NHS GRAMPIAN
Minute of Formulary Group Meeting
Tuesday 15 August 2023 at 14:30 via Microsoft Teams

PRESENT	APOLOGIES	APPROVED
Miss R Anderson	Ms A Davie	
Ms L Cameron		
Dr V Chieng		
Ms F Doney (Vice-Chair)		
Dr E Elias		
Dr L Elliot (Chair)		
Mrs G McKerron		
Dr M Metcalfe (Vice-Chair)		
Mrs E Milne		
Mr M Paterson		

IN ATTENDANCE
Ms Dawn Bruce, Specialist Pharmacy Technician
Dr Andrew Hannah, Consultant Cardiologist, for item 3
Mrs Christine Standen, Formulary and Medicines Management Pharmacist

OBSERVER
Ms Lynne Davidson, Clinical Pharmacist, Cardiology, for item 3

Note some items were taken outwith agenda order.

ITEM	SUBJECT	ACTION
	WELCOME The Chair 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 20 JUNE 2023** 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 final approval.	**FD**
3.	**DISCUSSION - SGLT2 INHIBITORS FOR THE TREATMENT OF SYMPTOMATIC CHRONIC HFPEF** The Chair welcomed Dr Andrew Hannah, Consultant Cardiologist, to the meeting to discuss the formulary requests for the sodium-glucose cotransporter-2 (SGLT2) inhibitors, dapagliflozin and empagliflozin, for the treatment of symptomatic chronic heart failure with preserved ejection fraction (HFpEF). Dr Hannah provided the Group with an overview of HFpEF in the context of SGLT2 inhibitors for the management of HFpEF. Dr Hannah confirmed that: • heart failure with reduced ejection fraction (HFrEF) is generally defined as a left ventricular ejection fraction (LVEF) ≤40%, and above 40% EF has historically been defined as the HFpEF group. Although in the last few years there has been a bit of a distinction to patients with mildly reduced EF and those with entirely preserved EF.	

- patients with EF >40% is being discussed here, so includes a range of EFs, sometimes with EF entirely in the normal range
- this group of patients:
  - have the syndrome of heart failure despite not having reduced EF
  - is said to account for approximately 50% of all heart failure patients
  - is potentially a very heterogeneous group, with higher incidences in older populations and a significant proportion will die from non-cardiovascular reasons
- the two SGLT2 inhibitor trials are unique in HFpEF studies, as these are the first studies to show statistically positive primary outcomes. Although, there are some doubts over the magnitude of the benefits, as the benefit shown in the primary [composite] outcome was driven by a decrease in hospitalisations for heart failure.
- compared to EMPEROR-Preserved* the composite primary outcome of DELIVER† included urgent heart failure visits to outpatient or emergency departments in addition to cardiovascular death and heart failure hospitalisation
- in DELIVER reductions in the primary outcome were consistent in patients with and without recent hospitalisation
- it is difficult to exactly define HFpEF, but local protocols could be designed to ensure the SGLT2 inhibitors are not used if the diagnosis is doubtful - by being reasonably robust in the criteria to be met, e.g., elevated N-terminal pro–B-type natriuretic peptide (NT-proBNP) levels, echocardiographic left atrial dilation or left ventricular hypertrophy, as well as the clinical syndrome of heart failure
- SGLT2 inhibitor prescribing is justified in other conditions, e.g. type II diabetes mellitus, chronic kidney disease, both of which are risk factors for HFpEF. These would represent significant co-morbid groups so the numbers of 'pure' symptomatic HFpEF patients may not necessarily be a large number.

Dr Hannah answered questions from members, and confirmed that:

- these are relatively expensive drugs that have shown evidence of reduced hospitalisation [for heart failure]
- there is a limited but positive evidence base for SGLT2 inhibitors in HFpEF
- meta-analysis of all of the SGLT2 inhibitor trials (heart failure with reduced ejection fraction (HFrEF) and HFpEF trials) were largely consistent with somewhat linear benefits across all subgroups. Very high EFs may not benefit as much, but there was not a clear step-wise change when the trials were amalgamated.
- in DELIVER the relative benefits for patients with and without recent hospitalisation were similar but the absolute benefits were better in the recently hospitalised population
- there is a national discussion about SGLT2 inhibitors in HFpEF, and there is a range of views being expressed by Cardiologists
- the average length of hospital stay for people with decompensating heart failure is 8 to 12 days, and drugs that prevent hospitalisation do help the overall burden of cost of healthcare
- the mainstay of managing these patients is diuretics and will remain diuretics
- SGLT2 inhibitors:
  - are not difficult to use, there is no titration and they are used in other indications
  - provide an opportunity to impact how we deliver services to this patient group, with the potential to reduce bed days and have an impact on (re)admissions

The Chair thanked Dr Hannah for the informative discussion. Dr Hannah and Ms Davidson left before decision-making.

