terms of the proportion of patients experiencing a ≥50% reduction in focal seizure frequency.
It was classified 1b- available for restricted use under specialist supervision and 8c - treatment to be initiated in hospital prior to handover. **FTEAM**

8.2. FG1SMC 2401 - RISDIPLAM (5Q SPINAL MUSCULAR ATROPHY (SMA))

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

The Group considered the request for risdiplam for the treatment of 5q spinal muscular atrophy (SMA) in patients 2 months of age and older, with a clinical diagnosis of SMA type 1, type 2 or type 3 or with one to four SMN2 [survival of motor neuron 2].

The Group noted that:
- SMA is a rare, debilitating, progressive, neuromuscular disorder
- risdiplam:
  - is an orphan medicine and the first oral treatment option for SMA
  - [for this indication] meets SMC orphan criteria, and was accepted for use in NHS Scotland following the output from the PACE process and application of the appropriate SMC modifiers that can be applied when encountering high cost-effectiveness ratios
  - improves the ability to sit up, stand or walk for people with type 1, 2 and 3 SMA and it may be effective for people before they start showing symptoms of SMA. There is some evidence suggesting that people with type 1 SMA live for longer on

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risdiplam. However, there is no direct evidence comparing risdiplam with best supportive care for type 1 SMA, and there is no long-term evidence of benefit for risdiplam overall.
- patient numbers in the trials were small and there are no data against best supportive care or nusinersen, the most relevant comparator
- treatment will be developed for local use and guidance is awaited from the Scottish Muscle Network
- treatment should be initiated by a physician with experience in the management of SMA
- patient numbers will be small but there is a potential that some of the patients currently receiving nusinersen may wish to switch to risdiplam
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of risdiplam, and the PAS is not available in Primary Care
- nusinersen, the relevant comparator, is included in the National Services Scotland Ultra-orphan medicines Risk Share Scheme, and it is not clear if risdiplam will be included in the scheme
- risdiplam is also available for patients with one to four SMN2 copies, this is a new population (i.e., not currently available for treatment with nusinersen)

The Group accepted the restricted local need for risdiplam for the treatment of SMA, as outlined in SMC 2401.

SMC 2401 - Risdiplam 0.75mg/mL powder for oral solution (Evrysdi®) ▼ is routinely available in line with national guidance (SMC 2401).
Indication under review: for the treatment of 5q spinal muscular atrophy (SMA) in patients 2 months of age and older, with a clinical diagnosis of SMA type 1, type 2 or type 3 or with one to four SMN2 [survival of motor neuron 2] copies.
Evidence from two phase II/III studies has indicated that risdiplam improves motor milestones and motor function in patients with type 1, 2 and 3 SMA.
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. It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only. Treatment with risdiplam should be initiated by a physician with experience in the management of SMA. FTEAM

8.3. FG1SMC 2307 - MEXILETINE 167MG CAPSULES (MYOTONIA)

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

The Group considered the request for mexiletine capsules, as Namuscla®, for the symptomatic treatment of myotonia in adults with non-dystrophic myotonic disorders.

The Group noted that:
- people with non-dystrophic myotonias mainly experience stiffness in skeletal muscles but can also experience muscle weakness, pain and impairment in physical activity
- generic mexiletine hydrochloride capsules (50mg, 100mg, 200mg) are currently included on the formulary, as licensed, for life-threatening ventricular arrhythmias
- mexiletine as Namuscla®:
  - is an orphan medicine and is the only medicine licensed for non-dystrophic myotonic disorders
  - [for this indication] was accepted for use in NHS Scotland following a resubmission assessed under the orphan process, the output from the PACE process and application of SMC modifiers that can be applied when encountering high cost-effectiveness ratios
  - was shown to be more effective than placebo at reducing muscle stiffness, and

