Drug Comparisons Chart [DCC01]

DPP-4 Inhibitors ▪ V7.1.1

September 2016

Coventry & Warwickshire Area Prescribing Committee

Clinical effectiveness, cost and safety comparisons
Refer to individual SPCs

Not to be used for commercial purposes

POSITIONING	LEGEND: **SU** = sulfonylurea **M** = Metformin **P** = Pioglitazone	Daily cost (Drug Tariff July 2016)	Dose	Mono - therapy	Dual - therapy				Triple therapy			Cautions			Clinical Efficacy Evidence	CVD Outcomes Data -------- Head to Head ------ Safety	NICE Clinical Guideline NG 28
					with metformin	with SU	with pioglitazone	with insulin	with metformin and SU	with metformin and pioglitazone	with metformin and insulin	Renal Impairment	Hepatic impairment	Elderly			
FIRST LINE	**Alogliptin▼** [Vipidia®▼] ---------- Marketed since: **Sep 2013**	£0.95	25 mg daily	No	Yes	Yes	Yes	Yes	No (safety and efficacy not fully established)	Yes	Yes	☑ Mild 50% Moderate 25% Severe 25% ESRD	☑ Mild ☑ Moderate ☒ Severe	◆Over 60 ◆Over 75	Alogliptin as add-on therapy reduces HbA1c by around 5.5 mmol/mol (0.5%) compared with placebo (4 RCTs of dual therapy lasting 26 weeks, 2 RCTs of triple therapy lasting 26 and 52 weeks).	EXAMINE study demonstrated non inferiority to placebo for CVD ischaemic events in people with type 2 diabetes who had had a recent acute coronary syndrome (median of 18 months, n= 5380) Ref: N Engl J Med 2013; 369:1327-1335 http://www.nejm.org/doi/full/10.1056/NEJMoa1305889 ✖ No serious safety concerns have emerged so far. Proportionally more hypoglycaemia and drug-related skin and subcutaneous disorders with alogliptin triple therapy compared with dual therapy, but statistical significance not reported (1 RCT of 52 weeks)	Initial drug treatment option if metformin is contraindicated or not tolerated. First and second intensification options
	Sitagliptin [Januvia®] Marketed since: **Oct 2009**	£1.19	100 mg daily	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	☑ Mild 50% Moderate 25% Severe 25% ESRD	☑ Mild ☑ Moderate ☒ Severe	☑ Over 60 ? Over 75	4 x Phase II trials [12 - 40 weeks] & 5 x Phase III trials [18 - 104 weeks]	In patients with type 2 diabetes and established cardiovascular disease, TECOS (n=14671) did not increase the risk of major adverse cardiovascular events, hospitalisation for heart failure, or other adverse events. http://www.nejm.org/doi/full/10.1056/NEJMoa1501352#t=abstract ✖ Serious adverse reactions including pancreatitis and hypersensitivity reactions have been reported. Hypoglycemia has been reported in combination with sulphonylurea (4.7%-13.8%) and insulin (9.6%). In 11 large clinical trials of up to 2 years in duration, over 3,200 patients have received treatment with Januvia 100 mg per day alone or in combination with metformin, a sulphonylurea (with or without metformin), insulin (with or without metformin), or a PPARγ agonist (with or without metformin). In a pooled analysis of 9 of these trials, the rate of discontinuation due to adverse reactions was 0.8 % with 100 mg per day and 1.5 % with other treatments. (Source: SmPC)	Initial drug treatment option if metformin is contraindicated or not tolerated. First and second intensification options
SECOND LINE	**Linagliptin▼** [Trajenta®▼] ---------- Marketed since: **Oct 2011**	£1.19	5 mg daily	Yes	Yes	No	No	Yes	Yes	No	Yes	☑ Mild ☑ Moderate ☑ Severe ☑ ESRD	? Mild ? Moderate ? Severe	☑ Over 60 ? Over 75	4 x Phase II trials & 9 x Phase III trials [12 - 78 weeks, total patients 4,687 T2DM]	Linagliptin was not associated with increased CV risk versus pooled active comparators or placebo in patients with T2DM. http://www.ncbi.nlm.nih.gov/pubmed/25990013 ✖ The safety of Trajenta has been evaluated overall in 6,602 patients with T2DM of which 5,955 patients received the target dose of 5 mg. In placebo-controlled studies, 6,666 patients were included and 4,302 patients were treated with the therapeutic dose of 5 mg linagliptin. 