* EMPagliflozin outcomE tRial in Patients With chrOnic heaRt Failure With Preserved Ejection Fraction (EMPEROR-Preserved)

† Dapagliflozin Evaluation to Improve the LIVES of Patients With PReserved Ejection Fraction Heart Failure (DELIVER)

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4.2. SODIUM-GLUCOSE COTRANSPORTER-2 (SGLT2) INHIBITORS FOR HFPEF
- SMC 2523 EMPAGLIFLOZIN 10MG FILM-COATED TABLET (JARDIANCE®)
- SMC 2577 DAPAGLIFLOZIN 5MG, 10MG FILM-COATED TABLETS (FORXIGA®)

Mr Paterson declared a personal non-specific interest in relation to AstraZeneca UK Limited.

The Group considered the requests to include dapagliflozin and empagliflozin on the formulary for the treatment of symptomatic chronic HFpEF.

Members accepted that:

- the number of 'pure' symptomatic chronic HFpEF may not necessarily be very large, as a significant proportion of patients will have other pathologies that would require SGLT2 inhibitor treatment
- the SGLT2 inhibitors have shown benefit in the HFpEF population
- hospitalisation for heart failure is costly and associated with a high risk for subsequent rehospitalisation
- this request represents the introduction of an additional agent to the treatment regimen for HFpEF patients who are often an older population, and the adverse events profile in trials may not be representative of clinical practice
- there are no properly controlled studies on EF levels, but robust criteria could be developed by the specialist service
- DELIVER showed greater absolute benefits in the recently hospitalised population

The Group accepted the restricted local need for dapagliflozin in adults for the treatment of symptomatic chronic HFpEF. Acceptance is subject to the service developing robust protocol(s) for use. **AH/LD**

SMC 2577 - Dapagliflozin 5mg, 10mg film-coated tablets (Forxiga®) is routinely available in line with national guidance (SMC 2577).
Indication under review: in adults for the treatment of symptomatic chronic heart failure with left ventricular ejection fraction (LVEF) >40%.
SMC has issued separate advice for dapagliflozin in adults for the treatment of symptomatic chronic heart failure with reduced ejection fraction (SMC 2322).
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**

SMC 2523 – Empagliflozin 10mg film-coated tablets (Jardiance®) is not routinely available as there is a local preference for alternative medicines.
Indication under review: in adults for the treatment of symptomatic chronic heart failure with preserved ejection fraction (left ventricular ejection fraction [LVEF] >40%).
Not routinely available as there is a local preference for alternative medicines. **FTEAM**
People currently established on empagliflozin may continue to receive empagliflozin if they are subsequently diagnosed with symptomatic chronic heart failure with preserved ejection fraction.

4. MATTERS ARISING

4.1. ACTION LOG

The action log was noted.

Ms Doney reported that a 500microgram tablet of Jorveza® (budesonide orodispersible tablet) is now marketed, and the Formulary Team will contact the Gastroenterology Service to confirm if there is a local need for Jorveza® for the maintenance treatment of eosinophilic oesophagitis. **FTEAM**

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Jorveza®, as the 1mg strength, was accepted by SMC and included on the formulary only for the induction of remission. The new strength of Jorveza® and the licence extension to include maintenance treatment is considered outwith remit for SMC.

Item closed. **FTEAM**

4.3. ADRENALINE AUTO-INJECTORS

Ms Doney reported that in June the Medicines and Healthcare products Regulatory Agency (MHRA), with the support of allergy awareness advocates, launched a safety campaign to raise awareness of anaphylaxis and provide advice on the use of adrenaline auto-injectors. A toolkit of resources is now available for health and social care professionals to support the safe and effective use of adrenaline auto-injectors.

The formulary section will be updated with the new information and resources, and the information shared with prescribers via MedWatch. **LC**

Item closed. **FTEAM**

5. FORMULARY GROUP DECISIONS JUNE 2023 - PUBLISHED 03/07/2023

Members ratified the decisions of the June 2023 meeting as published.

6. NETFORMULARY/FORMULARY REVIEW

6.1. FORMULARY UPDATES - AUGUST 2023

Mr Paterson declared a personal non-specific interest in relation to AstraZeneca UK Limited.

The Group reviewed the Formulary Team's summary document highlighting some new products, new generic medicines and discontinued medicines.

The Group ratified the Formulary Team's decision to categorise and publish GoResp® Digihaler® as non-formulary as the Respiratory Managed Clinical Network (MCN) has not reviewed the evidence for use, the product costs £75.63 per device, and there are disposal issues (it contains a lithium-manganese dioxide battery and must not be thrown away via household waste).

The Group supported the changes proposed by the Formulary Team:

- minor changes to the current formulary website entries for the new generic medicines that have been included on the Scottish Drug Tariff (apixaban, sitagliptin, lacosamide and calcipotriol 0.005%/betamethasone dipropionate 0.05% gel and ointment), amend the entries to remove the brand names and where appropriate add a note advising to prescribe generically
- note sitagliptin as the preferred first-choice dipeptidyl peptidase 4 inhibitor, with alogliptin (Vipidia®) changed to the second-choice product
- minor change to the current website entry for the non-formulary medicine adefovir dipivoxil (Hepsera®), amend to note that this product is now withdrawn from use/discontinued
- create an entry for generic fluticasone propionate nasal drops, with advice to prescribe generically, and note that Flixonase® Nasule® are discontinued
- minor change to the current website entry for the formulary medicine Suboxone® sublingual film, amend to note that this product is now discontinued
- create entries for the non-formulary product sufentanil citrate, noting that the brand Zalviso® is withdrawn and Dzuveo® as non-formulary **FTEAM**