evidence comes from a small study (n=25)
- there is a lack of long-term study data
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of Namuscla® 167mg capsules
- the SmPC advises that all patients should have:
  - cardiac evaluation (ECG, 24-48-hour Holter-monitoring and echocardiography) before treatment, repeated shortly after it is started (e.g., within 48 hours)
  - electrolyte evaluation prior to initiation treatment. If patient shows electrolyte imbalance, this needs to be corrected before administering Namuscla®.
- during Namuscla® maintenance treatment, the SmPC advises that in patients with or prone to cardiac abnormalities a detailed cardiac evaluation (including ECG, 24-48 hour Holter-monitoring and echocardiography) is recommended at least annually, or more frequently if considered necessary as part of routine cardiac assessment

Members noted the potential cardiac arrhythmogenic effects of mexiletine, and confirmed that mexiletine should only be prescribed by a neurologist and after cardiology review, with monitoring as outlined in the SmPC.
Members agreed that for Primary Care to take over prescribing when patients are established on treatment the specialist service should confirm that all baseline monitoring is completed, and the arrangements for ongoing cardiac assessment.

The Group accepted the restricted local need for mexiletine 167mg hard capsules for the symptomatic treatment of myotonia in adults with non-dystrophic myotonic disorders, as outlined in SMC 2307.

SMC 2307 - Mexiletine 167mg hard capsules (Namuscla®) is routinely available in line with national guidance (SMC 2307).
Indication under review: for the symptomatic treatment of myotonia in adults with non-dystrophic myotonic disorders.
In a short-term, phase III, crossover study, mexiletine significantly improved muscle stiffness compared with placebo when measured on a visual analogue scale.
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 views from a Patient and Clinician Engagement (PACE) meeting.
It was classified 1b- available for restricted use under specialist supervision and 8c - treatment to be initiated in hospital prior to handover. FTEAM

8.4. FG1SMC 2420 - PEMBROLIZUMAB (CARCINOMA OF THE OESOPHAGUS, GASTROESOPHAGEAL JUNCTION ADENOCARCINOMA)

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

The Group considered the request for pembrolizumab in combination with platinum and fluoropyrimidine based chemotherapy for the first-line treatment of patients with locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma, as outlined in SMC 2420.

The Group noted that:
- pembrolizumab:
  - [for this indication] was accepted for use in NHS Scotland following a full submission assessed under the end of life medicine process, the output from the PACE process and application of SMC modifiers that can be applied when encountering high cost-effectiveness ratios
  - is used in combination with doublet chemotherapy, and in the clinical trial treatment

with pembrolizumab or chemotherapy was continued until unacceptable toxicity, disease progression or a maximum of 24 months
- evidence from KEYNOTE-590 showed that (for patients with PD-L1 CPS ≥ 10) pembrolizumab plus chemotherapy versus chemotherapy showed a statistically significant improvement in the primary efficacy outcome measures of progression-free survival (PFS) and overall survival
- interim analysis, July 2020, median overall survival 13.5 months versus 9.4 months; median PFS 7.5 months versus 5.5 months
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of pembrolizumab
- KEYNOTE-590 used three-weekly pembrolizumab, but a six-weekly regimen is now licensed and will be the preferred regimen locally

The Group accepted the restricted local need for pembrolizumab as outlined in SMC 2420.

SMC 2420 - Pembrolizumab 25mg/mL concentrate for solution for infusion (Keytruda®) is routinely available in line with national guidance (SMC 2420).
Indication under review: in combination with platinum and fluoropyrimidine-based chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a CPS≥10.
Restriction: treatment with pembrolizumab is subject to a two-year clinical stopping rule.
In a phase III study, pembrolizumab in combination with chemotherapy was associated with significantly improved progression-free survival and overall survival compared with chemotherapy 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.
This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.
It was classified as 1b – available for restricted use under specialist supervision and 8b recommended for hospital use only. Treatment must be initiated and supervised by specialist physicians experienced in the treatment of cancer. FTEAM

8.5. FG1SMC 2428 - DAPAGLIFLOZIN (CHRONIC KIDNEY DISEASE)

Mr Paterson declared a personal, non-specific interest in AstraZeneca UK Limited and took part in decision-making.

