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Barnsley Hospital NHS Foundation Trust | South West Yorkshire Partnership NHS Foundation Trust | South Yorkshire Integrated Care Board

GLP-1 agonists: Liraglutide (Victoza®) Lixisenatide (Lyxumia®) Dulaglutide (Trulicity®) Semaglutide (Ozempic®▼ injection and Rybelsus® ▼oral tablets) Amber G guideline

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (https://www.medicinescomplete.com/#/) and the SPC (https://www.medicines.org.uk/emc/) remain authoritative.

Background Information	GLP-1 agonists bind to and activate the GLP-1 (glucagon-like peptide-1) receptor to increase insulin secretion, suppress glucagon secretion and slow gastric emptying. Treatment with liraglutide, lixisenatide dulaglutide or semaglutide is associated with the prevention of weight gain and possible promotion of weight loss which can be beneficial in overweight patients. They are given by subcutaneous injection or orally (in the case of semaglutide (Rybelsus® ▼)) for the treatment of type 2 diabetes mellitus. Three GLP-1 agonists, liraglutide (Victoza®), dulaglutide (Trulicity®) and semaglutide (Ozempic®▼ and Rybelsus®▼) are on the Barnsley Joint Formulary. Liraglutide as the brand Victoza is now discontinued but remains in the guidance for information Exenatide twice daily (Byetta®) exenatide weekly (Bydureon®) and lixisenatide (Lyxumia®), are non-formulary but may be prescribed for those patients already stabilised on these. Byetta®, Bydureon® and lixisenatide (Lyxumia® shouldn't be started in new patients. Lixisenatide remains in this guidance for information but has been discontinued as the brand Lyxumia® NICE guidance (NG28) advises that GLP-1 mimetic therapy should be continued only when people have a beneficial metabolic response (a reduction of at least 11mmol/mol (1.0%) in HbA1c and a weight loss of at least 3% of initial body weight in 6 months). For adults with type 2 diabetes, only offer combination therapy with a GLP-1 agonist and insulin along with specialist care advice and ongoing support from a consultant-led multidisciplinary team.
BNF therapeutic class	06.01.02.03

Indication	• Four licensed GLP-1 agonists, liraglutide (Victoza®), dulaglutide (Trulicity®) and semaglutide (Ozempic® injection and Rybelsus® oral tablets) are on the Barnsley Joint Formulary. Lixisenatide as the brand Lyxumia® has been discontinued and liraglutide as the brand Victoza® has also been discontinued but both remain in the guidance for information. • **NICE NG28** states a GLP-1 agonist can be used as third-line adjunctive therapy, but does not make any recommendations as to which GLP-1 agonist should be used over another. • **NICE NG28** advise that if triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, consider triple therapy by switching one drug for a GLP-1 agonist for adults with type 2 diabetes who: ➢ have a body mass index (BMI) of 35 kg/m^2 or higher (adjust accordingly for people from Black, Asian and other minority ethnic groups) **and** specific psychological or other medical problems associated with obesity **or** ➢ have a BMI lower than 35 kg/m^2 **and:** ○ for whom insulin therapy would have significant occupational implications **or** ○ weight loss would benefit other significant obesity-related comorbidities. **[2015, amended 2022]** ○ Patients currently prescribed a DPP4 inhibitor should have their medication reviewed and the DPP4 stopped prior to commencing a GLP-1 agonist. DPP4 inhibitors and GLP-1 agonists should not be used in combination.
	SIGN 154 states that 'for individuals with type 2 diabetes and established cardiovascular disease, GLP-1 receptor agonist therapies with proven cardiovascular benefit (currently liraglutide) should be considered. The APC endorsed the position taken by **SIGN 154** in March 2018, and recommended that a GLP-1 agonist with proven cardiovascular benefit (currently liraglutide), be used first-line. If a weekly dose preparation is required then semaglutide should be prescribed as the 1st line formulary choice Since **SIGN 154** was published further trials have been undertaken and three of the formulary products (liraglutide, semaglutide and dulaglutide) have evidence of Cardiovascular benefit. Patients currently being prescribed lixisenatide that have cardiovascular risk or a cardiovascular outcome should be reviewed and changed to dulaglutide, liraglutide or semaglutide.
Dosage and administration	• Administered by subcutaneous injection in the thigh, abdomen, or upper arm • Semaglutide (Rybelsus 3mg) is an oral tablet which should be swallowed whole with a sip of water (up to 120ml). Tablets should not be split, crushed or chewed as it is not known whether this impacts absorption of oral semaglutide. • When added to existing therapy of a sulphonylurea or insulin, a reduction in the dose of sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia. • Blood glucose self-monitoring may be necessary to adjust the dose of sulfonylurea when GLP-1 agonist is initiated. For specific drug dosage and administration see drug summary table (Appendix 1)
Cautions and Contraindications	Hypersensitivity to the active substance or to any of the excipients
Pregnancy and breast feeding	GLP-1 agonists are unlicensed for use in pregnancy or breast feeding.