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6.2. RESPIRATORY UPDATE

Ms Doney reported that:

- the Respiratory MCN supports AeroChamber® Plus Flo-Vu® as its preferred spacer device because it considers that this device demonstrates strong evidence for increased lung deposition of inhaled medication.
  Devices are considered outwith remit for the Formulary Group, however information will be linked to the formulary to highlight the MCN's preferred spacer device. **FTEAM**
- another 'generic Fostair® pressurised metered dose inhaler' has come to market, Bibecfo®, it costs significantly less than Luforbec®.
  Lupin, the manufacturer of Luforbec®, is currently reviewing its pricing to be more competitive. The change may take 6 to 10 weeks to come through the MHRA but the MCN is not minded to change its prescribing advice so soon after publication.

The Formulary Team will monitor the price of Luforbec®. **FTEAM**

6.3. SBAR - BUCCAL MIDAZOLAM (EPISTATUS® OROMUCOSAL SOLUTION PRE-FILLED SYRINGES)

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

The Group considered the information submitted on behalf of the Specialist Paediatric Epilepsy Service requesting addition of three new strengths of buccal midazolam, as Epistatus® pre-filled syringes.

The Group noted that:

- Epistatus® as the licensed 10mg pre-filled syringe, and unlicensed 5mL multi-dose bottle is included on the formulary for the treatment of prolonged, acute, convulsive seizures
- the 10mg pre-filled syringe is licensed for children and adolescents 10 years to less than 18 years, and is used off-label in adults
- the pre-filled syringes do not have volume graduations
- in NHS Grampian children's services, buccal midazolam is commonly prescribed under the direction of the paediatric epilepsy service as rescue treatment for status epilepticus
- due to safety concerns with other licensed brands of buccal midazolam, Epistatus® 10mg/1mL oromucosal solution remains the recommended brand option within Scotland, in line with the guidance from the Scottish Paediatric Epilepsy Network (SPEN)
- pre-filled syringes allow quick administration of buccal midazolam in an emergency situation without the need to draw up a specific volume from a multi-dose bottle
- buccal midazolam continues to be prescribed within Scotland using weight-based dosing of 0.3mg/kg (maximum 10mg) and therefore patients' midazolam doses will be rounded to the nearest appropriate pre-filled syringe size. It may be necessary for some patients to remain on the unlicensed multi-dose bottle under the direction of the paediatric epilepsy team.
- looking at medicines costs alone, the cost per dose of licensed Epistatus® is higher than the unlicensed multi-dose bottle, however once opened the multi-dose bottle has an in-use shelf-life, so four doses may not be administered within this period and if this happens the cost per dose is higher than the pre-filled syringes. Also, there may be additional charges applied to orders (handing/carriage fees) for unlicensed products.
- unlicensed Epistatus® is no longer included on the Scottish Drug Tariff so prices may increase with time, particularly if usage falls with the introduction of the new strength syringes

The Formulary Group accepted the restricted local need for Epistatus® 2.5mg, 5mg and 7.5mg pre-filled syringes without the need for a full submission. Acceptance is subject to dissemination of information for prescribers to ensure patients are not switched to these

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new products before patients/caregivers have undertaken training on the use of the new syringes. The service/requestor to liaise with Medicines Information and the Medication Safety Officer before releasing the information. **RACH**

SBAR - Midazolam 2.5mg, 5mg, 7.5mg oromucosal solution in pre-filled oral syringe (Epistatus®) is routinely available in line with local guidance.
Indication under review: for the treatment of prolonged, acute, convulsive seizures in infants, toddlers, children and adolescents aged from 3 months to less than 18 years.
Epistatus® must only be used by parents/caregivers where the patient has been diagnosed to have epilepsy.
For infants between 3 - 6 months of age treatment should be in a hospital setting where monitoring is possible and resuscitation equipment is available.
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**

6.4. COVID MEDICINES FORMULARY SECTION UPDATE

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

Ms Doney reported that the NICE/SMC collaboration advice for COVID medicines was published after the June meeting, and subsequently the Antibiotic Pharmacists requested that dexamethasone, which is also used in the management of COVID, is included in the COVID-19 therapeutics section of the formulary.

Following review of national guidance the Formulary Team proposed update of the COVID-19 therapeutics formulary section to include:

- dexamethasone on formulary, with a link to national guidance
- Molnupiravir®. Although currently under appeal with National Institute for Health and Care Excellence (NICE) it is still available within the current prescribing pathway. The proposal is to include on formulary with a link to the national guidance.
- Ronapreve® (casirivimab plus imdevimab), noting that this product has been discontinued. [The Conditional Marketing Authorisation was discontinued by the manufacturer, this was a business decision due to a reduced patient need].

The Group supported the proposed updates to the COVID-19 therapeutics section of the formulary. **FTEAM**

7. OTHER BUSINESS

7.1. CHIEF MEDICAL OFFICER SCOTLAND ANNUAL REPORT 2022 - 2023

Members noted the content of the Chief Medical Officer Scotland annual report.

