# NHS GRAMPIAN
## Minute of Formulary Group Meeting
## Tuesday 19 October 2021 at 14:30 via Microsoft Teams

| PRESENT | APOLOGIES | APPROVED |
|---|---|---|
| Ms L Cameron | Ms M Galvin | |
| Ms A Davie | Mrs G McKerron | |
| Ms F Doney | Mr R Sivewright | |
| Dr L Elliot | | |
| Dr J Fitton (from item 3 until item 8.10) | | |
| Professor J McLay (Chairman) | | |
| Dr M Metcalfe (until 8.10) | | |
| Mrs L Montgomery | | |
| Mrs K Neave | | |
| Dr J Newmark (from item 8.1 until 8.10) | | |
| Mrs S O'Beirne | | |
| Mr M Paterson | | |

Note some items were taken outwith the agenda order.

**IN ATTENDANCE**
Dr Lindsay Robertson, Consultant Rheumatologist and Clinical Lead for Rheumatology (for items 8.1 to 8.3)
Ms Christine Hay, Formulary and Medicines Management Pharmacist
Mrs Anne Rembisz, Formulary Team Administrator (observer)

| ITEM | SUBJECT | ACTION |
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| | The Chairman welcomed members, opened the meeting and noted that a quorum was present. | |
| | The Chairman confirmed that two new members joined the Group in October, Ms Lindsay Cameron the Medication Safety Officer, and Mrs Grace McKerron, Chief Nurse Corporate. | |
| | Mrs McKerron was unable to attend today, but the Chairman welcomed Ms Cameron to the meeting. | |
| | The Chairman also welcomed Mrs Anne Rembisz to the meeting as an observer. Mrs Rembisz is a new member of the Formulary Team and in future will attend meetings as the minute-taker. | |
| **1.** | **APOLOGIES** | |
| | Apologies for absence were requested and noted. | |
| **2.** | **DRAFT MINUTE OF THE MEETING HELD 21 SEPTEMBER 2021** | |
| | The Group accepted the draft note of the September meeting subject to minor typographical changes. | **FTEAM** |
| | The corrected final approved minute will be in the public domain within 21 days of approval. | **FD** |
| **3.** | **PRESENTATION/DISCUSSION** | |
| | Dr Lindsay Robertson, Consultant Rheumatologist and Clinical Lead for Rheumatology, attended the meeting to discuss the submissions for the Janus Kinase (JAK) inhibitors, upadacitinib and filgotinib. | |
| | Dr Robertson provided the Group with an update on the use of JAK inhibitors in rheumatological conditions and the need for additional disease-modifying antirheumatic | |

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drugs (DMARDs) for patients that are refractory to treatment or those that experience treatment waning with current agents.

Dr Robertson confirmed that:
- biologic DMARDs (bDMARDs) have transformed the outcomes for rheumatoid arthritis (RA)
- despite having a lot of different DMARDs/bDMARDs there are patients that are refractory to current treatment options, and those that experience treatment waning and progress to third, fourth and fifth bDMARDs
- new drugs with different targets/that work on different pathways/parts of pathway are always welcomed
- two JAK inhibitors, tofacitinib and baricitinib, are already on the formulary, they inhibit the JAK1, JAK2 and JAK3 enzymes by varying degrees
- filgotinib and upadacitinib only block JAK1, which may be more favourable as it seems they have less adverse events in respect of bone marrow suppression and less anaemia. In addition, less inhibition of the stimulating factors that reduce white cell function suggesting a more favourable infection side-effect profile (fewer infections).
- JAK1 is critical for anti-viral responses, and there have been reports of increased zoster infection with inhibitors of JAK1
- the JAK inhibitors are a 'newer' drug group with no long-term data
- there is a safety signal with tofacitinib suggesting increased risk of lung cancer, lymphoma and major adverse cardiovascular events
- newer drugs blocking JAK1 are an exciting addition to the armamentarium of treatments for rheumatological conditions
- JAK inhibitors adversely affect lipids levels and patients on JAK inhibitors require lipid monitoring. As a lipid profile is not part of routine monitoring for conventional DMARDs, the lipid monitoring will be managed by the Rheumatology Service.
- patients with RA have a high cardiovascular risk linked to disease activity
- in view of the safety signal with tofacitinib, use of this agent may decline with time

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

Items 8.1 and 8.2 were taken together.