	Patients should be advised to use effective contraception whilst using GLP-1 agonists. (Note the side effect of sickness and diarrhoea that may impact oral contraceptive effectiveness). Initial advice regarding contraception should be provided by initiating clinician with follow up in primary care if needed. Patients of child bearing age will be provided with the FSRH GLP-1 agonist contraceptive patient information leaflet at the time of initiation. If a patient wishes to become pregnant, or pregnancy occurs then treatment with GLP-1 agonist should be discontinued. Please check the correct SPC for up-to-date washout information. Women of childbearing age should be recommended to use effective contraception when treated with GLP-1 agonists. Semaglutide should be discontinued at least 2 months before a planned pregnancy due to the long half-life. Exenatide should be discontinued at least 12 weeks before a planned pregnancy due to the long half-life.
Adverse Drug Reactions	• Most common side effects are: nausea, vomiting, diarrhoea, constipation, abdominal pain, dyspepsia – these reactions are mostly mild and transient. Nausea may be minimised by stopping eating before satiety. • Headache and dizziness. • Hypoglycaemia has been reported in patients also taking a sulfonylurea and/or basal insulin • Decreased appetite • Injection site reactions (usually mild) Rare or very rare (>1 in 100 to >1 in 1000): acute pancreatitis. GLP-1 agonists should be avoided in patients considered to be at high risk of pancreatitis e.g. gallstones, severe hypertriglyceridaemia, or alcohol use. Patients suspected to have pancreatitis should have the GLP-1 agonist discontinued, be admitted to hospital and the diabetes team should be informed. For drug specific adverse drug reactions please see drug summary table (Appendix 1), BNF or specific drug SPC. Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme: www.mhra.gov.uk/yellowcard
Monitoring	Monitoring of the patient's response to the treatment by measuring HbA1c and weight at 3 months will be undertaken by the diabetic team or the specialist prescriber in the practice. The patients' weight and HbA1c should then be reviewed in primary care at 6months and once stable every 6 months thereafter. Daily blood glucose monitoring is not routinely required; however, blood glucose monitoring is necessary for patients initiating a GLP-1 agonist who are also taking a sulfonylurea or basal insulin where a dose adjustment of the sulfonylurea or insulin may be necessary. Renal function should be monitored annually, or more frequently in patients whose renal function is approaching moderate impairment. Renal function should also be monitored prior to initiating concomitant medication that may affect renal function and periodically thereafter.
Interactions	For drug specific drug interactions please see drug summary table (Appendix 1), BNF or specific drug SmPC.

Additional information[9]	Storage of GLP-1 agonists is in a refrigerator (2 °C – 8 °C). Do not freeze. See Appendix 1 drug summary for further information on storing the products once opened. Patients prescribed a GLP-1 agonist will require a prescription for GlucoRx® Carepoint insulin pen needles of suitable size and length. Clinicians should note that oral semaglutide has low absolute bioavailability (1%) and variable absorption (2-4% of patients will not have any exposure). Food, large volumes of water and other oral medicines reduce the absorption.

