deficiency states in a Dutch family. Clin Exp Immunol 1996;105:511–6.

Gudjonsson JE, Tsoi LC, Ma F, Billi AC, van Straalen KR, Vossen ARJV, et al. Contribution of plasma cells and B cells to hidradenitis suppurativa pathogenesis. JCI Insight 2020;5:e139930.

Hoffman LK, Tomalin LE, Schultz G, Howell MD, Anandasabapathy N, Alavi A, et al. Integrating the skin and blood transcriptomes and serum proteome in hidradenitis suppurativa reveals complement dysregulation and a plasma cell signature. PLoS One 2018;13:e0203672.

Kanni T, Zenker O, Habel M, Riedemann N, Giamarellos-Bourboulis EJ. Complement activation in hidradenitis suppurativa: a new pathway of pathogenesis? Br J Dermatol 2018;179:413–9.

Li C, Shah A, Ebsworth K, Dunlap C, Kilgour J, Sullivan K, et al. Complement activation and C5aR elevation in hidradenitis suppurativa patients lesions. Paper presented at: Symposium on Hidradenitis Suppurativa Advances SHSA Conference. 10–11 October 2020; Montreal, Canada.

Merle NS, Noe R, Halbwachs-Mecarelli L, Fremeaux-Bacchi V, Roumenina LT. Complement system part II: role in immunity. Front Immunol 2015;6:257.

Mollnes TE, Jokiranta TS, Truedsson L, Nilsson B, Rodriguez de Cordoba S, Kirschfink M. Complement analysis in the 21st century. Mol Immunol 2007;44:3838–49.

Nilsson PH, Thomas AM, Bergseth G, Gustavsen A, Volokhina EB, van den Heuvel LP, et al. Eculizumab-C5 complexes express a C5a neoepitope in vivo: consequences for interpretation of patient complement analyses. Mol Immunol 2017;89:111–4.

Oppermann M, Götze O. Plasma clearance of the human C5a anaphylatoxin by binding to leucocyte C5a receptors. Immunology 1994;82:516–21.

Peakman M, Lobo-Yeo A, Senaldi G, Nilsson M, Tee DE, Vergani D. Quantification of C3d in biological fluids by an enzyme-linked immunosorbent assay. J Immunol Methods 1987;104:51–6.

van der Zee HH, de Ruiter L, van den Broecke DG, Dik WA, Laman JD, Prens EP. Elevated levels of tumour necrosis factor (TNF)-α, interleukin (IL)-1β and IL-10 in hidradenitis suppurativa skin: a rationale for targeting TNF-α and IL-1β. Br J Dermatol 2011;164:1292–8.

Wagner JL, Hugli TE. Radioimmunoassay for anaphylatoxins: a sensitive method for determining complement activation products in biological fluids. Anal Biochem 1984;136:75–88.

GLP-1 Analogs and SGLT2 Inhibitors Do Not Increase Risk of Bullous Pemphigoid

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TO THE EDITOR

The association of bullous pemphigoid (BP) and dipeptidyl peptidase-4 inhibitors (DPP-4is) used for diabetes mellitus (DM) has recently attracted special interest in the field of BP research. (Nishie and Tasanen, 2019; Varpuluoma et al., 2018a). However, other diabetes drugs have been studied to a lesser extent in this context. In our previous case-control study of 3,397 patients with BP diagnosed in Finland between 1997 and 2013, we did not find increased risk of BP associated with oral DM drugs other than DPP-4is (Varpuluoma et al., 2018b). However, owing to the limited number of either cases or controls on newer drugs, we were unable to study all the DM drugs in the Finnish market. This study aims to analyze the association of DM drugs and BP, especially focusing on the newer regimens.

This is a retrospective case-control study of patients with BP older than 40 years diagnosed in Finland between 1 January 1997 and 31 December 2018. Data on patient records were obtained from the Finnish Care Register for Health Care. Patients were selected by a diagnosis of BP (International Classification of Diseases-10 code L12.0). The control population was composed of patients diagnosed with basal cell carcinoma and matched by age, sex, and year of diagnosis (within 2 years) in a 1:4 ratio. Data on purchased DM drugs for the 2 years immediately preceding diagnosis were obtained from the drug reimbursement register of the database of the Social Insurance Institution of Finland (Supplementary Table S1). Associations between DM drug usage and BP were evaluated using a conditional logistic regression model. Results were adjusted with DM, several neurological diseases, and use of aldosterone antagonists, anticholinergics, antipsychotics, and dopaminergic drugs that have been associated with increased risk for BP (Liu et al., 2020). Because several new DM drugs were approved for use in Finland during the study period, for these drugs, we included only cases and controls diagnosed after the approval. Methods and databases are described in detail in our previous studies (Varpuluoma et al., 2018a, 2018b).