Ms Doney confirmed that the Formulary Team will consider if it may be possible to add something to the reviews/decision-making to support sustainability and realistic medicine. **FTEAM**

8. NEW PRODUCT REQUESTS

8.1. SMC 2474 - PEMBROLIZUMAB (ENDOMETRIAL CARCINOMA)

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

The Group considered the request for pembrolizumab in combination with lenvatinib, for the treatment of advanced or recurrent endometrial carcinoma in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation.

The Group noted that:

- pembrolizumab:
  - was accepted for restricted use in NHS Scotland following a full submission assessed under the end-of-life and orphan equivalent medicine process, the output from the PACE process, and application of SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios
  - is administered as an intravenous infusion over 30 minutes at a dose of either 200mg every 3 weeks or 400mg every 6 weeks
  - [for this indication] is given in combination with lenvatinib at a dose of 20mg (2 x 10mg capsules) orally once a day
  - is already included on the formulary for multiple indications
- the SMC advice takes account of the benefits of Patient Access Schemes that improve the cost-effectiveness of both pembrolizumab and lenvatinib
- lenvatinib is available as two different brands, Kisplyx® and Lenvima®. Only the Lenvima® brand is licensed in combination with pembrolizumab for this indication
- Lenvima® is already included on formulary for hepatocellular and thyroid carcinoma
- evidence comes from KEYNOTE-775:
  - pembrolizumab plus lenvatinib improved the median progression-free survival (PFS) by about 3 months and overall survival (OS) by about 5 to 7 months. The median duration of treatment in the pembrolizumab-lenvatinib group was 7.59 months.
  - which only recruited patients with an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1
- SMC has restricted treatment with pembrolizumab to 2 years, but if patients reach 2 years of treatment they will continue on lenvatinib monotherapy
- dostarlimab is included on formulary for a sub-group of this patient population – for the treatment of adults with mismatch repair deficient/ microsatellite instability-high recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen. The service wishes to have both regimens available.
- minimal offset is available from the displacement of cisplatin plus doxorubicin

The Group accepted the restricted local need for pembrolizumab in combination with lenvatinib, for the treatment of advanced or recurrent endometrial carcinoma in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation, as outlined in SMC 2474.

SMC 2474 - Pembrolizumab 25mg/mL concentrate for solution for infusion (Keytruda®) is routinely available in line with national guidance (SMC 2474).
Indication under review: in combination with lenvatinib, for the treatment of advanced or recurrent endometrial carcinoma in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation.
Restriction: treatment with pembrolizumab is subject to a two-year clinical stopping rule.
Pembrolizumab in combination with lenvatinib improved progression-free and overall survival compared with chemotherapy in patients with advanced or recurrent endometrial cancer who had disease progression on or after platinum-based chemotherapy.
This advice takes account of the benefit of Patient Access Schemes (PAS) that improve the cost effectiveness of pembrolizumab and lenvatinib. This advice is contingent upon the continuing availability of these PAS in NHS Scotland or list prices that are equivalent or lower.
This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

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	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**
	SMC 2474 - Lenvatinib 4mg, 10mg hard capsules (Lenvima®) is routinely available in line with national guidance (SMC 2474). **Indication under review: in combination with pembrolizumab, for the treatment of advanced or recurrent endometrial carcinoma in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation.** **This advice takes account of the benefit of Patient Access Schemes (PAS) that improve the cost effectiveness of pembrolizumab and lenvatinib. This advice is contingent upon the continuing availability of these PAS in NHS Scotland or 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 should be initiated and supervised by a healthcare professional experienced in the use of anticancer therapies.**	**FTEAM**

8.2. SMC 2538 - PEMBROLIZUMAB (TRIPLE-NEGATIVE BREAST CANCER (TNBC))

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

The Group considered the request for pembrolizumab in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, for the treatment of adults with locally advanced, or early stage triple-negative breast cancer (TNBC) at high risk of recurrence.

The Group noted that:

- patients should be treated with neoadjuvant pembrolizumab in combination with chemotherapy for 8 doses of 200mg every 3 weeks or 4 doses of 400mg every 6 weeks or until disease progression that precludes definitive surgery or unacceptable toxicity, followed by adjuvant treatment with pembrolizumab as monotherapy for 9 doses of 200mg every 3 weeks or 5 doses of 400mg every 6 weeks or until disease recurrence or unacceptable toxicity
- pembrolizumab is already included on formulary with paclitaxel or nab-paclitaxel for the treatment of locally recurrent unresectable or metastatic TNBC in adults whose tumours express programmed death-ligand 1 (PD-L1) with a combined positive score (CPS)≥10 and who have not received prior chemotherapy for metastatic disease
- pembrolizumab for this indication is licensed for use in patients at high-risk of recurrence, and the service plan to use the same criteria for high-risk as KEYNOTE-522
- evidence for this indication comes from KEYNOTE-522:
  - patients had an ECOG score of 0 or 1
  - the difference in pathological complete response rate was 7.5% favouring chemotherapy plus pembrolizumab
  - the difference in event-free survival rate at 42 month follow up was 8.6% favouring the chemotherapy plus pembrolizumab arm
- this represents a new cost in the (neo)adjuvant setting, however, the service has stated that patients receiving (neo)adjuvant pembrolizumab would not receive any PD1/PDL1 treatment in the advanced disease setting

The Group accepted the restricted local need for pembrolizumab in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, for the treatment of adults with locally advanced, or

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early stage TNBC at high risk of recurrence.