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References

1. eMC. Lyxumia 20 micrograms solution for injection SmPC. Available at: https://www.medicines.org.uk/emc/product/2966/smpc < Accessed 27/03/2023>.
2. eMC. Trulicity 1.5mg solution for injection in pre-filled pen SmPC.Available at: https://www.medicines.org.uk/emc/product/3634/smpc <Accessed27/03/2023>.
3. eMC Trulicity 4.5mg solution for injection in pre-filled pen SmPC. Available at: https://www.medicines.org.uk/emc/product/11930/smpc <Accessed27/03/2023)
4. eMC. Victoza 6 mg/ml solution for injection in pre-filled pen SmPC.Available at: https://www.medicines.org.uk/emc/product/6585 < Accessed 27/03/2023>.
5. eMC. Ozempic 0.25mg/0.5mg/1mg for injection in pre-filled pen SmPC. Available at: https://www.medicines.org.uk/emc/product/9748 <Accessed 27/03/2023>.
6. eMC Rybelsus 3mg tablets SmPC. Available at:https://www.medicines.org.uk/emc/product/11507/smpc. <Accessed 27/03/2023>
7. eMC Mounjaro solution for injection in pre-filled pens. Available at:https://www.medicines.org.uk/emc/browse-medicines/M?offset=451&limit=50 <Accessed 17/04/2024>
8. NICE NG28 (2015, Updated Jun 22). Type 2 Diabetes in Adults: Management. Accessed Online. Available at: https://www.nice.org.uk/guidance/ng28 <Accessed 27/03/2023>.
9. SIGN 154 (2017). Pharmacological management of glycaemic control in people with type 2 diabetes.Available at: https://www.sign.ac.uk/media/1090/sign154.pdf <Accessed 27/03/2023>
10. Kidney disease stages and eGFR banding. Kidney.org.uk. Available at: https://www.kidney.org/sites/default/files/heat_map-Patient.jpg <Accessed 27/03/2023>
11. Needles for pre-filled and reusable Pens Area Prescribing Committee Position Statement (APC approved). Available at: https://best.barnsleyccg.nhs.uk/clinical-support/medicines/prescribing-guidelines/Insulin%20Pen%20Needles%20Position%20Statement.pdf?UNLID=209820332202212149 1413 < Accessed 27/03/2023>
12. Faculty of Sexual & Reproductive Healthcare statement: GLP-1 agonists and oral contraception. Available at: https://fsrh.org/Common/Uploaded%20files/documents/Patient-information-GLP-1-agonists-and-contraception.pdf?_gl=1*srv0yt*_ga*NzM5NjAzMTk1LjE3MjUwMTAzMDY.*_ga_S2TDH89J5C*MTc0NTQwMDEwMC4zLjAuMTc0NTQwMDEwOS4wLjAuMA. Accessed 22/04/2025

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Development Process

This guidance has been produced by Joy Power Medicines Management Pharmacist following an AMBER-G classification status of GLP-1 agonists by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by specialists listed and was ratified by the Area Prescribing Committee on 11/10/2023. Interim update March 2024, May 2024 and March 2025. Review date October 2026.

Appendix 1 -GLP-1 agonists – Drug summary (*Please see the full Summary of Product Characteristics for more information. Available at www.medicines.org.uk/emc*)

