Drug Comparisons Chart [DCC002]

GLP-1 analogues ▪ V4.2 July 2017

Coventry & Warwickshire Area Prescribing Committee

* GLP-1s: If triple therapy with metformin and 2 other oral drugs is not effective, not tolerated or contraindicated, consider combination therapy with metformin, a sulfonylurea and a glucagon‑like peptide‑1 (GLP‑1) mimetic for adults with type 2 diabetes who:
have a BMI of 35 kg/m2 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/m2 and:
for whom insulin therapy would have significant occupational implications or weight loss would benfit other significant obesity related comorbidities

Only continue GLP‑1 analogue therapy 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).

LEGEND: **SU** = sulfonylurea **M** = Metformin **P** = Pioglitazone	**28 Day cost**	**Frequency of administration**	**Preparation (all are pre-filled pens)**	**Dose**	**Mono - therapy**	**Dual therapy**			**Triple therapy**		**With Insulin (consider reducing the dose to prevent hypoglycaemia)**	**Renal impairment**			**Hepatic impairment**	**Elderly**	**NICE Guidance***	**Evidence** **(inc only those trials published in full and linked to sources)**	**CVD Outcomes Data** **Head to Head** **Safety**
						with Metformin	**with SU** (consider reducing dose of SU to reduce risk of hypoglycaemia)	**with Pioglitazone**	***with metformin and SU** (consider reducing dose of SU to reduce risk of hypoglycaemia)	**with metformin and pioglitazone**		**Mild**	**Moderate**	**Severe or end stage renal disease**				
Exenatide standard [Byetta®] First Marketed **Mar 2007** Specialist Drugs List Status SA	£63.69	**Daily**	5 micrograms solution per dose in prefilled pen 10 micrograms solution per dose in prefilled pen	5 micrograms **BD** increasing to 10 micrograms **BD**	No	Yes	Yes	Yes	Yes	Yes	As adjunctive therapy to basal insulin + metformin or pioglitazone, or metformin plus pioglitazone	No dosage adjustment	Caution-dose escalation from 5 mcg to 10 mcg should proceed conservatively	Not recommended	No dosage adjustment	Proceed with dose escalation from 5 to 10mcg with caution in those >70 years Experience in >75 years is very limited	NG 28: in triple therapy with M+SU*	Six fully published RCTs with three double blind RCTs each of 30 weeks duration. The primary outcome was the surrogate marker HbA1c reduction from baseline at trial completion.	Due 2018 (EXSCEL) X **3 x 30 week RCTs** *Use since 2007* SPC: Post marketing - Rare cases of acute pancreatitis and acute renal failure
Liraglutide [Victoza®] First Marketed **Jul 2009** Specialist Drugs List Status SA	£73.25 - £109.87	**Daily**	6 mg/mL solution for injection in pre-filled pen (3ml pens)	Starting dose is 0.6 mg **daily** Increase after at least one week to 1.2 mg	No	Yes	Yes	Yes	Yes	Yes	Yes - basal insulin	No dosage adjustment	No doasage adjustment	Not recommended	Limited experience - **not recommended**	No dose adjustment but experience in >75 years is limited	NG 28: in triple therapy with M+SU*	LEAD 1, 2, 3^, 4, 5 ,6* all Phase III 26 week (^52 week) randomised (except*) RCTs. The randomised trials were multi centre and totaled 4,337 volunteers. The primary outcome in studies LEAD 1,2,3,4,5 was change in HbA1c from baseline.	LEADER - primary endpoint of showing non-inferiority as well as demonstrating superiority, with a statistically significant reduction in cardiovascular risk. Exenatide PR (Marginally superior) **5 x 26 week RCTs** *Use since 2009* SPC: Post marketing - Rare cases of acute pancreatitis
Lixesenatide ▼ [Lymuxia®q] First Marketed **May 2013** Specialist Drugs List Status SA	£57.93 (20 micrograms)	**Daily**	10 micrograms and 20 micrograms solution for injection in pre-filled pen	Starting dose: 10 micrograms once **daily** for 14 days A fixed maintenance dose of 20 micrograms once daily is started on Day 15	No	Yes	Yes	Yes	Yes	Yes	Yes - Licensed with basal insulin +/- oral glucose lowering agents. However it should not be given in combination with basal insulin and SU due to increased risk of hypoglycaemia	No dosage adjustment	Caution	Not recommended	No dosage adjustment	No dose adjustment but experience in >75 years is limited	NG 28: in triple therapy with M+SU*	GetGoal-mono (12 weeks) & GetGoal-L-Asia (24 weeks), both Phase III double blind RCTs. Both showed HbA1c reductions from baseline between 0.5 - 0.9% better than placebo. HbA1c was reduced to less than 7% (53mmol/mol) in 20-30% more patients than placebo.	ELIXA-ACS: In patients with type 2 diabetes and a recent acute coronary syndrome, the addition of lixisenatide to usual care did not significantly alter the rate of major cardiovascular events or other serious adverse events. Exenatide (Non-inferior) **7 x ongoing trials** *Use since 2013* SPC: 2,600 patients in 8 placebo controlled or active-controlled trials
