

Table 1. Differentiating pharmacokinetics and clinical characteristics of currently approved GLP-1 receptor agonists.

Drug	Year of approval	Sequence homology to human GLP-1	Peak plasma concentration	Elimination half-life	Bioavailability	Dosing	Timing of administration	Formulation
Exenatide	2006	53%	2.1 h	2.4 h	65 – 75 %	5 mcg twice daily for 1 m, then 10 mcg twice daily.	Within 60 min prior to morning and evening meals, at least 6 h apart	Subcutaneous injection
Liraglutide	2009	97%	8-12 h	13 h	55%	0.6 mg for 1 wk, then increase to 1.2 mg daily. Option to increase to 1.8 mg daily	Anytime, independent of meals	Subcutaneous injection
Exenatide	2011	53%	Two peaks: Week 2 (related to initial diffusion out of exenatide). Week 6-7 (with hydrolysis and erosion of microspheres)	2.4 h once released	22 – 25%	2 mg once weekly	Anytime, independent of meals	Subcutaneous injection
Lixisenatide	2013		1-3.5 h	3 h	32%	10 mcg once daily for 14 d, then 20 mcg once daily on day 15.	Within the hour prior to any meal of the day	Subcutaneous injection
Albiglutide	2014		3-5 d	5 d	-	30 mg once weekly. Option to increase to 50 mg	Anytime, independent of meals	Subcutaneous injection
Dulaglutide	2014	90%	48 h	5 d	0.75 mg – 65% 1.5 mg – 47%	0.75 mg once weekly if taking as monotherapy, 1.5 mg once weekly if using as add-on therapy	Anytime, independent of meals	Subcutaneous injection
Semaglutide	2017	94%	1-3 d	7 d	89%	0.25 mg once weekly for 4 wks, then increased to 0.5 mg once weekly for at least 4 wks. Option to increase to 1 mg once weekly	Anytime, independent of meals	Subcutaneous injection
Semaglutide	2019 (USA)	94%	1 h	7 d	0.4 – 1%	3 mg once daily for 30 d, then 7 mg once daily for 30 d. Option to increase to 14 mg once daily	Taken on an empty stomach at least 30 mins prior to first meal of the day	Oral tablet

Table 3. Differentiating pharmacokinetics and clinical characteristics of currently approved DPP-4 inhibitors

Drug	Year of approval	Elimination half-life	Bioavailability	Dosing	Formulation
Sitagliptin	2006	8-14 h	87%	100 mg daily	Oral tablet
Vildagliptin	2007	2-3 h	85%	50 mg twice daily when used as monotherapy, 50 mg once daily if used in combination with sulfonylurea	Oral tablet
Saxagliptin	2009	2.5 h (saxagliptin), 3.1 h (main metabolite)	75%	2.5 mg or 5.0 mg once daily	Oral tablet
Linagliptin	2011	24 h	30%	5 mg once daily	Oral tablet
Alogliptin	2013	12-21 h	100%	25 mg once daily	Oral tablet

Table 2. Head to head studies comparing different GLP-1 receptors in patients with T2DM. Efficacy and tolerability data is presented.