3,964 patients were exposed to linagliptin 5 mg once daily for ≥ 12 weeks. In the pooled analysis of the placebo-controlled trials, the overall incidence of adverse events in patients treated with placebo was similar to linagliptin 5 mg (63.1% versus 60.3%). The most frequently reported adverse reaction was **hypoglycaemia** observed under the triple combination, linagliptin plus metformin plus sulphonylurea 14.6% versus 7.6% in placebo. In the placebo-controlled studies 6.2% of patients experienced "hypoglycaemia" as an adverse reaction under linagliptin. Of these, 5.1% were mild and 1.0% were moderate and 0.1% were classified as severe. **Pancreatitis** was reported more often in patients randomized to linagliptin (5 events in 4,302 patients receiving linagliptin versus 1 event in 2,364 patients receiving placebo). (Source: SmPC)	Initial drug treatment option if metformin is contraindicated or not tolerated. First and second intensification options
QUALIFIED CHOICE	**Saxagliptin** [Onglyza®] ---------- Marketed since: **Oct 2009**	£1.13	5 mg daily	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	☑ Mild 50% Moderate 50% Severe ☒ ~~ESRD~~	☑ Mild ? Moderate ☒ Severe	☑ Over 60 ? Over 75	2 x Phase II & 6 x Phase III trials [12 - 52 weeks]	SAVOR–TIMI 53 study reported that adding saxagliptin to other blood-glucose-lowering medication did not reduce the risk of CV events or some renal outcomes. However, saxagliptin increased the risk of hypoglycaemia and may also have increased the risk of admission to hospital because of heart failure (n=16492, median follow up 2.1 years) Ref:N Engl J Med DOI: 10.1056/NEJMoa1307684 http://www.nejm.org/doi/full/10.1056/NEJMoa1307684 ✖ There were 4,148 patients with type 2 diabetes, including 3,021 patients treated with Onglyza, randomised in six double-blind, controlled clinical safety and efficacy studies conducted to evaluate the effects of saxagliptin on glycaemic control. In a pooled analysis, the overall incidence of adverse events in patients treated with saxagliptin 5 mg was similar to placebo. Discontinuation of therapy due to adverse events was higher in patients who received saxagliptin 5 mg as compared to placebo (3.3% as compared to 1.8%). (Source: SmPC)	Initial drug treatment option if metformin is contraindicated or not tolerated. First and second intensification options
	Vildagliptin [Galvus] ---------- Marketed since: **Dec 2011**	£1.19 (50 mg twice daily) & £0.60 (50 mg daily)	50 mg twice daily* & 50 mg daily**	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	☑ Mild 50% Moderate 50% Severe ☒ ~~ESRD~~ In ESRD - vildagliptin 50 mg (50%) dose	☒ Mild ☒ Moderate ☒ Severe	☑ Over 60 ☑ Over 75	9 core trials of 24 -52 week duration[Total patients; 4,977]	A meta-analysis of 17446 patients indicates that vildagliptin is not associated with an increased risk of adjudicated Major Adverse Cardiac Events relative to comparators. http://www.ncbi.nlm.nih.gov/pubmed/26250051 ✖ The majority of adverse reactions in trials were mild and transient, not requiring treatment discontinuations. No association was found between adverse reactions and age, ethnicity, duration of exposure or daily dose. Rare cases of hepatic dysfunction (including hepatitis) have been reported. In these cases, the patients were generally asymptomatic without clinical sequelae and liver function returned to normal after discontinuation of treatment. In data from controlled monotherapy and add-on therapy trials of up to 24 weeks in duration, the incidence of ALT or AST elevations ≥ 3x ULN (classified as present on at least 2 consecutive measurements or at the final on-treatment visit) was 0.2%, 0.3% and 0.2% for vildagliptin 50 mg once daily, vildagliptin 50 mg twice daily and all comparators, respectively. These elevations in transaminases were generally asymptomatic, non-progressive in nature and not associated with cholestasis or jaundice. Rare cases of angioedema have been reported on vildagliptin at a similar rate to controls. A greater proportion of cases were reported when vildagliptin was administered in combination with an angiotensin converting enzyme inhibitor (ACE-Inhibitor). The majority of events were mild in severity and resolved with ongoing vildagliptin treatment. (Source: SmPC)	Initial drug treatment option if metformin is contraindicated or not tolerated. First and second intensification options

** in monotherapy or dual therapy with metformin or pioglitazone*

*** in combination with an SU*

◆ = Conservative dosing recommended