Table 1. Characteristics of Bullous Pemphigoid Cases and Basal Cell Carcinoma Controls Retrieved from the Finnish Care Register for Health Care

Characteristic	Cases n = 5,079 (%)	Controls n = 19,663 (%)[1]
Female	2,968 (58.44)	11,523 (58.60)
Male	2,111 (41.56)	8,140 (41.40)
Age, y, mean (range)	77.6 (40–104)	77.7 (40–104)

[1]Matched by age, sex, and year of diagnosis in a 1:4 ratio. Owing to the lack of data in the drug imbursement register, 581 cases had fewer than the intended 4 controls.

Abbreviations: BP, bullous pemphigoid; DM, diabetes mellitus; DPP-4i, dipeptidyl peptidase-4 inhibitor

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Table 2. Diabetes Drugs Used by Bullous Pemphigoid Cases and Basal Cell Carcinoma Controls 2 Years Before the Diagnosis and OR for Bullous Pemphigoid

Diabetes Drug	Group[1]	Total	n (%)	OR (95% CI)	Adjusted OR (95% CI)[2]	Adjusted OR (95% CI)[3]	Adjusted OR (95% CI)[4]
Biguanides	Case	5,079	758 (14.9)	1.72 (1.57–1.89)	1.19 (1.04–1.35)	1.22 (1.07–1.39)	1.21 (1.06–1.38)
	Control	19,663	1,852 (9.4)	Reference	Reference	Reference	Reference
Metformin	Case	5,079	758 (14.9)	1.72 (1.57–1.89)	1.19 (1.04–1.35)	1.22 (1.07–1.39)	1.21 (1.06–1.38)
	Control	19,663	1,852 (9.4)	Reference	Reference	Reference	Reference
Sulfonylureas	Case	5,079	269 (5.3)	1.58 (1.36–1.82)	1.13 (0.91–1.39)	1.15 (0.93–1.42)	1.16 (0.94–1.44)
	Control	19,663	675 (3.4)	Reference	Reference	Reference	Reference
Glipizide	Case	5,079	36 (0.7)	1.47 (0.99–2.17)	1.55 (0.87–2.77)	1.56 (0.87–2.82)	1.55 (0.86–2.79)
	Control	19,663	92 (0.5)	Reference	Reference	Reference	Reference
Glimepiride	Case	5,042	235 (4.7)	1.58 (1.35–1.84)	1.09 (0.87–1.35)	1.11 (0.89–1.38)	1.12 (0.90–1.40)
	Control	19,510	590 (3.0)	Reference	Reference	Reference	Reference
Combinations of oral blood glucose–lowering drugs	Case	4,194	113 (2.7)	2.87 (2.24–3.66)	1.93 (1.42–2.63)	2.02 (1.48–2.75)	1.97 (1.44–2.70)
	Control	16,282	160 (1.0)	Reference	Reference	Reference	Reference
Metformin and rosiglitazone	Case	4,194	11 (0.3)	1.38 (0.69–2.77)	2.20 (0.87–5.57)	2.21 (0.87–5.59)	2.21 (0.87–5.59)
	Control	16,282	32 (0.2)	Reference	Reference	Reference	Reference
Metformin and pioglitazone	Case	3,742	11 (0.3)	3.79 (1.63–8.77)	3.90 (1.18–12.9)	3.81 (1.14–12.7)	3.96 (1.02–15.4)
	Control	14,374	12 (0.1)	Reference	Reference	Reference	Reference
Metformin and sitagliptin	Case	3,303	62 (1.9)	2.67 (1.93–3.69)	1.38 (0.91–2.09)	1.42 (0.93–2.16)	1.40 (0.91–2.13)
	Control	12,567	94 (0.7)	Reference	Reference	Reference	Reference
Metformin and vildagliptin	Case	3,459	26 (0.8)	4.80 (2.70–8.56)	3.45 (1.78–6.67)	4.36 (2.10–9.05)	4.83 (2.22–10.5)
