Minutes of the SMC Committee Meeting

Tuesday 02 July 2019, The Merchants House of Glasgow, 7 West George Street, Glasgow, G2 1BA

Present:	Dr Alan MacDonald (Chairman) Ms Gail Caldwell Dr Jacob Dreyer Mr Roy Foot Dr Jane Goddard Professor Charlie Gourley Dr Roger Hardman Ms Alex Jones Mr Gordon Loughran Dr Catriona McMahon Dr Scott Muir Dr Avideh Nazeri Dr Paul Neary Mr Graham Scotland Mr Colin Sinclair Ms Alice Wilson
Observers:	Ms Gillian Jardine Mr Aaron Linstead Prof Alison Strath Ms Carole Wilkinson
In Attendance:	Mrs Corinne Booth Ms Ailsa Brown Ms Alison Culpan Mrs Jennifer Dickson Mrs Noreen Downes Ms Caroline Foulkes Mrs Sharon Hems Mr Scott Hill Ms Eileen Holmes Mrs Anne Lee

	Ms Rosie Murray Ms Marion Pirie Mrs Shonagh Ramsay Mr Jonathan Sim Ms Louise Taylor Scott Mrs Catherine Tait
Apologies:	Ms Ailene Botfield Paul Catchpole Jenny Coutts Ms Clare Dunn Michael Eddleston Irene Fazakerley Professor Jacob George Dr Christine Hepburn Dr Brian Jones Dr Jan Jones Mrs Lindsay Lockhart Mark MacGregor Mrs Pauline McGuire David Meiklejohn William Moore Mr Gerry O'Brien Alison Stillie Mr Scott Urquhart Catherine Tait

1.	**Welcome and Apologies for Absence**
1.1	The Chairman welcomed members to the meeting and apologies for absence were noted.
1.2	Welcome to the following observers: Mr Joe Brogan, Health and Social Care Board, Northern Ireland Mr Rohan Deogaonkar, Health Economist, SHTG & SMC Ms Gillian Jardine, Lead Pharmacist, NHS Ayr Ms Lynn Keenan, Health and Social Care Board, Northern Ireland Mr Aaron Linstead, Pharmaceutical Analyst, SMC Mrs Shonagh Ramsay, SMC Operations Manager and will be in post for one year to cover Donna Leith's maternity leave. Ms Carole Wilkinson, Chair, Healthcare Improvement Scotland
1.3	Thank you and goodbye Nothing to report
2.	**Declarations of Interest**
2.1	The Chairman reminded members to declare interests in the products to be discussed and the comparator medicines as noted on the assessment reports.
3.	**Minutes of the Previous Meeting (Tuesday 04 June 2019)**
3.1	The minutes of the SMC meeting held on Tuesday 04 June 2019 were accepted as an accurate record of the meeting.
4	**Matters Arising**
4.1	**Deferred Advice**
	empagliflozin plus linagliptin 10mg/5mg, 25mg/5mg film-coated tablets (Glyxambi®) SMC No. (1236/17) Boehringer Ingelheim Ltd SMC reviewed an abbreviated submission for empagliflozin/linagliptin (Glyxambi®), in adults aged 18 years and older with type 2 diabetes mellitus: • To improve glycaemic control when metformin and/or sulphonylurea (SU) and one of the monocomponents of Glyxambi® do not provide adequate glycaemic control • When already being treated with the free combination of empagliflozin and linagliptin in April 2017. Advice was withheld pending product availability. The medicine is now available and SMC advice will be distributed to NHS Boards and ADTCs on Friday 5 July 2019 and published on the SMC website on Monday 12 August 2019.