The Group considered the request for dapagliflozin for the treatment of chronic kidney disease in adults.

The Group noted:
- dapagliflozin (Forxiga®) is a selective and reversible sodium-glucose co-transporter-2 (SGLT2) inhibitor
- blocking the action of SGLT2 supports heart function in patients with heart failure and kidney function in patients with chronic kidney disease, regardless of having diabetes
- the cardiac and renal benefits of dapagliflozin are not solely dependent on the blood glucose-lowering effect and not limited to patients with diabetes mellitus
- dapagliflozin:
  - is the first SGLT2 inhibitor licensed for the treatment of chronic kidney disease
  - [for this indication] was superior to placebo in preventing the primary composite endpoint of ≥50% sustained decline in estimated glomerular filtration rate (eGFR), reaching end-stage kidney disease, cardiovascular or renal death (HR 0.61 [95%

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CI 0.51, 0.72]; p < 0.0001). The number needed to treat per 27 months was 19 (95% CI 15, 27). Based on the Kaplan-Meier curves, the dapagliflozin and placebo event curves began to separate early (4 months) and continued to diverge over the study period.
  - is taken at a dose of 10mg once a day, with a 5mg starting dose recommended for those with severe hepatic impairment
  - costs £36.59 (for 28 tablets regardless of dose)
- this will be a new additional cost for the Health Board, as dapagliflozin will be added to maximum tolerated renin-angiotensin-aldosterone system (RAAS) therapies
- that costs will be cumulative as this will be a long-term treatment option

Members discussed the significant changes in the use of SGLT2 inhibitors with the demonstration of reductions in cardiovascular events and there was a feeling that there are educational needs for Primary Care prescribers.
Members supported restricting prescribing in CKD patients to 'on the advice of a Renal Consultant/Physician'.

The Group accepted the restricted local need for dapagliflozin for the treatment of chronic kidney disease in adults, as outlined in SMC 2428.

SMC 2428 - Dapagliflozin 5mg, 10mg film-coated tablets (Forxiga®) is routinely available in line with national guidance (SMC 2428).
Indication under review:
For the treatment of chronic kidney disease in adults:
- **with an estimated glomerular filtration rate of ≥25 to ≤75mL/min/1.73m^2 at treatment initiation, and**
- **are receiving an angiotensin converting enzyme inhibitor or angiotensin receptor blocker (unless these are not tolerated or contraindicated), and**
- **have a urine albumin creatinine ratio of at least 23mg/mmoL, or type 2 diabetes mellitus or both**

Restriction: start treatment on the advice of a Renal Consultant/Physician.
In a randomised, double-blind, phase III study in patients with chronic kidney disease, treatment with dapagliflozin added to standard of care significantly reduced the risk of first occurrence of ≥50% sustained decline in estimated glomerular filtration rate, end stage renal disease, cardiovascular death or renal death when compared with standard of care alone.
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**

9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE - ISSUED AUGUST 2022

The Group noted the SMC provisional advice issued August 2022.

If the negative SMC recommendation is published next month, this medicine will not be included on the formulary for the indication in question.

10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS

10.1. PRESS STATEMENTS PUBLISHED JULY 2022

The Group noted the SMC advice published July 2022.

Following publication of the non-submission statements for enfortumab vedotin (Padcev®) ▼ SMC 2505 and vedolizumab (Entyvio®) SMC 2506, these medicines will not be included on the Grampian Joint Formulary for the indications in question.

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

- SMC 2438 crizanlizumab (Adakveo®) ▼ (submission received)
- SMC 2439 solriamfetol (Sunosi®) (clinicians not responded)
- SMC 2451 pegcetacoplan (Aspaveli®) ▼ (submission expected)
- SMC 2453 delafloxacin (Quofenix®) ▼ (submission expected)

Local advice for these medicines and indications will be included in the August 2022 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts'. **FTEAM**

UMAR SMC 2411 - ODEVIXIBAT (BYLVAY®)

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

Members noted the content of the SMC ultra-orphan medicines assessment report (UMAR) for odevixibat (Bylvay®).