**8.1 FG1SMC 2365 - FILGOTINIB (RHEUMATOID ARTHRITIS) AND**

**8.2 FG1SMC 2315 - UPADACITINIB (RHEUMATOID ARTHRITIS)**

Dr Fitton declared a personal, non-specific interest in Gilead Sciences Ltd, and took part in decision-making.

The Group reviewed the requests for filgotinib and upadacitinib for severe RA and active psoriatic arthritis.

The Group noted that:
- both Marketing Authorisation Holders (MAHs) asked the SMC to consider use in moderate to severe RA, but the SMC accepted use in severe disease only
- both are oral agents, taken once daily
- the service plans to supply both agents via homecare arrangements
- the SMC advice for both medicines take account of the benefits of patient access schemes (PASs) that improve the cost-effectiveness of treatment
- cost offset will be available from alternative formulary medicines, including other JAK inhibitors
- as with all new drugs, clinicians need to be mindful of the lack of long-term data, and that safety issues may not show up until the drug use is more widespread

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Mindful of the safety signal for tofacitinib, that RA patients have an increased risk for cardiovascular disorders, and the adverse effect JAK inhibitors have on lipid profiles, the Group noted that patients should have cardiovascular risk factors (e.g., hypertension, hyperlipidaemia) fully assessed, e.g. using QRISK or equivalent.

The Group accepted the restricted local need for filgotinib and upadacitinib for the management of severe active RA as outlined in SMC 2365 and SMC 2315.

**SMC 2365 - Filgotinib 100mg, 200mg film coated tablets (Jyseleca®) ▼ is routinely available in line with national guidance (SMC 2365).**
**Indication under review: for the treatment of moderate to severe active rheumatoid arthritis in adults who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs). Filgotinib may be used as monotherapy or in combination with methotrexate (MTX).**
**Restriction: patients with severe disease (a disease activity score [DAS28] greater than 5.1) that has not responded to intensive therapy with a combination of conventional DMARDs and in patients with severe disease inadequately controlled by a TNF antagonist in whom rituximab is not appropriate.**
**In two phase III studies, filgotinib compared with placebo (both in combination with MTX), significantly improved signs and symptoms of rheumatoid arthritis in patients with an inadequate response to conventional or biologic DMARDs. Filgotinib was non-inferior to a biologic DMARD in patients who had an inadequate response to MTX.**
**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, 8b - Recommended for hospital use only. Treatment with filgotinib should be initiated by a physician experienced in the treatment of rheumatoid arthritis.** FTEAM

**SMC 2315 - Upadacitinib 15mg prolonged-release tablets (Rinvoq®) ▼ is routinely available in line with national guidance (SMC 2315).**
**Indication under review: for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs). Upadacitinib may be used as monotherapy or in combination with methotrexate.**
**Restriction: in patients with severe disease (a disease activity score [DAS28] greater than 5.1) that has not responded to intensive therapy with a combination of conventional DMARDs and in patients with severe disease inadequately controlled by a TNF antagonist in whom rituximab is not appropriate.**
**Upadacitinib (with or without methotrexate) compared with placebo, significantly improved signs and symptoms of RA in patients with an inadequate response to conventional DMARDs and in patients with an inadequate response to biological DMARDs. Upadacitinib was non-inferior to a biologic DMARD in patients who had an inadequate response to methotrexate.**
**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 upadacitinib should be initiated and supervised by physicians experienced in the diagnosis and treatment of conditions for which upadacitinib is indicated.** FTEAM

### 8.3 FG1SMC 2361 - UPADACITINIB (PSORIATIC ARTHRITIS)

The Group considered the request for upadacitinib for the treatment of adults with active psoriatic arthritis.