4.2	**Amended advice**
	Nothing to report
5	**Chairman's Business**
5.1	Nusinersen A new ultra-orphan definition and approach for assessing medicines for extremely rare conditions started in October 2018. Nusinersen for spinal muscular atrophy (SMA) has been categorised as an ultra-orphan according to the new definition. From July 2019 it can be prescribed for patients with types 2 and 3 SMA for a period of up to three years while further evidence on its effectiveness is generated. The company will then provide an updated submission for reassessment to allow a final decision on its routine use in this patient group in NHSScotland. More information on the ultra-orphan pathway is available on the SMC website and was also recently covered in Dr Catherine Calderwood's column in the Scotsman.
5.2	Testosterone replacement therapy Testosterone-containing products used in testosterone replacement therapy for the treatment of male hypgonadism are now out of remit for SMC assessment. The out of remit criteria on the SMC web-site has been updated and NHS Boards and ADTCs informed.
5.3	Reporting of p-values for secondary outcomes across SMC Detailed Advice Documents The SMC Clinical Assessment Group has noted inconsistent reporting of p-values for secondary outcomes across Detailed Advice Documents and wish to adopt a standard approach. In future, p-values for secondary comparisons not controlled for the risk of false positive results, according to the study's statistical plan, will not be included in SMC Detailed Advice Documents. The effect estimates for each treatment for a given outcome will still be included for key secondary outcomes. The 95% confidence intervals for less robust comparisons will continue to be included where appropriate, but will be clearly identified as descriptive only. Descriptive p-values will continue to be reported in the clinical checklist where appropriate and will be clearly identified as descriptive only.
6.	**NDC ASSESSMENT REPORTS**
	FULL SUBMISSIONS
6.1	inotersen 284mg solution for injection in pre-filled syringe (Tegsedi®) Akcea Therapeutics UK Ltd SMC2188 No interests were declared in relation to this product/comparator medicines. Representatives of the submitting company were invited to the committee table to respond to specific queries regarding this submission, comment on matters of factual accuracy and provide clarification on any outstanding issues. Representatives of the Patient Group were invited to the committee table to respond to specific queries regarding the Patient Group submission, and provide clarification on any outstanding issues.

	A member of the SMC Executive provided an overview of the assessment, draft advice, expert comments, revised data/analysis, and comments received from the company. A member of the Public Involvement Team presented a Patient Group submission from Amyloidosis Research Consortium UK (ARC UK). Detailed discussion followed and, after a vote of the members, it was decided that inotersen (Tegsedi), should be accepted for within NHSScotland. Indication under review: for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis (hATTR). In a phase II/III study of adults with hATTR and polyneuropathy, inotersen was associated with significantly less worsening compared with placebo, measured by the change in modified neuropathy impairment score +7 (mNIS+7) and in Norfolk Quality of Life-Diabetic Neuropathy (QOL-DN) questionnaire from baseline to 66 weeks. This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of inotersen. This advice is contingent upon the continuing availability of the PAS in NHSScotland or a list price that is equivalent or lower. This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
6.2	lumacaftor and ivacaftor 200mg/125mg, 100mg/125mg film-coated tablets and 100mg/125mg,150mg/188mg granules in sachets (Orkambi®) Vertex Pharmaceuticals (Europe) Limited SMC2182 No interests were declared in relation to this product/comparator medicines. Representatives of the submitting company were invited to the committee table to respond to specific queries regarding this submission, comment on matters of factual accuracy and provide clarification on any outstanding issues. Representatives of the Patient Group were invited to the committee table to respond to specific queries regarding the Patient Group submission, and provide clarification on any outstanding issues. The NDC Co-Vice Chair provided an overview of the assessment, draft advice, expert comments, revised data/analysis, and comments received from the company. A member of the Public Involvement Team presented a Patient Group submissions from Cystic Fibrosis Trust and Quest for a CF Cure. Detailed discussion followed and, after a vote of the members, it was decided that lumacaftor-ivacaftor (Orkambi), should not be recommended for use within NHSScotland. Indication under review: the treatment of cystic fibrosis in patients aged 6 years and older (tablets) and aged 2 to 5 years (granules) who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

	lumacaftor-ivacaftor, compared with placebo, improved measures of lung function in patients with cystic fibrosis who were homozygous for the F508del mutation in the CFTR gene. The submitting company's justification of the treatment's cost in relation to its health benefits was not sufficient and in addition the company did not present a sufficiently robust clinical and economic analysis to gain acceptance by SMC. This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
6.3	<u>tezacaftor and ivacaftor 100mg/150mg film-coated tablets (Symkevi®) Vertex Pharmaceuticals (Europe) Ltd SMC2183</u> No interests were declared in relation to this product/comparator medicines. Representatives of the submitting company were invited to the committee table to respond to specific queries regarding this submission, comment on matters of factual accuracy and provide clarification on any outstanding issues. Representatives of the Patient Group were invited to the committee table to respond to specific queries regarding the Patient Group submission, and provide clarification on any outstanding issues. The NDC Co-Vice Chair provided an overview of the assessment, draft advice, expert comments, revised data/analysis, and comments received from the company. A member of the Public Involvement Team presented a Patient Group submissions from Cystic Fibrosis Trust and Quest for a CF Cure. Detailed discussion followed and, after a vote of the members, it was decided that tezacaftor and ivacaftor (Symkevi) should not be recommended for use within NHSScotland. Indication under review: In a combination regimen with ivacaftor 150mg tablets for the treatment of patients with cystic fibrosis (CF) aged 12 years and older who are homozygous for the F508del mutation or who are heterozygous for the F508del mutation and have one of the following mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene: P67L, R117C, L206W, R352Q, A455E, D579G, 711+3A→G, S945L, S977F, R1070W, D1152H, 2789+5G→A, 3272-26A→G, and 3849+10kbC→T. In phase III studies in patients ≥12 years of age with cystic fibrosis who were homozygous for the F508del CFTR mutation or heterozygous for the F508del CFTR mutation and a second allele with a CFTR mutation with residual function, tezacaftor-ivacaftor was superior to placebo for absolute change in the percent predicted forced expiratory volume in one second ($ppFEV_1$) from the baseline. The submitting company's justification of the treatment's cost in relation to its health benefits was not sufficient and in addition the company did not present a sufficiently robust clinical and economic analysis to gain acceptance by SMC.