SMC 2538 - Pembrolizumab 25mg/mL concentrate for solution for infusion (Keytruda®) is routinely available in line with national guidance (SMC 2538).
Indication under review: in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, for the treatment of adults with locally advanced, or early stage triple-negative breast cancer (TNBC) at high risk of recurrence.
In a randomised, double-blind phase III study, the addition of pembrolizumab to neoadjuvant chemotherapy followed by adjuvant pembrolizumab monotherapy significantly improved the pathological complete response rate and event-free survival compared with placebo.
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. Therapy must be initiated and supervised by specialist physicians experienced in the treatment of cancer. **FTEAM**

8.3. SMC 2525 - POLATUZUMAB (DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL))

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

The Group considered the request for polatuzumab in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) for the treatment of adults with previously untreated diffuse large B-cell lymphoma (DLBCL). The company asked the SMC to restrict use to patients with an International Prognostic Index (IPI) score of 2 to 5.

The Group noted that:

- polatuzumab:
  - is currently included on the formulary, on an interim basis subject to ongoing evaluation and future reassessment, in combination with bendamustine and rituximab for the treatment of adults with relapsed or refractory DLBCL who are not candidates for haematopoietic stem cell transplant
  - [for this indication] was accepted for restricted use in NHS Scotland following a full submission assessed under the end-of-life and orphan equivalent medicine process and the output from the PACE process
  - is administered intravenously at a dose of 1.8mg/kg every 21 days in combination with R-CHP for 6 cycles. Cycles 7 and 8 consist of rituximab monotherapy.
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of polatuzumab
- In the POLARIX trial there was a statistically significant improvement in investigator PFS in the pola-R-CHP group compared with the R-CHOP group. The number of events was 107 vs 134 and the Kaplan-Meier (KM) estimated PFS at 24 months was 77% vs 70% for pola-R-CHP vs R-CHOP respectively.
- the available data do not show a benefit in OS for polatuzumab plus R-CHP over R-CHOP. At the pre-specified final analysis, OS results were still immature and did not meet the pre-specified threshold for statistical significance.
- subgroup analysis did not show a clear benefit with pola-R-CHP in patients 60 years of age or younger, patients with the germinal-center B-cell-like subtype of DLBCL, patients who had bulky disease, and patients who had lower IPI scores. However, subgroup analyses were exploratory and the POLARIX study was not powered to compare subgroups.
- the Service stated that polatuzumab in combination with R-CHP will be used first-line in patients who are fit to receive R-CHOP, so minimal offset is available as polatuzumab will replace vincristine

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The Group accepted the restricted local need for polatuzumab in combination with R-CHP for the treatment of adults with previously untreated DLBCL and an IPI score of 2 to 5.

SMC 2525 - Polatuzumab vedotin 30mg, 140mg powder for concentrate for solution for infusion (Polivy®) ▼ is routinely available in line with national guidance (SMC 2525).
Indication under review: in combination with rituximab, cyclophosphamide, doxorubicin and prednisone (R-CHP) for the treatment of adults with previously untreated diffuse large B-cell lymphoma (DLBCL) and an International Prognostic Index (IPI) score of 2 to 5.
Polatuzumab vedotin, in combination with R-CHP, resulted in a statistically significant improvement in investigator-assessed progression-free survival compared with rituximab, cyclophosphamide, vincristine, doxorubicin and prednisone (R-CHOP).
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. Polatuzumab must only be administered under the supervision of a healthcare professional experienced in the diagnosis and treatment of cancer patients. FTEAM

8.4. SMC 2524 - POLATUZUMAB (RELAPSED OR REFRACTORY DLBCL)

The Group considered the SMC reassessment, considered under the end of life and orphan equivalent medicine process, for polatuzumab in combination with bendamustine and rituximab for the treatment of adults with relapsed or refractory DLBCL who are not candidates for haematopoietic stem cell transplant.

It was confirmed that:
- in 2020 polatuzumab vedotin was accepted on an interim basis for adults with relapsed or refractory DLBCL who are not candidates for haematopoietic stem cell transplant (SMC 2282), as at that time polatuzumab had a Conditional Marketing Authorisation
- polatuzumab now has a full marketing authorisation and was accepted by SMC for use in NHS Scotland following a reassessment under the end of life and orphan equivalent medicine process (SMC 2524)
- on review of the SMC reassessment and supporting documentation, the only change identified between the interim advice and the reassessment, is a change in the PAS price of polatuzumab

The Group accepted the restricted local need for polatuzumab in combination with bendamustine and rituximab for the treatment of adults with relapsed or refractory DLBCL who are not candidates for haematopoietic stem cell transplant, without the need for a full submission.

SMC 2524 - Polatuzumab vedotin 30mg, 140mg powder for concentrate for solution for infusion (Polivy®) ▼ is routinely available in line with national guidance (SMC 2524).
Indication under review: in combination with bendamustine and rituximab for the treatment of adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant (HSCT).
In a phase Ib/II study, polatuzumab vedotin in combination with bendamustine and rituximab resulted in an increase in complete response rate compared with bendamustine and rituximab alone.