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The Group noted that:

- upadacitinib:
  - is the second JAK inhibitor, after tofacitinib, licensed for the treatment of psoriatic arthritis
  - can be used as monotherapy or in combination with methotrexate, unlike tofacitinib that is only licensed for use in combination with methotrexate
  - is taken once daily, at a dose of 15mg
- the service plans to supply via homecare arrangements
- patient numbers are expected to be small but will potentially increase with time
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of upadacitinib
- JAK inhibitors adversely affect lipids levels and patients on JAK inhibitors require lipid monitoring. As a lipid profile is not part of routine monitoring for conventional DMARDs, the lipid monitoring will be managed by the Rheumatology Service.

The Group accepted the restricted local need for upadacitinib for the treatment of active psoriatic arthritis in adults whose disease has not responded adequately to at least two conventional DMARDs, given either alone or in combination as outlined in SMC 2316.

**SMC 2316 - Upadacitinib 15mg prolonged-release tablets (Rinvoq®) ▼ is routinely available in line with national guidance (SMC 2316).**
**Indication under review: for the treatment of active psoriatic arthritis in adults whose disease has not responded adequately to at least two conventional DMARDs, given either alone or in combination.**
**Upadacitinib may be used as monotherapy or in combination with methotrexate.**
**Upadacitinib offers an additional treatment choice in the therapeutic class of Janus Kinase (JAK) inhibitors in this setting.**
**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 upadacitinib should be initiated and supervised by physicians experienced in the diagnosis and treatment of conditions for which upadacitinib is indicated.** **FTEAM**

## 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.

### 4.2. MAGNESIUM KORA HEALTHCARE 4MMOL (97MG) TABLETS

Ms Davie updated the Group on the options to highlight Magnesium Kora Healthcare 4mmoL (97mg) tablets in GP clinical systems.

Ms Davie confirmed that:

- Magnesium Kora Healthcare 4mmoL (97mg) tablet:
  - is not listed as a 'brand' on either of the GP clinical systems
  - is listed as the salt, i.e. magnesium citrate, and currently Magnesium Kora is the only citrate salt
- the clinical systems link to the DM&D code, and this cannot be changed unless it is requested by the Marketing Authorisation Holder (MAH)
- at present, selection of the correct salt will be used to promote use of Magnesium Kora Healthcare 4mmoL (97mg) tablets in primary care, with information shared with prescribers and Community Pharmacies

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**5. FORMULARY GROUP DECISIONS SEPTEMBER 2021 - PUBLISHED 04/10/2021**

Members ratified the decisions of the September 2021 meeting as published.

**6. NETFORMULARY/FORMULARY REVIEW**

**6.1. SENNOSIDES NEW LABELLING REQUIREMENTS**

The Group noted the Specialist Pharmacy Service (SPS) document outlining the new labelling requirements for senna.

The Chairman reported that due to regulatory changes, products containing sennosides as the active substance can no longer be labelled as senna. The formulary entry has been updated to include dual naming [senna/sennosides] and a link added to the SPS document. Dual naming will be reviewed after update of the Summary of Product Characteristics (SmPCs) and the Scottish Drug Tariff (SDT).

**6.2. UNLICENSED NEOMYCIN 500MG TABLETS**

The Group considered the SBAR outlining a proposal to substitute unlicensed neomycin 500mg tablets after discontinuation of the only neomycin 500mg tablet licensed in the UK.

The Group noted that:

- October 2020, the Group accepted the preoperative use of the oral antibiotics (OABs) metronidazole and neomycin, [in addition to induction prophylactic intravenous antibiotics] combined with mechanical bowel preparation (MBP), MoviPrep®, to reduce the risk of surgical site infections in adult patients undergoing elective colorectal surgery
- the request to substitute unlicensed neomycin is supported by the Antimicrobial Management Team (AMT) and the regimen will be subject to audit
- other Health Boards using this regimen have switched to unlicensed neomycin
- no safety concerns are anticipated from the use of the unlicensed product. No safety issues have been reported by other Health Boards that are using unlicensed neomycin for this indication.
- use will be limited to the managed service, and although the unlicensed neomycin is more costly, the increased costs are manageable within the existing service budget
- the Quality Assurance department has reviewed suitable products and has provided a risk assessment for a preferred option

The Group accept the restricted local need for unlicensed neomycin 500mg tablets as part of a preoperative OAB and MBP regimen (in addition to induction prophylactic intravenous antibiotics) to reduce SSI in adult patients undergoing elective colorectal resection.