Exenatide PR [Bydureon®] First Marketed - **Jul 2011** Specialist Drugs List Status SA	£73.36	**Weekly**	2 mg powder and solvent for prolonged release suspension for injection (pre-filled pen)	2 mg (one vial) **weekly**	No	Yes	Yes	Yes	Yes	Yes	No	No dosage adjustment	Not recommended	Not recommended	No dose adjustment **No clinical experience**	No dose adjustment based on age Experience in >75 years is limited	NG 28: in triple therapy with M+SU*	Four fully published Phase III RCTs (DURATION 1,2,3,4), 670 volunteers in total, in which the primary outcome was the change in HbA1c from baseline.	Due 2018 (EXSCEL) ✓ Liraglutide v. (Marginally inferior) 7 x core safety studies < 12 months *Use since Dec 2011* SPC: Post marketing - Rare cases of acute pancreatitis and acute renal failure
Albiglutide ▼ (Eperzan® ▼) Marketed March 2014 Drugs List Status SI	£71	**Weekly**	30 micrograms and 50 micrograms Powder/solvent for solution for injection in pre-filled pen)	30 mg weekly . Increase to 50 mg once weekly based on individual response	Yes	Yes	Yes	Yes	Yes	Yes	Licensed with insulin +/- oral glucose lowering agents	No dosage adjustment	No dosage adjustment	Not recommended	No dosage adjustment	No dose adjustment is required based on age. The clinical experience in patients ≥75 years is very limited	NG 28: in triple therapy with M+SU*	8 phase III studies. In HARMONY 2, over the 52-week treatment period, HbA1c decreased in both albiglutide groups and increased in the placebo group. The treatment difference was significant for both doses t (albiglutide 30mg: -0.84% [95% CI -1.11% to -0.58%], p<0.0001; albiglutide 50mg: -1.04% [-1.31% to -0.77%], p<0.0001). *http://www.ncbi.nlm.nih.gov/pubmed/26577795* HARMONY 3 (104 week study) compared weekly albiglutide with daily sitagliptin, glimepiride and placebo when used in combination with metformin. Results oshowed that albiglutide, when added to metformin, was superior in terms of HbA1c reduction compared to placebo (-0.9% [95% CI -1.2% to -0.7%], p<0.0001), sitagliptin (-0.4% [95% CI -0.5% to -0.2%], p<0.0001) and glimepiride (-0.3% [95% CI -0.5% to -0.1%], p=0.0033) .*http://www.ncbi.nlm.nih.gov/pubmed/24898304* Albiglutide was inferior to pioglitazone 30 to 45mg daily in HARMONY 5 and inferior to liraglutide 1.8mg daily in HARMONY 7. In HARMONY 4, which had a non-inferiority margin of 0.3%, albiglutide demonstrated non-inferiority to insulin glargine, and in HARMONY 6, which had a non-inferiority margin of 0.4%, albiglutide was non-inferior to pre-prandial insulin lispro.	Meta-analysis of eight phase 3 trials and one phase 2b trial. Major adverse cardiovascular event alone was also not significantly different (52 events vs 53; HR, 0·99; 95% CI, 0·65–1·49 *http://www.thelancet.com/journals/landia/article/PIIS2213-8587(15)00233-8/abstract* Liraglutide (Albiglutide inferior to liraglutide) *http://www.thelancet.com/journals/landia/article/PIIS2213-8587(13)70214-6/abstract* European Public Assessment Report: the long-term safety concerns are the same as for the other GLP-1 receptor agonists, i.e. potential increased risk for pancreatitis and thyroid and pancreatic tumours. *http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/002735/WC500165119.pdf*
Dulaglutide▼ (Trulicity® ▼) Marketed Nov 2014 Drugs List Status SI	£73.25	**Weekly**	0.75 mg and 1.5 mg solution for injection in pre-filled pen	0.75 mg increasing to 1.5 mg once weekly	Yes	Yes	Yes	Yes	Yes	Yes	Licensed with insulin +/- oral glucose lowering agents	No dosage adjustment	No dosage adjustment	Not recommended	No dosage adjustment	No dose adjustment is required based on age However, the therapeutic experience in patients ≥ 75 years is very limited and in these patients 0.75 mg once weekly can be considered as a starting dose.	NG 28: in triple therapy with M + SU*	6 phase III randomised controlled trials (RCTs). In AWARD 1, dulaglutide 1.5 mg or 0.75 mg once weekly was superior to placebo (treatment difference −11.5 mmol/mol [-1.05% points] and −9.2 mmol/mol [-0.84% points], respectively) *http://www.ncbi.nlm.nih.gov/pubmed/24879836*	EPAR -cardiovascular outcome study is underway and is estimated to report in 2020 - http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002825/human_med_001821.jsp&mid=WC0b01ac058001d124 Liraglutide (AWARD 6 -non inferior) http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)60976-4/abstract Exenatide twice daily (AWARD 1-superior) ttp://www.ncbi.nlm.nih.gov/pubmed/24879836 According to the European public assessment report (EPAR) possible long-term safety concerns of pancreatitis and pancreatic and thyroid cancers are consistent with other GLP-1 receptor agonists*http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002825/human_med_001821.jsp&mid=WC0b01ac058001d124*