	This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
6.4	venetoclax 10mg, 50mg, and 100mg film-coated tablets (Venclyxto®) AbbVie Ltd SMC2166 No interests were declared in relation to this product/comparator medicines. Representatives of the submitting company were invited to the committee table to respond to specific queries regarding this submission, comment on matters of factual accuracy and provide clarification on any outstanding issues. Representatives of the Patient Group were invited to the committee table to respond to specific queries regarding the Patient Group submission, and provide clarification on any outstanding issues. A member of the SMC Executive provided an overview of the assessment, draft advice, expert comments, revised data/analysis, and comments received from the company. A member of the Public Involvement Team presented a Patient Group submissions from Chronic Lymphocytic Leukaemia Support Association (CLLSA) and Leukaemia CARE. Detailed discussion followed and, after a vote of the members, it was decided that venetoclax (Venclyxto), should be accepted for use within NHSScotland. Indication under review: in combination with rituximab for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy. Progression-free survival was significantly longer in the venetoclax plus rituximab group compared with chemoimmunotherapy in a phase III study of patients with relapsed or refractory CLL. This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of venetoclax. This advice is contingent upon the continuing availability of the PAS in NHSScotland or a list price that is equivalent or lower. This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
6.6	buprenorphine 8/16/24/32/64/96/128 mg prolonged-release solution for injection (Buvidal®) Camurus AB SMC2169 No interests were declared in relation to this product/comparator medicines. Representatives of the submitting company were invited to the committee table to respond to specific queries regarding this submission, comment on matters of factual accuracy and provide clarification on any outstanding issues.

	Representatives of the Patient Group were invited to the committee table to respond to specific queries regarding the Patient Group submission, and provide clarification on any outstanding issues. A member of the SMC Executive provided an overview of the assessment, draft advice, expert comments, revised data/analysis, and comments received from the company. A member of the Public Involvement Team presented a Patient Group submissions from Scottish Families Affected by Alcohol and Drugs, Scottish Recovery Consortium, Faces & Voices of Recovery UK and Scottish Drugs Forum. Detailed discussion followed and, after a vote of the members, it was decided that buprenorphine (Buvidal), should be accepted for restricted use within NHSScotland. Indication under review: treatment of opioid dependence within a framework of medical, social and psychological treatment. Treatment is intended for use in adults and adolescents aged 16 years or over. SMC restriction: Use in patients in whom methadone is not suitable and for whom the use of buprenorphine is considered appropriate. In a phase III study in patients with opioid dependence, subcutaneous buprenorphine was non-inferior to sublingual buprenorphine/naloxone for the mean percentage of urine samples with test results negative for illicit opioids. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
6.7	<u>tildrakizumab 100mg solution for injection in pre-filled syringe (Ilumetri®) Almirall Limited SMC2167</u> No interests were declared in relation to this product/comparator medicines. Representatives of the submitting company were invited to the committee table to respond to specific queries regarding this submission, comment on matters of factual accuracy and provide clarification on any outstanding issues. Representatives of the Patient Group were invited to the committee table to respond to specific queries regarding the Patient Group submission, and provide clarification on any outstanding issues. A member of the SMC Executive provided an overview of the assessment, draft advice, expert comments, revised data/analysis, and comments received from the company. A member of the Public Involvement Team presented a Patient Group submissions from The Psoriasis Association and Psoriasis and Psoriatic Arthritis Alliance (PAPAA). Detailed discussion followed and, after a vote of the members, it was decided that tildrakizumab (Ilumetri) should be accepted for restricted for use within NHSScotland. Indication under review: the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy. SMC restriction: for use in patients who have failed to respond to conventional systemic therapies (including ciclosporin, methotrexate and phototherapy), are intolerant to, or have a contraindication to these treatments.