	HbA1c Reduction (%)	Body Weight Reduction (kg)	Gastrointestinal Symptoms (%)				Injection Site Reactions (%)	Pancreatitis (N)
			Nausea	Vomiting	Diarrhoea	Constipation		
DURATION-1 Exenatide 2 mg Once Weekly Vs Exenatide 10 mcg Twice Daily	-1.9 vs -1.5	-3.7 vs -3.6	26.4 vs 34.5	10.8 vs 18.6	13.5 vs 13.1	10.8 vs 6.2	22.3 vs 11.7	No cases
DURATION-5 Exenatide 2mg Once Weekly Vs Exenatide 10 mcg Twice Daily	-1.6 vs -0.9	-2.3 vs 1.4	14.0 vs 35.0	4.7 vs 8.9	9.3 vs 4.1	-	13.0 vs 10.0	0 vs 1
DURATION-6 Exenatide 2mg Once Weekly Vs Liraglutide 1.8 mg	-1.28 vs -1.48	-2.68 vs -3.57	9.0 vs 21.0	4.0 vs 11.0	6.0 vs 13.0	5.0 vs 5.0	15.0 vs 3.0	2 vs 0
GETGOAL-X Lixisenatide 20 mcg Vs. Exenatide 10 mcg	-0.79 vs -0.96	-2.96 vs -3.98	24.5 vs 35.1	10.1 vs 13.3	10.4 vs 13.3	-	8.5 vs 1.6	No cases
LEAD-6 Liraglutide 1.8 mg Vs. Exenatide 10 mcg Twice Daily	-1.12 vs -0.79	-3.24 vs -2.87	25.5 vs 28.0	6.0 vs 9.9	12.3 vs 12.1	5.1 vs 2.6	8.9 vs 9.1	1 vs 0
HARMONY-7 Albiglutide 30 mg Titrated to 50 mg Vs. Liraglutide 0.6 mg Titrated to 1.8 mg	-0.78 vs 0.99	-0.64 vs -2.19	9.9 vs 29.2	5.0 vs 9.3	14.9 vs 13.5	-	6.9 vs 1.2	1 vs 2
AWARD-1 Dulaglutide 1.5 mg Vs Dulaglutide 0.75 mg Vs Exenatide 10 mg Twice Daily	-1.51 vs -1.30 vs -0.99	-1.30 vs 0.20 vs -1.07	29.0 vs 17.0 vs 28.0	17.0 vs 6.0 vs 12.0	13.0 vs 9.0 vs 8.0	6.0 vs 2.0 vs 2.0	-	1 vs 0 vs 0
AWARD-6 Dulaglutide 1.5 mg Vs. Liraglutide 1.8 mg	-1.42 vs -1.36	-2.90 vs -3.61	20.0 vs 18.0	7.0 vs 8.0	12.0 vs 12.0	4.0 vs 6.0	<1.0	No cases
SUSTAIN-3: Semaglutide 1.0 mg Vs. Exenatide 2 mg Once Weekly	-1.5 vs -0.9	-5.6 vs -1.9	22.3 vs 11.9	7.2 vs 6.2	11.4 vs 8.4	6.4 vs 5.2	1.2 vs 22.0	2 vs 3
SUSTAIN-7: Semaglutide 0.5 mg or 1.0mg Vs. Dulaglutide 0.75 mg or 1.5mg	Low Dose: -1.5 vs -1.1 High Dose: -1.8 vs -1.4	-4.6 vs -2.3 -6.5 vs -3.0	23.0 vs 13.0 21.0 vs 20.0	10.0 vs 4.0 10.0 vs 10.0	14.0 vs 8.0 14.0 vs 18.0	5.0 vs 3.0 5.0 vs 5.0	1.0 vs 1.0 2.0 vs 3.0	No cases
SUSTAIN-10: Semaglutide 1.0 mg Vs. Liraglutide 1.8 mg	-1.7 vs -1.0	-5.8 vs 1.9	21.8 vs 15.7	10.4 vs 8.0	15.7 vs 12.2	5.9 vs 3.5	-	0 vs 1
PIONEER-4: Oral Semaglutide 14mg Vs. Subcutaneous Liraglutide 1.8 mg	-1.2 vs -1.1	-4.4 vs 3.1	20.0 vs 18.0	9.0 vs 5.0%	15.0 vs 11.0	8.0 vs 4.0	-	1 vs 1

Table 4. Tolerability and Safety of Incretin Based Therapies in Neurodegenerative Diseases

Disease	N	Drug	Weight Loss (N)	Nausea (N)	Gastrointestinal Side Effects			Injection Site Reactions (N)	Pancreatitis or Pancreatic Cancer (N)
					Vomiting (N)	Diarrhoea (N)	Constipation (N)		
PD	44	Exenatide 10 mcg Twice daily Vs Placebo	19 vs 8	13 vs 8	-	7 vs 5	18 vs 14	2 vs 0	-
PD	60	Exenatide 2 mg Once Weekly Vs Placebo	24 vs 18	16 vs 10	2 vs 0	8 vs 6	12 vs 11	27 vs 26	0 vs 1 ^a
WS	1	Liraglutide 0.9 mg Once Daily (Case Study)	Yes, but stabilised	-	-	-	-	-	-
AD	21	Exenatide 10 mcg Twice Daily Vs. Placebo	4 vs 0	5 vs 0	-	3 vs 1	-	1 vs 1	-
AD	38	Liraglutide 1.8 mg Once Weekly Vs. Placebo	Yes ^b	Yes ^b	-	-	-	-	-

a Developed pancreatic cancer shortly after the end of the trial monitoring

b Number not provided in paper.