GLP-1 (Glucagon-like peptide-1) AGONISTS (Increase insulin secretion, suppress glucagon secretion, and slow gastric emptying)			
DRUG	**NOTES**	**FORMULARY CHOICE**	**PRECAUTIONS / CONTRA-INDICATIONS / LESS DESIRABLE PATIENT GROUPS**
Lixisenatide (Lyxumia®▼)  **Cost per month (Dec 2015):** 20 mcg daily £57.93	**Once daily subcutaneous injection** • **Lixisenatide is currently the GLP-1 agonist with the lowest acquisition cost.** **Dual/Triple therapy:** As per exenatide (Byetta®▼) **Licensed in combination with:** oral glucose-lowering medicinal products and/or basal insulin when these, together with diet and exercise, do not provide adequate glycaemic control. There is no specific NICE guidance for lixisenatide.	Prescriber to decide most appropriate GLP-1 agonist after discussion with patient. If all other patient factors are equal prescribe the GLP-1 agonist with the lowest acquisition cost.	**DUAL THERAPY - continue lixisenatide <u>only</u> if the person has a reduction in HbA1c of ≥11mmol/mol (1%) after 6 months.** **TRIPLE THERAPY - continue lixisenatide <u>only</u> if the person has a reduction in HbA1c of ≥11mmol/mol (1%) and a 3% loss of initial bodyweight after 6 months.** No long term safety data available. **Renal impairment (CrCl, SPC):** 50-80ml/min – no dose adjustment 30-50ml/min – use with caution <30ml/min – not recommended No dose adjustment required based on age, but limited therapeutic experience in patients > 75yrs. See exenatide for information on hypoglycaemia risk and warning about **pancreatitis risk** (applies to all GLP-1 agonists).
Exenatide prolonged release (Bydureon®▼)  **Cost per month (Dec 2015):** 2 mg weekly £73.36	**Once weekly subcutaneous injection** **APC advice:** Exenatide modified release can be considered if tolerability and compliance remains a major issue with conventional GLP-1 agonist therapy among patients whose HbA1c remains >59 mmol/mol and BMI>35kg/m^2. **Exenatide MR is NOT licensed in combination with insulin**. ***Triple therapy: Met + (Glic or Pio) + Exenatide MR*** *Prolonged-release exenatide in triple therapy regimens (that is, in combination with metformin and a sulfonylurea, or metformin and a thiazolidinedione) is recommended as a treatment option for people with type 2 diabetes as described*	Prescriber to decide most appropriate GLP-1 agonist after discussion with patient. If all other patient factors are equal prescribe the GLP-1 agonist with the lowest	**Continue exenatide MR <u>only</u> if the person has a reduction in HbA1c of ≥11mmol/mol (1%) and a 3% loss of initial bodyweight after 6 months.** No long term safety data available. See exenatide for information on hypoglycaemia risk and warning about **pancreatitis risk** (applies to all GLP-1 agonists).

	in 'Type 2 diabetes in adults: management' (NICE NG28); that is, when control of blood glucose remains or becomes inadequate (HbA_{1c} ≥ 59 mmol/mol or agreed individualised target), and the person has:
	• *a body mass index (BMI) ≥ 35 kg/m2 in those of European family origin (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with obesity* ***or***
	• *a BMI < 35 kg/m2* ***and****:*
	  ○ *for whom insulin therapy would have significant occupational implications* ***or***
	  ○ *weight loss would benefit other significant obesity-related comorbidities.*
	
	Licensed as:
	• Dual therapy with metformin, a sulfonylurea or pioglitazone.
	• Triple therapy with metformin & sulfonylurea or metformin and pioglitazone.
		acquisition cost.	

Liraglutide (®▼) Amb1 **Cost per month (Dec 2015):** 1.2 mg daily £78.48	**Once daily subcutaneous injection** **APC advice:** Liraglutide should only be used if the patient has not tolerated lixisenatide, exenatide or exenatide has been shown to be ineffective (after 6 months treatment). **Liraglutide is NOT licensed to be added to basal insulin although basal insulin can be added to it**. ***Triple therapy: Met + (Glic or Pio) + Liraglutide*** *Liraglutide 1.2 mg daily in triple therapy regimens (in combination with metformin + sulfonylurea, or metformin + thiazolidinedione) is recommended as an option for the treatment of people with type 2 diabetes, only if used as described in NICE NG28; that is, when control of blood glucose remains or becomes inadequate* *(HbA1c ≥ 59mmol/mol, or agreed individualised target), and the person has BMI:* • *a body mass index (BMI) ≥ 35 kg/m2 in those of European family origin (with appropriate adjustment*	Prescriber to decide most appropriate GLP-1 agonist after discussion with patient. If all other patient factors are equal prescribe the GLP-1 agonist with the lowest acquisition cost.	**Liraglutide 1.8 mg daily is not recommended for the treatment of people with type 2 diabetes.** **Continue liraglutide only if the person has a reduction in HbA1c of ≥11mmol/mol[2] (1%) and a 3% loss of initial bodyweight after 6 months.** No long term safety data available. Liraglutide is not recommended for use in patients with an eGFR <60mL/min. See exenatide for information on hypoglycaemia risk and warning about **pancreatitis risk** (applies to all GLP-1 agonists).

