South East London Integrated Medicines Optimisation Committee
Formulary recommendation

Reference	**097**
Intervention:	**Cariprazine hydrochloride (Reagila™) for the treatment of schizophrenia in adults** (Cariprazine is a 2nd generation, oral antipsychotic agent)
Date of Decision	**January 2019, reviewed in December 2021 and recategorised from Red to Amber 2. Updated June 2023 following report on outcome data and time limit to formulary approval removed**
Date of Issue:	**February 2019, reissued in February 2022 (one year time limited approval) and July 2023**
Recommendation:	**Amber 2 – specialist initiation and prescribing for a minimum of 12 months and until the patient is stable. GP may be requested to prescribe after this period.**
Further Information:	• Cariprazine is approved for **restricted** use in adult patients with schizophrenia who: – Continue to have prominent and debilitating negative symptoms on their current antipsychotic regimen **and** – Have a Scale for the Assessment of Negative Symptoms* (SANS) score of ≥50. • Negative symptoms include emotional apathy, lack of drive, poverty of speech, social withdrawal, and self-neglect. • Monitoring the response to cariprazine will include the patient's overall clinical status and improvements in the SANS score. The SANS score should be measured at baseline and again at 6 months. Treatment with cariprazine will only be continued if there is a ≥50% improvement in the SANS score. • Prescribing and supply will be carried out by the mental health trusts for a minimum of 12 months. Only consultants may initiate cariprazine using the internal process agreed within the Trusts. • The use of cariprazine as a first line antipsychotic agent is **not** supported by this recommendation. • **May 2023:** The re-issued formulary recommendation in February 2022 requested a further report back to the Committee after 12 months outlining the number of patients initiated on treatment and transferred to primary care, outcomes and safety data. Primary care prescribing data demonstrates prescribing in primary care within the last 12 months. The outcomes data presented indicated improvements in SANS score, reduced hospital admissions and bed days. Whilst there were no significant safety concerns, some patients did discontinue treatment due to adverse effects. The Committee agreed the time limit on the formulary approval could be removed and requested further outcome data are presented in two years. *Further information on the parameters covered by the SANS scale is available at: https://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/GetPdf.cgi?id=phd000807.2
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	• In 2019, the local mental health trusts have estimated that approximately 67 patients might be suitable for treatment with cariprazine in SEL (50 under SLaM and 17 under Oxleas). This would result in a cost impact of around £65K in SEL. • As a comparison, data presented to the Committee in December 2021 showed that 35 patients had been started on cariprazine since January 2019. There may be savings from reduced admissions and shorter inpatient stay. This is difficult to quantify but will be included as part of the data reported back to the Committee.

Usage Monitoring & Impact Assessment	**Mental Health and Acute Trusts:** • Monitor and audit usage of cariprazine as agreed and report back to the Committee in two years (data to be collated and presented no later than July 2025).
	SEL 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. glucagon-like peptide (GLP-1) analogue pathway for adults aged 18 years and over with Type 2 Diabetes Mellitus (T2DM), available here. 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.