South East London Integrated Medicines Optimisation Committee
(SEL IMOC, formerly the SEL Area Prescribing Committee)
Formulary recommendation

Reference	**124**
Intervention:	**Oral semaglutide tablets (Rybelsus™) for type 2 diabetes mellitus** (Semaglutide is a glucagon-like peptide-1 [GLP-1] receptor agonist.)
Date of Decision	**December 2020**
Date of Issue:	**February 2021 – TIME LIMITED approval to November 2021 to support COVID-19 response.**
Recommendation:	**Amber 3 – initiation and supply by specialist diabetes teams. GPs may be asked to take on prescribing after 3 months.**
Further Information:	• The oral tablet formulation of semaglutide (all strengths) is accepted for use in South East London to support reduced face to face contact during the COVID-19 pandemic. • During this time use is approved in line with the local GLP-1 agonist pathway, which has been updated to reflect this time limited approval. • Within this pathway, use of oral semaglutide is supported in line with the NICE recommendations for the use of injectable GLP-1 agonists (NICE clinical guideline 28 – last updated December 2020). • NICE recommends a GLP-1 agonist can be considered in a triple therapy regimen in combination with metformin and a sulfonylurea for patients with type 2 diabetes if certain caveats are met (refer to the NICE guideline/ SEL GLP-1 agonist pathway for details). • In line with NICE, treatment with oral semaglutide will only be continued if the person with type 2 diabetes has had a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months). • Oral semaglutide should only be offered in combination with insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team*. • During COVID-19, oral semaglutide will be an option alongside the injectable GLP-1 agonists on the SEL formulary. The decision on choice of GLP-1 agent and the most clinically appropriate route of administration (sub-cutaneous vs. oral) during the COVID-19 pandemic will be made by the initiating clinician in discussion with the patient, including individual patient factors, such as cardiovascular risk. • Patients who are already stabilised on injectable GLP-1 agonist therapy should **not** be switched over to oral semaglutide unless there is a robust clinical rationale to do so. • Patients commenced on oral semaglutide during this interim period of approval will be given the option to continue longer term if they and their diabetes specialist feel it is clinically appropriate to do so. • Over the period of this time limited approval, outcome data will be collated across SEL (determined and coordinated by the original formulary applicant) to include: - Number of patients started on oral semaglutide by organisation vs. total number of injectable GLP-1 agonist starts - Whether use is in line with this recommendation and if not, the main reasons for deviating. - Outcomes in patients, such as glycaemic control, weight loss and adverse effects. - The number of people stopping treatment with oral semaglutide and moving over to injectable GLP-1 therapy and the reasons for doing so and vice versa. • These data will be used to help inform and review the longer term positioning of oral semaglutide on the formulary once the pandemic situation stabilises. * The NICE guideline notes that a consultant-led multidisciplinary team may include a wide range of staff based in primary, secondary and community care.