	Control	13,192	22 (0.2)	Reference	Reference	Reference	Reference
Metformin and linagliptin	Case	2,174	7 (0.3)	13.6 (2.82–65.5)	10.3 (1.40–75.4)	17.9 (1.64–196)	16.5 (1.33–205)
	Control	8,095	2 (0.0)	Reference	Reference	Reference	Reference
Metformin and dapagliflozin	Case	1,771	0 (0.0)	—	—	—	—
	Control	6,478	2 (0.0)	—	—	—	—
Metformin and empagliflozin	Case	1,549	0 (0.0)	—	—	—	—
	Control	5,271	2 (0.0)	—	—	—	—
Thiazolidinediones	Case	4,662	43 (0.9)	2.39 (1.63–3.49)	1.79 (1.11–2.89)	1.80 (1.11–2.91)	1.73 (1.06–2.83)
	Control	18,025	72 (0.4)	Reference	Reference	Reference	Reference
Rosiglitazone	Case	4,662	8 (0.2)	1.12 (0.51–2.47)	0.59 (0.20–1.70)	0.56 (0.19–1.66)	0.56 (0.19–1.66)
	Control	18,025	28 (0.2)	Reference	Reference	Reference	Reference
Pioglitazone	Case	4,622	35 (0.8)	3.16 (2.03–4.92)	2.47 (1.44–4.22)	2.46 (1.43–4.23)	2.37 (1.36–4.10)
	Control	17,868	44 (0.2)	Reference	Reference	Reference	Reference
DPP-4 inhibitors	Case	3,599	457 (12.7)	3.96 (3.44–4.53)	2.42 (2.00–2.93)	2.48 (2.04–3.01)	2.42 (1.99–2.94)
	Control	13,777	541 (3.9)	Reference	Reference	Reference	Reference
Sitagliptin	Case	3,599	213 (5.9)	2.45 (2.05–2.92)	1.31 (1.04–1.66)	1.31 (1.03–1.66)	1.29 (1.02–1.64)
	Control	13,777	360 (2.6)	Reference	Reference	Reference	Reference
Vildagliptin	Case	3,489	126 (3.6)	6.59 (4.94–8.79)	4.03 (2.72–5.97)	4.53 (2.99–6.85)	4.50 (2.96–6.83)
	Control	13,350	80 (0.6)	Reference	Reference	Reference	Reference
Saxagliptin	Case	2,977	3 (0.1)	—	—	—	—
	Control	11,266	2 (0.0)	—	—	—	—
Linagliptin	Case	2,530	152 (6.0)	5.07 (3.96–6.48)	3.08 (2.25–4.21)	3.23 (2.34–4.46)	3.20 (2.32–4.42)
	Control	9,523	133 (1.4)	Reference	Reference	Reference	Reference
GLP-1 analogs	Case	3,661	15 (0.4)	2.57 (1.34–4.92)	1.24 (0.51–2.97)	1.04 (0.41–2.66)	1.08 (0.42–2.78)
	Control	14,047	23 (0.2)	Reference	Reference	Reference	Reference
Exenatide	Case	3,661	6 (0.2)	3.35 (1.13–9.99)	2.18 (0.46–10.3)	1.99 (0.40–9.81)	1.92 (0.37–9.90)
	Control	14,047	7 (0.0)	Reference	Reference	Reference	Reference
Liraglutide	Case	3,055	9 (0.3)	2.37 (1.04–5.42)	1.11 (0.37–3.37)	0.91 (0.27–3.09)	0.94 (0.27–3.22)
	Control	11,574	15 (0.1)	Reference	Reference	Reference	—
Dulaglutide	Case	1,691	0 (0.0)	—	—	—	—
	Control	5,970	2 (0.0)	—	—	—	—
Lixisenatide	Case	2,016	0 (0.0)	—	—	—	—
	Control	7,457	1 (0.0)	—	—	—	—
SGLT2 inhibitors	Case	2,076	39 (1.9)	2.77 (1.83–4.19)	1.18 (0.67–2.07)	1.43 (0.79–2.58)	1.40 (0.77–2.54)
	Control	7,715	58 (0.8)	Reference	Reference	Reference	Reference
Dapagliflozin	Case	2,076	13 (0.6)	2.36 (1.19–4.69)	1.03 (0.38–2.78)	1.63 (0.54–4.90)	1.59 (0.52–4.85)
	Control	7,715	22 (0.3)	Reference	Reference	Reference	Reference