	for other ethnic groups) and specific psychological or medical problems associated with obesity ***or*** • *a BMI < 35 kg/m2* ***and****:* ○ *for whom insulin herapy would have significant occupational implications* ***or*** ○ *weight loss would benefit other significant obesity-related comorbidities.* **Licensed in combination with:** • Metformin or a sulfonylurea, in patients with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin or sulfonylurea. • Metformin and a sulfonylurea or metformin and a thiazolidinedione in patients with insufficient glycaemic control despite dual therapy.		
Exenatide (Byetta®▼) Non-formulary since Aug 2014 Amb1 **Cost per month (Dec 2015):** 10 mcg twice daily £68.24	**Twice daily subcutaneous injection** ***Triple therapy: Met + (Glic or Pio) + Exenatide*** *Exenatide in triple therapy regimens (that is, in combination with metformin and a sulfonylurea, or metformin and a thiazolidinedione) is recommended as a treatment option for people with type 2 diabetes as described in 'Type 2 diabetes in adults: management' (NICE NG28); that is, when control of blood glucose remains or becomes inadequate (HbA_{1c} ≥ 59 mmol/mol or agreed individualised target), and the person has:* • *a body mass index (BMI) ≥ 35 kg/m2 in those of European family origin (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with obesity* ***or*** • *a BMI < 35 kg/m2* ***and****:* ○ *for whom insulin herapy would have significant occupational implications* ***or*** *weight loss would benefit other significant obesity-related comorbidities.* **Licensed as:** Dual therapy with metformin, a sulfonylurea or pioglitazone. Triple therapy with metformin and a sulfonylurea or	Continue for patients already using it.	**Continue exenatide only if the person has a reduction in HbA1c of ≥11mmol/mol (1%) and a 3% loss of initial bodyweight after 6 months.** No long term safety data available. Exenatide is not recommended for use in patients with an eGFR <30mL/min. **Applies to ALL GLP-1 agonists:** • Discuss the potential benefits and risks of treatment with a GLP-1 agonist with the person to enable them to make an informed decision. • Routine monitoring of blood glucose levels is only required if the GLP-1 agonist is given in combination with another agent likely to cause hypoglycaemia (eg sulfonylurea). • There have been reports of necrotising and haemorrhagic **pancreatitis** with GLP-1 agonists, some of which were fatal. If pancreatitis is suspected, treatment with the GLP-1 agonist should be suspended immediately; if pancreatitis is diagnosed, the GLP-1 agonist should be permanently

	metformin and pioglitazone. **In combination with insulin:** Exenatide is licensed for addition to patient currently receiving insulin +/- metformin and/or pioglitazone in adults who have not achieved adequate glycaemic control with these agents. **NG28:** *In adults with type 2 diabetes, only offer a GLP-1 mimetic in combination with insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team*		discontinued. For most people, however, the benefits of treatment with a GLP-1 agonist outweigh the risks of pancreatitis.

Dulaglutide (Trulicity® ▼) Non-formulary at the time of writing  **Cost per month (Dec 2015):** 0.75mg or 1.5mg weekly £73.25	**NICE Evidence Review ESNM59 (**15 June 2015) **Once weekly sc injection (0.75mg weekly as monotherapy, 1.5 mg weekly as add-on therapy)** ***NICE guidance (CG87):*** ***Dual/triple therapy:*** *Can be used in dual or triple therapy regimens when control of blood glucose remains or becomes inadequate (HbA1c ≥ 59mmol/mol or agreed individualised target). Patients should be on maximally tolerated doses of oral hypoglycaemic agents **and** have a BMI;* • *≥ 35.0 kg/m^2 in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight, or* • *< 35.0 kg/m^2, and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.* **Licensed as:** Monotherapy when metformin ineffective Add-on therapy with other drugs, including insulin	Prescriber to decide most appropriate GLP-1 agonist after discussion with patient. If all other patient factors are equal prescribe the GLP-1 agonist with the lowest acquisition cost	**Continue dulaglutide only if the person has a reduction in HbA1c of ≥11mmol/mol (1%) and a 3% loss of initial bodyweight after 6 months.** No long term safety data available. Dulaglutide can be used without dose adjustment in patients with renal disease **Applies to ALL GLP-1 agonists:** • Discuss the potential benefits and risks of treatment with a GLP-1 agonist with the person to enable them to make an informed decision. • Routine monitoring of blood glucose levels is only required if the GLP-1 agonist is given in combination with another agent likely to cause hypoglycaemia e.g. sulfonylurea. There have been reports of necrotising and haemorrhagic **pancreatitis** with GLP-1 agonists, some of which were fatal. If pancreatitis is suspected, treatment with the GLP-1 agonist should be suspended immediately; if pancreatitis is diagnosed, the GLP-1 agonist should be permanently discontinued. For most people, however, the benefits of treatment with a GLP-1 agonist outweigh the risks of pancreatitis.