**Neomycin 500mg tablets [unlicensed] is routinely available in line with local guidance.**
**Indication under review: as preoperative sterilisation of the bowel [in combination with metronidazole, induction prophylactic intravenous antibiotics, and mechanical bowel preparation (MBP)] to reduce the risk of surgical site infections in adult patients undergoing elective colorectal surgery.**
**It was classified 1b - available for restricted use under specialist supervision and 8b - recommended for hospital use only.** **FTEAM**

**Neomycin 500mg tablets (Nivemycin®) is now withdrawn from use/discontinued.**
**Indication: for preoperative sterilisation of the bowel and may be useful in the treatment of impending hepatic coma, including portal systemic encephalopathy.**
**This medicine is now withdrawn from use/discontinued.** **FTEAM**

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### 6.3. DISCONTINUED ITEMS

The Group noted the content of the letter from Alcon Eye Care UK Limited advising that Tears Naturale® (15mL), Tears Naturale® single dose and Isopto® Plain 0.5% are being discontinued in the UK. The discontinuation is a commercial decision related to manufacturer of hypromellose withdrawing their certification of suitability for the active ingredient (hypromellose).

Ms Doney confirmed the formulary would be updated, removing Tears Naturale®. **FTEAM**

## 7. OTHER BUSINESS

### 7.1. EMERADE® 300MICROGRAM AND 500MICROGRAM ADRENALINE AUTO-INJECTORS: RE-SUPPLY TO MARKET

The Group noted that:

- following corrections made to the device Emerade® 300microgram and 500microgram adrenaline auto-injectors will be resupplied to the UK market in October 2021
- Emerade® 150microgram auto-injectors will not be returning to market at this time
- Emerade® adrenaline auto-injectors were previously included on the formulary, and the potential for including on formulary can be discussed when Dr Herriot attends the December meeting

## 8. NEW PRODUCT REQUESTS

Dr Joshua Newmark, Registrar in Chemical pathology, provided the Group with a comprehensive update on the pharmacology of two lipid-lowering medicines recently accepted for use in NHS Scotland for the management of hypercholesterolaemia.

INCLISIRAN

Dr Joshua Newmark confirmed that:

- inclisiran:
  - is a first-in-class agent - small interfering ribonucleic acid (siRNA)
  - is given by subcutaneous injection, initially, again at 3 months followed by every 6 months
  - inhibits the production of proprotein convertase subtilisin/kexin type 9 (PCSK9). PCSK9 is a protein that can increase levels of LDL-cholesterol (LDL-C), by preventing its production, inclisiran helps to lower LDL-C levels.
  - reduces LDL-C significantly, providing similar absolute reductions in LDL-C to the PCSK9 inhibitors alirocumab and evolocumab
  - also reduces lipoprotein (a) (LP(a)), a potently atherogenic lipoprotein
  - offers the advantage of far fewer injections than PCSK9 inhibitors (two per year versus 26 injections) but this has to be balanced against its long washout period if the person does not tolerate treatment
  - is well tolerated with a safety profile similar to PCSK9 inhibitors
  - may have a role in severe atherosclerotic cardiovascular disease (ASCVD), and in the treatment pathways following ASCVD events
- data on cardiovascular outcomes are not available, and will not be available for several years

BEMPEDOIC ACID

Dr Joshua Newmark confirmed that:

- bempedoic acid works in a similar way to statins, but works higher up the cholesterol synthesis pathway in hepatocytes, reducing de novo cholesterol synthesis, which results in upregulation of the LDL receptors on the hepatocytes reducing the circulating LDL-C