	Dulaglutide (Trulicity®)	Liraglutide (Victoza®)	Lixisenatide (Lyxumia®)	Semaglutide (Ozempic®)	Semaglutide (Rybelsus®)
Indication / Licensing information	Treatment of type 2 diabetes alone when metformin is considered inappropriate, or in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.	Treatment of type 2 diabetes alone when metformin is considered inappropriate, or in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control. Liraglutide as the brand Victoza® has now been discontinued but remains in the guidance for information.	Treatment of type 2 diabetes mellitus in combination with oral antidiabetic drugs or basal insulin, or both, when adequate glycaemic control has not been achieved. Lixisenatide as the brand Lyxumia® has now been discontinued but remains in the guidance for information.	Treatment of type 2 Diabetes alone (when metformin inappropriate or patient is intolerant) or in combination with other medicinal products for the treatment of diabetes as an adjunct to diet and exercise.	Treatment of type 2 Diabetes alone (when metformin inappropriate or patient is intolerant) or in combination with other medicinal products for the treatment of diabetes as an adjunct to diet and exercise.
Relevant NICE guidance	**NICE Guidance NG28** NICE guidance states a GLP-1 agonist can be used If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, consider triple therapy by switching one drug for a GLP-1 mimetic for adults with type 2 diabetes who: • Have a body mass index (BMI) ≥ 35.0 kg/m^2 in those of European descent (with appropriate adjustment for black, asian and other minority ethnic groups) and specific psychological or medical problems associated with obesity, **or** • Have a BMI < 35.0 kg/m^2, and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities. Only continue GLP-1 agonist if the person has had a beneficial metabolic response (a reduction of at least 1.0 percentage point in HbA1c and a weight loss of at least 3% of initial body weight at 6 months).				
Dosing information	• Administered by subcutaneous injection in the thigh, abdomen, or upper arm. • When added to existing therapy of a sulphonylurea or insulin, a reduction in the dose of sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia.				• Administration orally • When added to existing therapy of a sulphonylurea or insulin, a reduction in

	Dulaglutide (Trulicity®)	**Liraglutide (Victoza®)**	**Lixisenatide (Lyxumia®)**	**Semaglutide (Ozempic®)**	**Semaglutide (Rybelsus®)**
	• Blood glucose self-monitoring may be necessary to adjust the dose of sulfonylurea when GLP-1 agonist is initiated.				the dose of sulphonylurea or insulin may be considered to reduce the risk of hypoglycaemia. • Blood glucose self-monitoring may be necessary to adjust the dose of sulfonylurea when GLP-1 agonist is initiated.
	• Adults over 18 years: *Monotherapy:* The recommended dose is 0.75 mg once weekly. *Add-on therapy:* The recommended dose is 1.5 mg once weekly. For potentially vulnerable populations 0.75 mg once weekly can be considered as a starting dose. For additional glycaemic control: • the 1.5 mg dose may be increased after at least 4 weeks to 3 mg once weekly. • the 3 mg dose may be increased after at	• Adults over 18 years: initially 0.6mg once daily, increased after at least 1 week to 1.2mg once daily. The dose can be increased to 1.8mg (however this is not standard procedure to further improve glycaemic control. • Daily doses higher than 1.8mg are not recommended. • Liraglutide should be administered at the same time each day.	• Adults over 18 years: maintenance dose 20micrograms once daily.	• Adults over 18yrs: starting dose initiated at 0.25mg once weekly. After 4 weeks the dose should be increased to 0.5mg once weekly. After at least a further 4 weeks the dose can be increased to 1mg once weekly to further improve glycaemic control. After at least 4 weeks with a dose of 1mg once weekly, the dose can be increased to 2mg once weekly to further improve glycaemic control.Weekly doses higher than 2mg are not recommended.	• Adults over 18yrs: starting dose is 3mg once daily for one month. The dose should then be increased to 7mg once daily, for at least one month. If further improvement in glycaemic dose needed the dose may be increased to a maintenance dose of 14mg daily. • The maximum recommended single daily dose of semaglutide is 14mg. Taking two 7mg tablets to achieve the effect of 14mg has not been studied and is therefore not recommended. • Tablet should be swallowed whole with a sip of water (up to half a glass or 120ml). • Tablet should not be split, crushed, or chewed, as it