ITEM	SUBJECT	ACTION
	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.** **SMC previously accepted polatutuzumab for use in this indication on an interim basis (SMC 2282). This supersedes that advice.** **It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only. Polatuzumab must only be administered under the supervision of a healthcare professional experienced in the diagnosis and treatment of cancer patients.**	FTEAM

8.5. FG1SMC 2545 - TRASTUZUMAB DERUXTECAN (HER2-POSITIVE BREAST CANCER)

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

The Group considered the request for trastuzumab deruxtecan (Enhertu®) as monotherapy for the treatment of adults with unresectable or metastatic HER2-positive breast cancer who have received one prior anti- human epidermal growth factor receptor 2 (HER2)-based regimen.

The Group noted that:

- trastuzumab deruxtecan as Enhertu® ▼:
  - is currently included on the formulary as monotherapy for the treatment of adults with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens, so this request would move treatment up to second-line
  - is administered at a recommended dose of 5.4mg/kg given as an IV infusion every three weeks until disease progression
- in DESTINY-Breast03:
  - only patients with an ECOG performance score of 0 or 1 were recruited, so efficacy and tolerability in poorer performance status is unknown
  - subgroup analysis in patients who had received 0 or 1 previous lines of therapy showed a PFS of 22.4 months versus 8 months for trastuzumab deruxtecan and trastuzumab emtansine respectively
  - the toxicities observed with trastuzumab deruxtecan were described as clinically significantly different from those observed with trastuzumab emtansine and tolerability of trastuzumab deruxtecan appears lower. An important safety concern is the risk of interstitial lung disease/pneumonitis.
  - the median duration of treatment in the trastuzumab deruxtecan group was 14.3 months and 6.9 months in the trastuzumab emtansine group
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of trastuzumab deruxtecan
- trastuzumab deruxtecan will replace trastuzumab emtansine in the second-line setting

The Group accepted the restricted local need for trastuzumab deruxtecan (Enhertu® ▼) for the treatment of adults with unresectable or metastatic HER2-positive breast cancer who have received one prior anti-HER2-based regimen, as outlined in SMC 2545.

SMC 2545 - Trastuzumab deruxtecan (Enhertu®) ▼ is routinely available in line with national guidance (SMC 2545).
Indication under review: as monotherapy for the treatment of adults with unresectable or metastatic HER2-positive breast cancer who have received one prior anti-HER2-based regimen.
In a phase III study, trastuzumab deruxtecan was associated with significantly improved progression-free survival compared with an antibody-drug conjugate medication.

ITEM	SUBJECT	ACTION
	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.** **SMC has previously issued advice (SMC 2388) accepting trastuzumab deruxtecan (Enhertu® ▼) for use within NHS Scotland on an interim basis subject to ongoing evaluation and future reassessment as monotherapy for the treatment of adults with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens. This advice remains valid.** **It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only.** **Enhertu® ▼ 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.** **Enhertu® ▼ should not be substituted with trastuzumab or trastuzumab emtansine.**	**FTEAM**

8.6. FG1SMC 2314 - BRIGATINIB (ALK-POSITIVE ADVANCED NSCLC)

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

The Group considered the request for brigatinib monotherapy for the treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with an ALK inhibitor.

The Group noted that:

- January 2021, following an abbreviated submission reviewed by the SMC executive, brigatinib was accepted for use in NHS Scotland as monotherapy for the treatment of adults with ALK-positive advanced NSCLC previously not treated with an ALK inhibitor
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of brigatinib
- brigatinib:
  - is currently included on formulary as monotherapy for the treatment of adults with ALK-positive advanced NSCLC previously treated with crizotinib, and this request would move treatment to first-line use
  - is administered orally, at a recommended starting dose of 90mg once-daily for 7 days, then 180mg once-daily
- the North Cancer Alliance (NCA) clinical management guideline for NSCLC recommends alectinib or brigatinib as first-line choices for stage III or IV disease
- alectinib is already included on the formulary for this indication
- there are no comparative data for alectinib and brigatinib, however an indirect treatment comparison submitted by the company for the NICE review [TA670], suggested the two agents had similar PFS
- compared with alectinib, brigatinib has a reduced treatment burden (1 tablet per day compared with 8 tablets per day)
- cost-offset is available as brigatinib will be an alternative first-line option to other oral tyrosine kinase inhibitors (TKIs)
- lorlatinib, another oral TKI, is also accepted by SMC for first-line use, but it is not included on the formulary, currently the service does not wish to add lorlatinib to formulary [for this indication]

The Group accepted the restricted local need for brigatinib monotherapy as an additional oral TKI treatment option for adults with ALK-positive advanced NSCLC previously not treated with an ALK inhibitor.