(*continued*)

Table 2. Continued

Diabetes Drug	Group[1]	Total	n (%)	OR (95% CI)	Adjusted OR (95% CI)[2]	Adjusted OR (95% CI)[3]	Adjusted OR (95% CI)[4]
Empagliflozin	Case	1,733	28 (1.6)	3.16 (1.92–5.23)	1.30 (0.68–2.49)	1.38 (0.71–2.67)	1.36 (0.70–2.65)
	Control	6,268	36 (0.6)	Reference	Reference	Reference	Reference
Other blood glucose–lowering drugs, excl. insulins	Case	5,079	47 (0.9)	1.76 (1.24–2.48)	1.11 (0.73–1.68)	1.13 (0.74–1.73)	1.13 (0.74–1.73)
	Control	19,663	104 (0.5)	Reference	Reference	Reference	Reference
Guar gum	Case	5,079	19 (0.4)	1.24 (0.74–2.09)	0.90 (0.50–1.63)	0.90 (0.50–1.64)	0.90 (0.50–1.64)
	Control	19,663	58 (0.3)	Reference	Reference	Reference	Reference
Repaglinide	Case	4,921	20 (0.4)	2.74 (1.55–4.85)	1.35 (0.64–2.84)	2.92 (1.07–7.98)	2.98 (1.10–8.04)
	Control	19,017	29 (0.2)	Reference	Reference	Reference	Reference

Abbreviations: CI, confidence interval; DPP-4, dipeptidyl peptidase 4.

[1]Including cases and controls diagnosed after the drug in question had been approved for use in Finland; see Supplementary Table S1.

[2]OR adjusted for diabetes.

[3]OR adjusted for diabetes, Alzheimer disease, vascular dementia, other/unspecified dementia, Parkinson disease, multiple sclerosis, subarachnoid hemorrhage, intracerebral hemorrhage, cerebral infarction, and epilepsy.

[4]OR adjusted for diabetes, Alzheimer disease, vascular dementia, other/unspecified dementia, Parkinson disease, multiple sclerosis, subarachnoid hemorrhage, intracerebral hemorrhage, cerebral infarction, epilepsy, dopaminergic agents (The Anatomical Therapeutic Chemical-code N04B), anticholinergic agents (N04A), aldosterone antagonists (C03DA), and antipsychotic agents (N05A).

We obtained data on drug use from 5,079 patients and 19,663 controls. The characteristics of the study populations are shown in Table 1. DM drugs used and their associations with BP or basal cell carcinoma are shown in Table 2. DPP-4is were associated with a 2-fold increased risk for BP. Of DPP-4is, vildagliptin was associated with the highest risk. Linagliptin, sitagliptin, and combinations of metformin with vildagliptin and linagliptin were also associated with increased risk of BP. Sulfonylureas, SGLT2 inhibitors, or GLP-1 analogs were not associated with increased BP risk. After adjustments, metformin, repaglinide, pioglitazone, and the combination of metformin and pioglitazone seemed to be associated with increased risk for BP. To rule out the possible effect of DPP-4i use, we performed further analyses for all aforementioned drugs using only data from those cases and controls who had not used DPP-4is during the study period. In these analyses, no statistically significant associations between metformin, repaglinide, pioglitazone, or metformin-pioglitazone combination and BP were found (data not shown).