	Dulaglutide (Trulicity®)	Liraglutide (Victoza®)	Lixisenatide (Lyxumia®)	Semaglutide (Ozempic®)	Semaglutide (Rybelsus®)
	least 4 weeks to 4.5 mg once weekly. The maximum dose is 4.5 mg once weekly.				is not known if this affects absorption. • Patients should wait at least 30minutes before eating, drinking or taking any other oral medicinal products. Waiting less than 30minutes decreases the absorption of oral semaglutide. A longer post-dose fasting period results in higher absorption.
Drug specific Adverse drug reactions	• Most common side effects are: nausea, vomiting, diarrhoea, constipation, abdominal pain, dyspepsia – these reactions are mostly mild and transient. Nausea may be minimised by stopping eating before satiety. • Headache and dizziness. • Hypoglycaemia has been reported in patients also taking a sulfonylurea and/or basal insulin • Decreased appetite • Injection site reactions (usually mild) • Fatigue <u>Rare or very rare (>1 in 100 to >1 in 1000):</u> acute pancreatitis. GLP-1 agonists should be avoided in patients considered to be at high risk of pancreatitis e.g. gallstones, severe hypertriglyceridaemia, or alcohol use. Patients suspected to have pancreatitis should have the GLP-1 agonist discontinued, be admitted to hospital and the diabetes team should be informed. • Anaphylactic reaction (Rare).				
	Drug specific common adverse reactions: Sinus tachycardia. First degree atrioventricular block.	Drug specific common adverse reactions: Nasopharyngitis. Bronchitis. Anorexia.	Drug specific common adverse reactions: Upper respiratory tract infection. cystitis. Influenza.	Drug specific common adverse reactions: Diabetic retinopathy complications. Cholelithiasis.	Drug specific common adverse reactions: Diabetic retinopathy complications.
Bioavailability	The mean absolute bioavailability of dulaglutide following single-dose subcutaneous	Absolute bioavailability of liraglutide following subcutaneous administration is approximately 55%.	There are no clinically relevant differences in the rate of absorption when lixisenatide is administered	Similar exposure was achieved with subcutaneous administration of semaglutide in the abdomen, thigh, or upper arm. Absolute	The estimated bioavailability of oral semaglutide is about 1%. Absorption of semaglutide oral is decreased if taken with food or large volumes of water. A

	Dulaglutide (Trulicity®)	Liraglutide (Victoza®)	Lixisenatide (Lyxumia®)	Semaglutide (Ozempic®)	Semaglutide (Rybelsus®)
	administration of single 1.5 mg and 0.75 mg doses was 47 % and 65%, respectively. Absolute bioavailabilities for 3 mg and 4.5 mg doses were estimated to be similar to 1.5 mg although they have not been specifically studied. Over the dose range 0.75 mg to 4.5 mg, the increase in dulaglutide concentration is approximately proportional.		subcutaneously in the abdomen, thigh, or arm. Lixisenatide has a moderate level of binding (55%) to human proteins.	bioavailability of subcutaneous semaglutide was 89%.	longer post-dose fasting period results in higher absorption.
Hepatic impairment	No dosage adjustment is necessary in patients with hepatic impairment.	No dose adjustment is recommended for patients with mild or moderate hepatic impairment. Victoza is not recommended for use in patients with severe hepatic impairment.	No dosage adjustment is needed in patients with hepatic impairment.	No dosage adjustment is needed in patients with hepatic impairment. Experience with the use of semaglutide in patients with severe hepatic impairment is limited. Caution should be exercised when treating these patients with semaglutide.	No dose adjustment is required for patients with hepatic impairment. Experience with the use of semaglutide in patients with severe hepatic impairment is limited. Caution should be exercised when treating these patients with semaglutide.
Renal impairment[8]	No dose adjustment is required in patients with mild, moderate or severe renal impairment (eGFR <	No dose adjustment is required for patients with mild, moderate or severe renal impairment (eGFR < 90 to ≥ 15 mL/min/1.73 m^{2}..	No dose adjustment is required for patients with mild to moderate renal impairment (eGFR 90 to ≥ 45ml/min). There is no therapeutic experience in patients with	No dose adjustment is required for patients with mild, moderate or severe renal impairment (eGFR < 90 to ≥ 15 mL/min/1.73 m^2).	No dose adjustment is required for patients with mild, moderate or severe renal impairment (eGFR < 90 to ≥ 15 mL/min/1.73 m^2).