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- ezetimibe:
  - reduces dietary cholesterol adsorption, faecal sterol excretion is increased
  - combined with simvastatin after acute coronary syndromes showed a small (2%) reduction in cardiovascular events compared to simvastatin alone
- bempedoic acid:
  - showed a 23% reduction of LDL-C (CLEAR Serenity)
  - is the first non-ezetimibe alternative to statins and is aimed at people that are unable to take their statin due to muscle-related adverse events
  - was well tolerated in patients with pre-existing statin intolerance
  - has no effect on triglyceride, HDL-C or LP(a) and reductions in LDL-C do not approach that achieved by a high intensity statin
  - provides a therapy for a cohort of patients that have historically been difficult to treat
- neither ezetimibe nor bempedoic acid have the additional benefits gained from statins, e.g., plaque stabilisation
- there is an option to co-administer bempedoic acid with ezetimibe
- the SMC does not include minimum cholesterol targets [for initiating therapy]

Members agreed that statin intolerance is often unproved, and people often do not take their statins regularly.
Members discussed the need for guidance for assessing intolerance to stains and the possibility of having a stopping policy for bempedoic acid.

Items 8.4 and 8.5 were taken together.

**8.4. FG1SMC 2363 - BEMPEDOIC ACID (HYPERCHOLESTEROLAEMIA) AND**

**8.5. FG1SMC 2406 - BEMPEDOIC ACID/EZETIMIBE (HYPERCHOLESTEROLAEMIA)**

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

The Group considered the requests for bempedoic acid for the management of hypercholesterolaemia.

The Group noted that:
- bempedoic acid:
  - is an oral tablet available as the single agent (Nilemdo®) and as a combination tablet with ezetimibe (Nustendi®)
  - is licensed for a wider population than accepted for use by SMC
  - has a significantly smaller LDL-C lower effect than high-intensity statins
- initial plans are for recommendations to initiate bempedoic acid to only come from the specialists in the lipid service
- treatment should be limited to people that are truly statin intolerant, and patient numbers have the potential to escalate if this is not adhered to
- ezetimibe is not a side-effect free drug
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of bempedoic acid as the single agent tablet or as the combination bempedoic acid plus ezetimibe tablet
- the flat pricing of the two preparations - bempedoic acid alone and the bempedoic acid plus ezetimibe combination
- bempedoic acid lacks mortality data because the studies so far are only efficacy and safety studies
- the cost of high-intensity statin therapy, e.g., atorvastatin 80mg, is approximately £30 per patient per year compared to bempedoic acid [at list price] at over £700 per patient per year

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The Group agreed that:
- statins are the treatment of choice for people with hypercholesterolaemia
- the greatest health gain would be achieved by people with hypercholesterolaemia taking their statins regularly
- at present bempedoic acid (with or without ezetimibe) is not associated with data showing a reduction in cardiovascular events

The Group requested that the Lipid Service produced guidance to help colleagues to assess/confirm that people are truly statin-intolerant. **FTEAM**

The Group accepted the restricted local need for bempedoic acid alone and bempedoic acid plus ezetimibe for the management of hypercholesterolaemia. Recommendations for treatment are limited to specialists in the Lipid Service as at present this medication/combination of medications is not associated with data showing a reduction in cardiovascular events.

**SMC 2363, SMC 2406 - Bempedoic acid 180mg film-coated tablets (Nilemdo®) ▼ and Nustendi® ▼ 180mg/10mg film coated tablets (bempedoic acid/ezetimibe) are routinely available in line with local guidance.**
**Indication under review: for primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet for use in adults who are:**
- **statin intolerant or for whom a statin is contra-indicated and**
- **where ezetimibe alone does not appropriately control LDL-C and**
- **where proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors or inclisiran are not appropriate**

**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 8d - treatment may be initiated in community on the recommendation of a consultant/specialist.**
**Note: at present, this medication/combination of medications is not associated with data showing a reduction in cardiovascular events.** **FTEAM**

### 8.6. FG1SMC 2358 - INCLISIRAN (HYPERCHOLESTEROLAEMIA)

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

The Group considered the request for inclisiran as an additional agent for the management of hypercholesterolaemia.