Shared Care/ Transfer of care required:	Yes - transfer of prescribing information sheet.
Cost Impact for agreed patient group	• For the current time limited approval, the cost of oral semaglutide is comparable to the injectable GLP-1 agonists already in use within SE London, with the advantage of not requiring needles or sharps disposal. Therefore, during the pandemic when used an alternative to injectable therapy, the budget impact is cost neutral. • Depending on the positioning longer term, availability of an oral GLP-1 agonist could increase overall GLP-1 agonist use by 10% (to include patients who may not have received a drug in this class e.g. due to needle phobia). Based on current levels of spend in SEL primary care on GLP-1 agonists, a cost impact of around £310K (or ~£16,000 per 100,000 population) is estimated for SEL longer term. This is potentially an overestimate and will be re-visited once outcome data for the time limited approval are available.
Usage Monitoring & Impact Assessment	**Providers:** • Monitor use and submit outcome data as requested in "Further Information" section by no later than **November 2021**.
	SEL CCG Borough Medicines Teams: • Monitor ePACT2 data. • Exception reports from GPs if inappropriate prescribing requests are made to primary care.
Evidence reviewed	**References (from evidence evaluation)** 1. Scottish Medicines Consortium. Semaglutide 0.25mg, 0.5mg and 1mg solution for injection in pre-filled pen (Ozempic®). SMC2092. Published 14 January 2019. 2. NICE. Type 2 diabetes in adults: management. NICE guideline [NG28]. Last updated August 2019. Accessed online via: https://www.nice.org.uk/guidance/ng28. Last accessed 03/09/19. 3. South East London Joint Medicines Formulary. Last accessed online here on 25/11/20. 4. South East London Area Prescribing Committee. South East London glucagon-like peptide (GLP-1) analogue pathway for adults aged 18 years and over with Type 2 Diabetes Mellitus (T2DM). 5. SPC. Rybelsus. Last updated May 2020. Last accessed online here on 25/11/20. 6. Rodbard HW et al (2019) Oral Semaglutide Versus Empagliflozin in Patients With Type 2 Diabetes Uncontrolled on Metformin: The PIONEER 2 Trial. Diabetes Care; 42(12):2272-2281 7. Effect of Additional Oral Semaglutide vs Sitagliptin on Glycated Hemoglobin in Adults With Type 2 Diabetes Uncontrolled With Metformin Alone or With Sulfonylurea. The PIONEER 3 Randomized Clinical Trial. JAMA; 321(15):1466-1480 8. Pieber TR et al (2019) Efficacy and safety of oral semaglutide with flexible dose adjustment versus sitagliptin in type 2 diabetes (PIONEER 7): a multicentre, open-label, randomised, phase 3a trial. The Lancet Diabetes & Endocrinology; 7(7):528-539 9. Pratley R et al (2019) Oral semaglutide versus subcutaneous liraglutide and placebo in type 2 diabetes (PIONEER 4): a randomised, double-blind, phase 3a trial. The Lancet; 394(10192):39-50 10. Yabe D et al (2020) Safety and efficacy of oral semaglutide versus dulaglutide in Japanese patients with type 2 diabetes (PIONEER 10): an open-label, randomised, active-controlled, phase 3a trial. The Lancet Diabetes & Endocrinology; 8(5):392-406 11. Zinman B et al (21019) Efficacy, Safety, and Tolerability of Oral Semaglutide Versus Placebo Added to Insulin With or Without Metformin in Patients With Type 2 Diabetes: The PIONEER 8 Trial. Diabetes Care; 42(12):2262-2271 12. Mosenzon O et al (2019) Efficacy and safety of oral semaglutide in patients with type 2 diabetes and moderate renal impairment (PIONEER 5): a placebo-controlled, randomised, phase 3a trial. The Lancet Diabetes & Endocrinology; 7(7):515-527 13. Husain M et al (2019) Oral Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes. NEJM; 381:841-851 14. Yamada Y et al (2020) Dose-response, efficacy, and safety of oral semaglutide monotherapy in Japanese patients with type 2 diabetes (PIONEER 9): a 52-week, phase 2/3a, randomised, controlled trial. The Lancet Diabetes & Endocrinology; 8(5):377-391 15. Aroda VR et al (2019) PIONEER 1: Randomized Clinical Trial of the Efficacy and Safety of Oral Semaglutide Monotherapy in Comparison With Placebo in Patients With Type 2 Diabetes. Diabetes Care; 42(9):1724-1732 16. Marso S et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes (2016). The New England Journal of Medicine; 375: pages 1834-1844. 17. European Medicines Agency. Rybelsus Assessment Report. 30 January 2020. Last accessed online here on 25/11/20 18. British National Formulary. Accessed online via https://bnf.nice.org.uk/. Last accessed on 25/11/20.

NOTES:

a) SEL IMOC recommendations and minutes are available publicly via the website.

b) This SEL IMOC recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.

c) Not to be used for commercial or marketing purposes. Strictly for use within the NHS.