	Dulaglutide (Trulicity®)	**Liraglutide (Victoza®)**	**Lixisenatide (Lyxumia®)**	**Semaglutide (Ozempic®)**	**Semaglutide (Rybelsus®)**
	90 to ≥ 15 mL/min/1.73 m^2). There is very limited experience in patients with end stage renal disease (< 15 mL/min/1.73 m^2), therefore dulaglutide cannot be recommended in this population.	There is no therapeutic experience in patients with end stage renal disease (creatinine clearance below 15ml/min) therefore, the use of liraglutide cannot be recommended for use in these patients.	severe renal impairment eGFR≤ 30ml/minute.or end-stage renal disease eGFR ≤ 15ml/min and therefore, it is not recommended for use in this population.	There is no therapeutic experience in patients with end stage renal disease eGFR ≤ 15ml/min, therefore, the use of semaglutide cannot be recommended for use in these patients.	There is no therapeutic experience in patients with end stage renal disease eGFR ≤ 15ml/min, therefore, the use of semaglutide cannot be recommended for use in these patients.
Precautions and contraindications	Acute pancreatitis - Use of glucagon-like peptide-1 (GLP-1) receptor agonists has been associated with a risk of developing acute pancreatitis. Patients should be informed of the characteristic symptoms of acute pancreatitis: persistent, severe abdominal pain. If pancreatitis is suspected, the GLP-1 agonist should be discontinued. Caution should be exercised in patients with a history of pancreatitis. Severe gastrointestinal disease - Use of GLP-1 receptor agonists may be associated with gastrointestinal adverse reactions. Delay in gastric emptying - The delay of gastric emptying with GLP-1 agonists may reduce the rate of absorption of orally administered medicinal products therefore use with caution in patients receiving oral medicinal products that require rapid gastrointestinal absorption, require careful clinical monitoring or have a narrow therapeutic ratio. Hypoglycaemia - Patients receiving a GLP-1 agonist with a sulfonylurea and/or with basal insulin may have an increased risk of hypoglycaemia. Reduction of the dose of the sulfonylurea or the basal insulin should be considered to reduce the risk of hypoglycaemia. Lixisenatide should not be given in combination with basal insulin **and** a sulfonylurea due to increased risk of hypoglycaemia. Dehydration - Patients treated with a GLP-1 receptor agonist should be advised of the potential risk of dehydration in relation to gastrointestinal adverse reactions and take precautions to avoid fluid depletion. Pregnancy -. Unlicensed for use in pregnancy or breast feeding.GLP-1 agonists should not be used during pregnancy. Patients are advised to use effective contraception (Note the side effect of sickness and diarrhoea that may impact oral contracptives effectiveness Children –. Unlicensed for children under 18yrs.				
Relevant monitoring	Monitor the patient's response to the treatment by measuring HbA1c and weight at 3 months, 6 months and then 6 monthly thereafter. Renal function should be monitored annually, or more frequently in patients whose renal function is approaching moderate impairment. Renal function should also be monitored prior to initiating concomitant medication that may affect renal function and periodically.				

	Dulaglutide (Trulicity®)	Liraglutide (Victoza®)	Lixisenatide (Lyxumia®)	Semaglutide (Ozempic®)	Semaglutide (Rybelsus®)
Storage	Store in a refrigerator (2 °C – 8 °C). Do not freeze. Once opened the pen may be stored at room temperature for up to 14 days,	Store in a refrigerator (2 °C – 8 °C). Do not freeze. Once opened the pen may be stored at room temperature for up to four weeks.	Store in a refrigerator (2 °C – 8 °C). Do not freeze. Once opened the pen may be stored at room temperature for up to four weeks.	Store in a refrigerator (2 °C – 8 °C). Do not freeze. Once opened the pen may be stored at room temperature for up to six weeks. The cap should always be replaced on the pen to protect the contents from light.	Store in the original blister pack to protect from light and moisture. Does not require any special storage conditions.
Drug Interactions	Dulaglutide delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products. Dulaglutide should be used with caution in patients receiving oral medicinal products that require rapid gastrointestinal absorption. For some prolonged release formulations, an increased release due to an extended gastric residence time may slightly increase drug exposure. Check BNF or SmPC section 4.5 for specific interactions.	No specific drug interactions listed. In vitro, liraglutide has shown very low potential to be involved in pharmacokinetic interactions with other active substances related to cytochrome P450 and plasma protein binding. The small delay of gastric emptying with liraglutide may influence absorption of concomitantly administered oral medicinal products. Interaction studies did not show any clinically relevant delay of absorption and therefore no dose adjustment is required. Few patients treated with liraglutide reported at least one episode of severe diarrhoea. Diarrhoea may affect the absorption of	Lixisenatide delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products. Lixisenatide should be used with caution in patients receiving oral medicinal products that require rapid gastrointestinal absorption. For some prolonged release formulations, an increased release due to an extended gastric residence time may slightly increase drug exposure. Patients receiving medicinal products of a narrow therapeutic ratio or that require careful clinical monitoring should be followed closely, especially at initiation of lixisenatide treatment. If such medicinal products are to be administered with food, patients should be advised	Semaglutide delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products. Semaglutide should be used with caution in patients receiving oral medicinal products that require rapid gastrointestinal absorption. For some prolonged release formulations, an increased release due to an extended gastric residence time may slightly increase drug exposure. Monitor INR more frequently when semaglutide started in patients on warfarin or other coumarin derivatives. Check BNF or SmPC section 4.5 for specific interactions.	Semaglutide delays gastric emptying which may influence the absorption other oral medicinal products. Monitor thyroid parameters when treating patients with semaglutide and levothyroxine. Semaglutide did not change the pharmacodynamic effects as measured by INR. However, upon initiation of semaglutide treatment in patients on warfarin or other coumarin derivatives, frequent INR monitoring is recommended. Interactions with medicinal products with very low bioavailability (F: 1%) have not been evaluated. Check BNF or SmPC section 4.5 for specific interactions.