The Group noted that:
- inclisiran is given as a single 284mg subcutaneous injection, initially, again at 3 months, followed by every 6 months
- the SMC advice takes account of the benefits of a PAS that improves the cost-effectiveness of inclisiran
- the clinic expects that, at least initially, patient numbers will be small, although treatment with inclisiran will be long-term and patient numbers will be cumulative
- the primary end point was LDL reduction, not cardiovascular events
- the SmPC specifies that 'Inclisiran is intended for administration by a healthcare professional' which may have implications for clinic capacity. This is different to the PCKS9 inhibitors that can be self-injected.

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The Group accepted the restricted local need for inclisiran for the management of hypercholesterolaemia, use is limited to the Lipid Clinic.

**SMC 2358 - Inclisiran 284mg solution for injection in pre-filled syringe (Leqvio®) ▼ is routinely available in line with national guidance (SMC 2358).**
**Indication under review: for adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, as an adjunct to diet:**

- **in combination with a statin or statin with other lipid lowering therapies in patients who are unable to reach LDL-C goals with the maximum tolerated dose of a statin, or**
- **alone or in combination with other lipid lowering therapies in patients who are statin intolerant, or for whom a statin is contraindicated.**

**Restriction: for specialist use only in patients at high cardiovascular risk as follows:**

- **patients with heterozygous familial hypercholesterolaemia (HeFH) and LDL-C ≥5.0mmol/L, for primary prevention of cardiovascular events or,**
- **patients with HeFH and LDL-C ≥3.5mmol/L, for secondary prevention of cardiovascular events or,**
- **patients with high risk due to previous cardiovascular events and LDL-C ≥4.0mmol/L or,**
- **patients with recurrent/polyvascular disease and LDL-C ≥3.5mmol/L.**

**In three phase III studies, both the percentage reduction in LDL-C to day 510 and the time adjusted percentage in LDL-C from day 90 to day 540 were significantly larger with inclisiran 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.** **FTEAM**

Items 8.7 and 8.8 were taken together.

### 8.7. FG1SMC 2319 - LEUPRORELIN ACETATE (EARLY BREAST CANCER)

### 8.8. FG1SMC 2320 - LEUPRORELIN ACETATE (ADVANCED BREAST CANCER)

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

The Group considered the requests for leuprorelin acetate injection for the management of breast cancer as licensed:

- as adjuvant treatment in combination with tamoxifen or an aromatase inhibitor, of endocrine responsive early stage breast cancer in pre- and perimenopausal women at higher risk of disease recurrence (young age, high grade tumour, lymph node involvement). In women who have received chemotherapy, premenopausal status must be confirmed after completion of chemotherapy.
- as treatment in pre- and perimenopausal women with advanced breast cancer suitable for hormonal manipulation.

The Group noted that:

- leuprorelin acetate is:
  - already included on the formulary for prostate cancer
  - available as a monthly and 3-monthly injection
  - the third gonadotropin-releasing hormone (GnRH) agonist licensed for breast cancer [after goserelin and triptorelin]
- for other indications, leuprorelin acetate is licensed to be given by either subcutaneous or intramuscular injection, but for breast cancer (early and advanced), it is only

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licensed to be given by subcutaneous injection. This may represent a training/educational need for those prescribing and/or administering leuprorelin acetate in breast cancer.
- cost offset is available as leuprorelin acetate will be used instead of goserelin
- the availability of a 3-monthly injection may be advantageous to patients and staff

Members discussed the potential for leuprorelin acetate to be administered inappropriately by the intramuscular route and requested that:
- the clinic letters specifically highlight that the injection should be administered by subcutaneous injection
- information regarding the appropriate route of administration is highlighted to nursing and Primary Care clinicians via a future medication safety newsletter, and potentially updating a summary table previously prepared by Ms Davie and Ms Doney — **LC AD/FD**

The Group accepted the restricted local need for leuprorelin acetate, as licensed for early stage and advanced breast cancer.