	Tildrakizumab was superior to placebo in improving the signs and symptoms of psoriasis in adults with moderate to severe plaque psoriasis, who were candidates for systemic therapy. This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of tildrakizumab. This advice is contingent upon the continuing availability of the PAS in NHSScotland or a list price that is equivalent or lower. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
	ABBREVIATED SUBMISSIONS
6.8	<u>perampanel 0.5mg/mL oral suspension (Fycompa®) Eisai Ltd SMC2172</u> No interests were declared in relation to this product/comparator medicines. The NDC Co-Vice Chair provided an overview of the assessment, and draft advice. Discussion followed and, after a vote of the members, it was decided that perampanel (Fycompa), should be accepted for restricted use within NHSScotland. Indication under review: for the adjunctive treatment of partial-onset seizures with or without secondarily generalised seizures in adult and adolescent patients from 12 years of age with epilepsy. SMC restriction: use as a second-line adjunctive treatment in patients with refractory partial onset epilepsy who are unable to swallow perampanel tablets. Treatment should be initiated only by physicians who have appropriate experience in the treatment of epilepsy. SMC has previously accepted perampanel tablets for restricted use as adjunctive treatment of partial-onset seizures with or without secondarily generalised seizures in patients with epilepsy aged 12 years and older. The oral suspension provides an alternative formulation for patients who have difficulty swallowing tablets. Depending on the dose, it may be more expensive than the tablets but any overall net budget impact is likely to be small. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
7.	**SMC User Group Forum (UGF)**
7.1	The next meeting of the SMC UGF is scheduled for Tuesday 09 July 2019, an update will be provided at the next meeting.
8.	**Forthcoming Submissions**
8.1	Noted
9.	**Area Drug & Therapeutics Committee (ADTC) Issues**
9.1	Nothing to report.

10.	**Any Other Business**
10.1	Nothing to report.
11.	**Closed Session**
	NON SUBMISSIONS
11.	lenalidomide 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg and 25mg hard capsules (Revlimid®) Celgene Ltd SMC2217 In the absence of a submission from the holder of the marketing authorisation lenalidomide (Revlimid) is not recommended for use within NHSScotland. Indication under review: as combination therapy with bortezomib and dexamethasone for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant. The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland. Note: SMC advice 1096/15 is still valid. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
11.2	perampanel 0.5mg/mL oral suspension (Fycompa®) Eisai Ltd 2218 In the absence of a submission from the holder of the marketing authorisation perampanel (Fycompa) is not recommended for use within NHSScotland. Indication under review: for the adjunctive treatment of primary generalised tonic-clonic seizures in adult and adolescent patients from 12 years of age with idiopathic generalised epilepsy. The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
11.3	pomalidomide 1mg , 2mg , 3mg and 4mg hard capsules (Imnovid®) Celgene Ltd SMC2219 In the absence of a submission from the holder of the marketing authorisation pomalidomide (Imnovid) is not recommended for use within NHSScotland. Indication under review: in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior treatment regimen including lenalidomide. The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.

11.4	rucaparib 200mg, 250mg and 300mg film-coated tablets (Rubraca®) Clovis Oncology UK Ltd SMC2221 In the absence of a submission from the holder of the marketing authorisation rucaparib (Rubraca) is not recommended for use within NHSScotland. Indication under review: as monotherapy treatment of adult patients with platinum sensitive, relapsed or progressive, BRCA mutated (germline and/or somatic), high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, who have been treated with two or more prior lines of platinum based chemotherapy, and who are unable to tolerate further platinum based chemotherapy. The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland. The SMC advice will be issued to the NHS Boards and ADTCs on Friday, 05 July 2019.
12.	**Any Other Business in Closed Session**
12.1	SMC Chair An advert for the role of SMC Chairman has recently been advertised by Healthcare Improvement Scotland and circulated by the SMC secretariat to SMC and NDC members, the closing date is Tuesday 2 July. Dr Alan MacDonald is happy to discuss further with interested parties. SMC Co-Vice Chair In addition, expression of interest are invited for the role of SMC Co-Vice Chair and will be considered by the SMC Executive. The closing date is 2 July.
13.	**Date of the Next Meeting**
13.1	The date of the next meeting was confirmed as Tuesday 06 August 2019 (lunch from 12 noon), at The Merchants House of Glasgow, 7 West George Street, Glasgow, G2 1BA.