	Dulaglutide (Trulicity®)	Liraglutide (Victoza®)	Lixisenatide (Lyxumia®)	Semaglutide (Ozempic®)	Semaglutide (Rybelsus®)
		concomitant oral medicinal products. Advise to monitor INR more frequently when liraglutide started in patients on warfarin or other coumarin derivatives. Check BNF or SmPC section 4.5 for specific interactions.	to, if possible, take them with a meal when lixisenatide is not administered. For oral medicinal products that are particularly dependent on threshold concentrations for efficacy, such as antibiotics, patients should be advised to take those medicinal products at least 1 hour before or 4 hours after lixisenatide injection. Gastro-resistant formulations should be administered 1 hour before or 4 hours after lixisenatide injection. No dose adjustment for warfarin is required when co-administered with lixisenatide; however, frequent monitoring of INR in patients on warfarin and/or coumarin derivatives is recommended at the time of initiation or ending of lixisenatide treatment. Check BNF specific interactions.		

	Dulaglutide (Trulicity®)	Liraglutide (Victoza®)	Lixisenatide (Lyxumia®)	Semaglutide (Ozempic®)	Semaglutide (Rybelsus®)
Other Information	The REWIND trial showed favourable CVD outcomes between Dulaglutide and placebo.	The Liraglutide Effect and Action in Diabetes Evaluation of Cardiovascular Outcome Results (LEADER) trial showed that Liraglutide was superior in preventing MACE (major adverse cardiovascular events: CV death, non-fatal myocardial infarction or non-fatal stroke) vs placebo. Liraglutide also significantly reduced the risk of expanded MACE (primary MACE, unstable angina pectoris leading to hospitalisation, coronary revascularisation, or hospitalisation due to heart failure).	The ELIXA trial did not show a difference in cardiovascular mortality or other cardiovascular outcomes between Lixisenatide and placebo.	The SUSTAIN 6 trial showed that Semaglutide was superior in preventing MACE (major adverse cardiovascular events: CV death, non-fatal myocardial infarction or non-fatal stroke) vs placebo. The lower cardiovascular risk was principally driven by the statistically significant decrease in the rate of non-fatal stroke and non-significant decrease in non-fatal MI. There was no significant difference in the rate of cardiovascular death. The SUSTAIN 7 trial compared Semaglutide with Dulaglutide and the results showed statistically significant reductions in both HbA1c and bodyweight for Semaglutide.	The PIONEER 6 trials showed that Semaglutide was superior in preventing MACE (major adverse cardiovascular events: CV death, non-fatal myocardial infarction or non-fatal stroke) vs placebo. Currently no trials have compared semaglutide oral versus other injectable GLP 1 agonists.