**SMC 2319 - Leuprorelin acetate 3.75mg, 11.25mg powder and solvent for prolonged-release suspension for injection in pre-filled syringe (Prostap® SR DCS, Prostap® 3 DCS) is routinely available in line with national guidance (SMC 2319).**
**Indication under review: as adjuvant treatment in combination with tamoxifen or an aromatase inhibitor, of endocrine responsive early stage breast cancer in pre- and perimenopausal women at higher risk of disease recurrence (young age, high grade tumour, lymph node involvement). In women who have received chemotherapy, premenopausal status must be confirmed after completion of chemotherapy.**
**Leuprorelin offers an additional treatment choice in the therapeutic class of gonadotropin-releasing hormone analogues for this indication.**
**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. May be initiated in the community on consultant/specialist recommendation. Prostap® should be prepared, reconstituted and administered only by healthcare professionals who are familiar with these procedures.** — **FTEAM**

**SMC 2320 - Leuprorelin acetate 3.75mg, 11.25mg powder and solvent for prolonged-release suspension for injection in pre-filled syringe (Prostap® SR DCS, Prostap® 3 DCS) is routinely available in line with national guidance (SMC 2320).**
**Indication under review: as treatment in pre- and perimenopausal women with advanced breast cancer suitable for hormonal manipulation.**
**Leuprorelin offers an additional treatment choice in the therapeutic class of gonadotropin-releasing hormone analogues for this indication.**
**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. Prostap® should be prepared, reconstituted and administered only by healthcare professionals who are familiar with these procedures.** — **FTEAM**

### 8.9. FG1 – VISUXL® GEL (MODERATE TO SEVERE DRY EYES)

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

The Group considered the request for VisuXL® gel as an additional agent for the management of moderate to severe dry eyes.

The Group noted that:
- VisuXL® gel:
  - is used twice a day, and the lower frequency of administration may be beneficial for

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patients
  - has a thumb lever to help administration
  - will mostly replace a non-formulary item - Celluvisc® single dose eye drops
- in Primary Care most recommendations for eye drops come from colleagues in ophthalmology

The Group agreed that VisuXL® gel has the advantage of only twice daily administration, and may provide the potential to be cost-minimising. However, members requested clarification on whether patients on Celluvisc® should be actively switched to VisuXL® gel.

The Group accepted the local need for VisuXL® gel as an additional agent for the management of moderate to severe dry eyes.

**VisuXL® Gel is routinely available in line with local guidance.**
**Indication under review: for the treatment of moderate to severe dry eye disease.**
**It was classified 1a - available for general use, 8e - may be initiated in either hospital or community.** **FTEAM**

The Group noted the high cost of Simple Eye ointment [£53.28 ex VAT for a 4g tube] and that the service feels there is still a place for Simple Eye ointment on the formulary. Simple Eye ointment is very thick and provides longer protection overnight and hence should only be prescribed for use at bedtime.

### 8.10. FG1SMC 2321 - TRIXEO® AEROSPHERE® (COPD)

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

Ms Doney reported that following review of the priming requirement for the Aerosphere® device the Respiratory Managed Clinical Network (MCN) does not support formulary inclusion of this product.

**SMC 2321 - Trixeo® Aerosphere® 5micrograms/7.2micrograms/160micrograms pressurised inhalation, suspension (formoterol fumarate dihydrate/glycopyrronium bromide/budesonide) is not routinely available as there is a local preference for alternative medicines.**
**Indication under review: maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of an inhaled corticosteroid and a long-acting $beta_2$-agonist or combination of a long-acting $beta_2$-agonist and a long-acting muscarinic antagonist.**
**SMC restriction: in patients with severe COPD (forced expiratory volume in one second [$FEV_1$] less than 50% predicted normal).**
**Formoterol fumarate dihydrate/glycopyrronium / budesonide (Trixeo® Aerosphere®) offers an additional treatment choice of long-acting $beta_2$-agonist (LABA), long-acting muscarinic antagonist (LAMA) and inhaled corticosteroid (ICS) in a single inhaler.**
**Not routinely available as there is a local preference for alternative medicines.** **FTEAM**

## 9. SCOTTISH MEDICINES CONSORTIUM PROVISIONAL ADVICE - OCTOBER 2021

The Group noted the SMC provisional advice issued October 2021.