ITEM	SUBJECT	ACTION

SMC 2314 - Brigatinib 30mg, 90mg, 180mg film-coated tablets (Alunbrig®) ▼ is routinely available in line with national guidance (SMC 2314).
Indication under review: as monotherapy for the treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with an ALK inhibitor.
Brigatinib offers an additional treatment choice in the therapeutic class of tyrosine kinase inhibitors for this indication.
Medicines within this therapeutic class have been accepted via the orphan process for this indication.
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 brigatinib should be initiated and supervised by a physician experienced in the use of anticancer medicinal products.
ALK-positive NSCLC status should be known prior to initiation of brigatinib therapy. A validated ALK assay is necessary for the selection of ALK-positive NSCLC patients. Assessment for ALK-positive NSCLC should be performed by laboratories with demonstrated proficiency in the specific technology being utilised. **FTEAM**

LORLATINIB (ALK-POSITIVE ADVANCED NSCLC)

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

The Group supported the position that there is currently not a local need for lorlatinib monotherapy as an additional oral TKI treatment option for adults with ALK-positive advanced NSCLC previously not treated with an ALK inhibitor.

SMC 2415 - Lorlatinib 25mg, 100mg film-coated tablets (Lorviqua®) ▼ is not routinely available as there is a local preference for alternative medicines.
Indication under review: as monotherapy for the treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously not treated with an ALK inhibitor.
Not routinely available as there is a local preference for alternative medicines. **FTEAM**

8.7. FG1SMC 2533 - AZACITIDINE (ACUTE MYELOID LEUKAEMIA (AML))

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

The Group considered the request for oral azacitidine, as Onureg®, as maintenance therapy in adults with acute myeloid leukaemia (AML) who achieved complete remission or complete remission with incomplete blood count recovery following induction therapy with or without consolidation treatment and who are not candidates for, including those who choose not to proceed to, haematopoietic stem cell transplantation.

The Group noted that:
- oral azacitidine, for this indication, was accepted for use in NHS Scotland following a full submission assessed under the end of life and orphan equivalent medicine process, the output from the PACE process, and application of SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of oral azacitidine
- Onureg® is the first licensed oral formulation of azacitidine, a subcutaneous formulation of azacitidine is licensed and included on formulary for other indications
- the oral and subcutaneous formulations of azacitidine should not be used

interchangeably due to differences in the exposure, dose, schedule recommendations and licensing
- currently there are no established maintenance treatments for most patients with AML who are ineligible for haematopoietic stem cell transplantation. People with FLT3 mutation positive AML have the option of maintenance therapy with midostaurin.
- for maintenance therapy, the recommended dose is 300mg azacitidine orally once daily. Each repeated 28-day cycle consists of a treatment period of 14 days followed by a 14-day treatment-free period.
- in the case of disease relapse [with 5% to 15% blasts in peripheral blood or bone marrow, in conjunction with a clinical assessment] an extension of the dosing schedule from 14 to 21 days of repeated 28-day cycles may be considered
- in the licensing study, QUAZAR AML-001, and the median OS was 24.7 months vs 14.8 months for oral azacitidine and placebo respectively
- patient numbers are expected to be small, and cost off-set is available for patients who are FLT3 mutation-positive, as azacitidine would be an alternative to midostaurin

The Group accepted the restricted local need for oral azacitidine maintenance therapy in adults with AML, in line with SMC 2533.

SMC 2533 - Azacitidine 200mg, 300mg film-coated tablets (Onureg®) is routinely available in line with national guidance (SMC 2533).
Indication under review: maintenance therapy in adults with acute myeloid leukaemia who achieved complete remission or complete remission with incomplete blood count recovery following induction therapy with or without consolidation treatment and who are not candidates for, including those who choose not to proceed to, haematopoietic stem cell transplantation.
Oral azacitidine plus best supportive care resulted in statistically significant improvements in overall survival and relapse-free survival, when compared with placebo plus best supportive care.
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 should be initiated and monitored under the supervision of a physician experienced in the use of chemotherapeutic medicinal products. **FTEAM**

SUBCUTANEOUS AZACITIDINE MONOTHERAPY FOR AML

Mrs Standen reported that:
- at the October 2022 meeting, it was noted that subcutaneous azacitidine monotherapy for the treatment of adults with AML would ultimately be replaced by combination therapy with venetoclax. However, there may be occasional patients where a step-down from venetoclax/azacitidine combination therapy was required.
- at the time, members felt that it was too early to remove azacitidine monotherapy for AML from the formulary, and requested review of this position in 6 to 9 months
- the haematology pharmacist has confirmed that in 2023 no AML patients have received azacitidine monotherapy but >5 patients have received azacitidine in combination with venetoclax

The Group accepted there was no longer a local need for subcutaneous azacitidine monotherapy for the treatment of adults who are not eligible for haematopoietic stem cell transplantation with AML.

ITEM	SUBJECT	ACTION
	Azacitidine 25mg/mL powder for suspension for injection is not routinely available as there is a local preference for alternative medicines. **Indication under review: as monotherapy for the treatment of adults who are not eligible for haematopoietic stem cell transplantation (HSCT) with acute myeloid leukaemia (AML).** **Not routinely available as there is a local preference for alternative medicines.**	**FTEAM**
	This item will be removed from the Action Log.	**FTEAM**

9. SMC PROVISIONAL ADVICE ISSUED - AUGUST 2023

The Group noted the SMC provisional advice issued August 2023.

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

10. PUBLISHED ADVICE - JULY AND AUGUST 2023

10.1. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE - JULY 2023

The Group noted the SMC advice published July 2023.