Ms Doney confirmed that:

- odevixibat (Bylvay®) has been validated as meeting SMC ultra-orphan (UO) criteria and from 11 July 2022 it was available for prescribing within the ultra-orphan pathway while further evidence on its effectiveness is generated. After three years, the company will provide an updated submission to SMC for reassessment to allow a decision on its routine use in NHS Scotland to be made.
- UO medicines undergoing an initial assessment of evidence by the SMC are considered outwith remit for the Formulary Group

In line with local processes, the Group recorded Bylvay® [SMC 2411] as not routinely available in NHS Grampian.

SMC 2411 - Odevixibat 200microgram, 400microgram, 600microgram, 1,200microgram hard capsules (Bylvay®) ▼ is not routinely available in NHS Grampian.
Indication: for the treatment of progressive familial intrahepatic cholestasis (PFIC) in patients aged 6 months or older.
Not routinely available in NHS Grampian. If local need identified treatment is available through the National Services Scotland Ultra-Orphan Medicines Risk Share Scheme. **FTEAM**

10.2. PRESS STATEMENTS PUBLISHED AUGUST 2022

The Group noted the SMC advice published August 2022.

Following publication of the negative SMC recommendation, for remimazolam (Byfavo®) ▼ SMC 2454, this medicine will not be included on the Grampian Joint Formulary for the indication in question.

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

- SMC 2334 Trimbow® (beclometasone dipropionate/formoterol fumarate dihydrate/glycopyrronium) (submission expected)
- SMC 2409 Sibnayal® (potassium citrate/potassium hydrogen carbonate) (Clinicians not responded)
- SMC 2447 daratumumab (Darzalex®) (submission expected)
- SMC 2461 roxadustat (Evrenzo®) ▼ (submission expected)
- SMC 2492 atezolizumab (Tecentriq®) ▼ (Clinicians not responded)
- SMC 2493 somatrogon (Ngenla®) ▼ (submission expected)

ITEM	SUBJECT	ACTION
	Local advice for these medicines and indications will be included in the August 2022 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts'.	FTEAM

11. GENERAL INFORMATION FROM SCOTTISH MEDICINES CONSORTIUM - JULY AND AUGUST 2022

None.

12. DOCUMENTS FOR INFORMATION

Items 12.1 (Drug Safety Update June 2022), 12.2 (Drug Safety Update July 2022), 12.3 (Primary Care Prescribing Group (PCPG) minute May 2022) and 12.4 (Grampian Area Drug and Therapeutics Committee (GADTC) minute March 2022) were noted.

13. AOCB

POTASSIUM PERMANGANATE

Ms Cameron highlighted the recent National Patient Safety Alert regarding the inadvertent oral administration of potassium permanganate [https://www.england.nhs.uk/2022/04/inadvertent-oral-administration-of-potassium-permanganate/]. The PCPG had enquired if potassium permanganate could to be added to the formulary webpages to ensure clinicians were aware that it should not be prescribed without prior recommendation from a consultant/specialist.

Potassium permanganate is not a licensed medicine so would be considered outwith remit for Formulary Group. However, members agreed to host information on the formulary as the benefits for patient safety and staff education outweighed any issues regarding product licensing.

Information will be presented at a future meeting. **LC**

PROPOSAL FOR A SUMMER BREAK

The Chair proposed planning future meeting dates to include a summer break by cancelling the July meeting. Members supported the proposal. **FTEAM**

DATE OF NEXT MEETING

Tuesday 20 September 2022 starting at 14.30 via Microsoft Teams

CHAIR'S SIGNATURE  **DATE 20 SEPTEMBER 2022**