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.

| ITEM | SUBJECT | ACTION |
|---|---|---|

**10. SCOTTISH MEDICINES CONSORTIUM PRESS STATEMENTS - OCTOBER 2021**

The Group noted the SMC advice published October 2021.

Following publication of the negative SMC recommendation, for liraglutide (Saxenda®) SMC 2378, and the non-submission statements, for isatuximab (Sarclisa®) SMC 2423, avapritinib (Ayvakyt®)▼ SMC 2424, and vericiguat (Verquvo®)▼ SMC 2425, these medicines will not be included on the Grampian Joint Formulary for the indications in question.

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

- SMC 2366 - olaparib (Lynparza®) (submission expected)
- SMC 2376 - cabotegravir (Vocabria®)▼ (submission received)
- SMC 2373 - chloroprocaine hydrochloride (Ampres®) (no submission)
- SMC 2386 - cabozantinib (Cabometyx®)▼ (submission expected)
- SMC 2392 - midazolam oral solution (Ozalin®) (submission expected)

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

SMC 2396 - EMPAGLIFLOZIN (JARDIANCE®) (SYMPTOMATIC CHRONIC HEART FAILURE WITH REDUCED EJECTION FRACTION)

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

The Group discussed the SMC advice for empagliflozin 10mg film-coated tablets (Jardiance®) for the treatment of symptomatic chronic heart failure with reduced ejection fraction (SMC 2396).

The Group noted:

- July 2021, dapagliflozin was included on the formulary for the management of symptomatic chronic heart failure with reduced ejection fraction (HFrEF)
- empagliflozin is the second sodium-glucose co-transporter-2 (SGLT2) inhibitor licensed for symptomatic chronic HFrEF
- empagliflozin is already included on the formulary for type 2 diabetes mellitus, in strengths of 10mg and 25mg film-coated tablets, however only the 10mg strength is licensed for symptomatic chronic HFrEF
- empagliflozin and dapagliflozin cost the same at £36.59 (£43.91 inc. VAT) for 28 days
- availability of a second SGLT2 inhibitor will not increase patient numbers, however SGLT2 inhibitors for this indication represents a new cost to Primary Care, as they are administered in conjunction with other heart failure therapies
- the Cardiology Service wishes to have both agents on formulary [for symptomatic chronic HFrEF] and the availability of empagliflozin may reduce questions about swapping people with type 2 diabetes mellitus from empagliflozin to dapagliflozin
- further licence extensions for SGLT2 inhibitors are expected, e.g., heart failure with preserved ejection fraction

The Group accepted the restricted local need for empagliflozin for adults for the treatment of symptomatic chronic HFrEF without the need for a full submission.

| ITEM | SUBJECT | ACTION |
|---|---|---|
| | **SMC 2396 - Empagliflozin 10mg film-coated tablets (Jardiance®) is routinely available in line with local guidance.<br>Indication under review: in adults for the treatment of symptomatic chronic heart failure with reduced ejection fraction.<br>Restriction: start treatment on the advice of a heart failure specialist/cardiologist.<br>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 |

**11.** GENERAL INFORMATION FROM SCOTTISH MEDICINES CONSORTIUM

Nil of note.

**12.** DOCUMENTS FOR INFORMATION

The Group noted items 12.1 and 12.2 (Drug Safety Update September and October 2021) were noted.

12.3 NORTHERN IRELAND FORMULARY – PREGABALIN REMOVED (NEUROPATHIC PAIN))

Members discussed item 12.3, pregabalin removed from the Northern Ireland Formulary for neuropathic pain.
Members supported sharing the document with other medicines management groups and linking with the pain team to start a discussion about the potential to review the position of pregabalin in the management of neuropathic pain. **FD**

**13. AOCB**

None.

**DATE OF NEXT MEETING**

Tuesday 16 November 2021 starting at 14.30 via Microsoft Teams.

**CHAIRMAN'S SIGNATURE** _____ **DATE 16 NOVEMBER 2021**