Following publication of the negative SMC recommendation, for ropeginterferon alfa-2b (Besremi®)▼ SMC 2563, this medicine will not be included on the Grampian Joint Formulary for the indication in question.

The following SMC accepted medicine has not been processed within a 60-day timescale:

- SMC 2579 - apalutamide (Erleada®) (submission expected)

Local advice for this medicine and indication will be included in the August 2023 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts'. **FTEAM**

10.1.1. UMAR SMC 2583 - BELUMOSUDIL

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

Ms Doney reported that since issuing the meeting papers the Scottish Government Medicines Policy Branch has confirmed that this medicine is available for prescribing within the ultra-orphan pathway, i.e., Sanofi has met all the conditions of the ultra-orphan pathway, including providing a data collection plan and a Patient Access Scheme.

In line with local processes, the Group recorded belumosudil (Rezurock®)▼ as 'not routinely available in NHS Grampian. If local need identified treatment is available through the National Services Scotland Ultra-orphan medicines Risk Share Scheme.'

SMC 2583 - Belumosudil 200mg film-coated tablet (Rezurock®)▼ is not routinely available in NHS Grampian.
Indication under review: treatment of patients aged 12 years and older with chronic graft-versus-host disease (chronic GvHD) who have received at least two prior lines of systemic therapy.
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**

ITEM	SUBJECT	ACTION

10.1.2. SMC 2546 - AVALGLUCOSIDASE ALFA

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

The Group noted that:

- Pompe disease is a rare metabolic disorder with treatments initiated on the direction of the Scottish Inherited metabolic disorders (IMD) service
- following an abbreviated submission the SMC accepted avalglucosidase alfa for use in NHS Scotland, and the advice takes account of the benefits of a PAS that improves the cost-effectiveness of avalglucosidase alfa
- to ensure the Health Board can access the appropriate funding stream, IMD risk-share, avalglucosidase alfa should be included on the formulary

The Formulary Group accepted the restricted local need for avalglucosidase alfa (Nexviadyme®) in line with SMC 2546.

SMC 2546 - Avalglucosidase alfa 100mg powder for concentrate for solution for infusion (Nexviadyme®)▼ is routinely available in line with national guidance (SMC 2546).
Indication under review: long-term enzyme replacement therapy for the treatment of patients with Pompe disease (acid α-glucosidase deficiency).
Avalglucosidase alfa offers an additional treatment choice of enzyme replacement therapy for acid α-glucosidase deficiency.
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 should be supervised by a physician experienced in the management of patients with Pompe disease or other inherited metabolic or neuromuscular diseases. **FTEAM**

10.2. NCMAG ADVICE PUBLISHED - JULY 2023

The Group noted the NCMAG advice published July 2023

The following NCMAG supported medicines have not been processed within a 60-day timescale

- NCMAG 109 - pemetrexed
- NCMAG 110 - abiraterone (submission expected)

Local advice for these medicines and indications will be included in the August 2023 decisions as 'Not routinely available as the ADTC is waiting for further advice from local clinical experts'. **FTEAM**

10.3. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE - AUGUST 2023

The Group noted the SMC advice published August 2023.

Following publication of the negative SMC recommendations and non-submission statements, Acarizax® (Dermatophagoides pteronyssinus and Dermatophagoides farina) SMC 2613, aflibercept (Eylea®) SMC 2612, baricitinib (Olumiant®) SMC 2572 and selumetinib (Koselugo®)▼ SMC 2540, 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 2602 - icosapent ethyl (Vazkepa®)▼
- SMC 2541 - tezepelumab (Tezspire®)▼ (submission expected)

ITEM	SUBJECT	ACTION
	Local advice for these medicines and indications will be included in the August 2023 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 2023

None.

12. DOCUMENTS FOR INFORMATION

ITEM 12.1 (DRUG SAFETY UPDATE JUNE 2023)

Miss Anderson confirmed that the local guidelines for the acute management of hyperkalaemia in adults has just been updated and published to ensure it aligns with the Adult Renal Association Clinical Practice Guidelines (2020) for the treatment of severe hyperkalaemia.

Items 12.2 (Drug Safety Update July 2023), 12.3 (MedWatch Vol.4 Issue 2 June 2023), 12.4 (Medicine Guidelines and Policies Group (MGPG) minute March 2023), 12.5 and 12.6 (Grampian Area Drug and Therapeutics Committee (GADTC) minute March and May 2023) were noted.

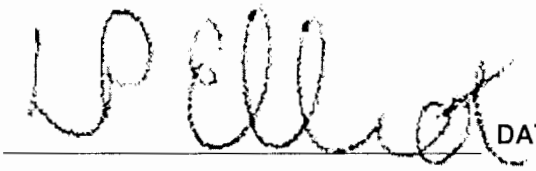
13. AOCB

THANK YOU AND GOODBYE

The Chair confirmed that Dr Elias was leaving NHS Grampian and this was his last meeting. The Chair thanked Dr Elias for all of his feedback and work within the Group, his input will be missed. Members wished him all the best for the future.

DATE OF NEXT MEETING

Tuesday 19 September 2023 starting at 14.30 via Microsoft Teams

CHAIR'S SIGNATURE  **DATE 19 SEPTEMBER 2023**