This study offers data to support the view that GLP-1 analogs and SGLT2 inhibitors are not associated with increased risk of BP. Previously, one case concerning GLP-1 agonist–related BP had been reported; a 62-year-old male with type 2 DM treated with metformin developed BP 2 months after dulaglutide and insulin were added to the treatment (Fukuda et al., 2019). To the best of our knowledge, no case reports have been published of SGLT2 inhibitor–related BP in the English scientific literature. One patient using empagliflozin was recently reported in a Spanish pharmacovigilance study, but no clinical details of the case were available (Reolid et al., 2020). Another pharmacovigilance study did not find disproportionality between reported pemphigoid cases and other DM drugs when the effect of DPP4is was taken into account (Arai et al., 2018). Combinations of DPP-4is and metformin have previously been reported to be associated with increased risk of BP (Plaquevent et al., 2019; Varpuluoma et al., 2018a), but metformin as monotherapy does not seem to carry such a risk (Kridin and Bergman, 2018; Varpuluoma et al., 2018a). In this study, metformin monotherapy was not associated with increased BP risk when the data were corrected for previous or concomitant DPP-4i medication. In contrast, a recent Taiwanese insurance register study of 124,619 patients with diabetes found metformin to be associated with increased BP risk (Wu et al., 2021). Authors suggest that this finding might be explained by their strict definition of the study group where they excluded patients with neurological diseases. Another Taiwanese study of the same insurance register did not find an association between thiazolidinedione, acarbose, glinide, and sulfonylurea and increased risk for BP (Guo et al., 2020).

This study strengthens the view of DPP-4is being the most evident risk factor for BP among DM drugs. In studies comparing DPP-4is with other antidiabetic drugs, DPP-4is were associated with increased risk of BP compared with the other second- and third-line antidiabetic drugs (Douros et al., 2019) or second-generation sulfonylureas (Lee et al., 2020). This study is also in line with recent meta-analyses of case-control studies (Phan, 2020) and of randomized controlled trials concerning DPP-4is (Silverii et al., 2020) that reported DPP4is being associated with a significantly increased risk of BP.

The strengths of this study are its use of comprehensive, real-life data on purchased drugs and a nationwide study design that is likely to cover most of the BP cases diagnosed in Finland during the study period. Limitations of the study include the absence of access to the clinical details. Because of the nature of the drug imbursement register, the drugs supplied to hospital inpatients

were not included in the study. The choice of control population can be considered a limitation because patients with basal cell carcinoma may represent a selected population.

This study offers updated data on the relation of BP and DM drugs and strengthens the view of DPP-4is carrying a significantly increased risk of BP. Further studies are needed to understand the pathogenesis of DPP-4i–associated BP.

Data availability statement

Our data are from the Finnish Care Register for Health Care, maintained by the Finnish Institute for Health and Welfare, and from the drug reimbursement register of Social Insurance Institution of Finland. According to Finnish law and regulations, the data in these registers and documents are confidential. Register authorities can grant permission to use register data and documents for purposes of scientific research.

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CONFLICT OF INTEREST

OV has received educational grants from Leo Pharma and Novartis Finland. LH has received educational grants from CSL Behring, Takeda, Janssen-Cilag, Novartis, AbbVie, and Leo Pharma; honoraria from Lilly, AbbVie, Takeda, Novartis, Sanofi Genzyme, and Union Chimique Belge Pharma for consulting and/or speaking; and is an investigator for AbbVie. KT has received educational grants from Sanofi Genzyme and honoraria from AbbVie, Novartis, Sanofi Genzyme, Janssen-Cilag and Union Chimique Belge Pharma for consulting and/or speaking. The remaining authors state no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization: OV, KT, LH; Formal Analysis: OV, JJ; Methodology: OV, JJ, KT, LH; Supervision: KT, LH; Writing - Original Draft Preparation: OV; Writing - Review and Editing: OV, KT, LH

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at www.jidonline.org, and at https://doi.org/10.1016/j.jid.2021.05.015.

REFERENCES

Arai M, Shirakawa J, Konishi H, Sagawa N, Terauchi Y. Bullous pemphigoid and dipeptidyl peptidase 4 inhibitors: a disproportionality analysis based on the Japanese adverse drug event report database. Diabetes Care 2018;41:e130–2.

Douros A, Rouette J, Yin H, Yu OHY, Filion KB, Azoulay L. Dipeptidyl peptidase 4 inhibitors and the risk of bullous pemphigoid among patients with type 2 diabetes. Diabetes Care 2019;42:1496–503.

Fukuda G, Yoshida T, Hirayama A, Umezawa Y, Takemoto M. Dulaglutide-related bullous pemphigoid in a patient with type 2 diabetes: a case report. Geriatr Gerontol Int 2019;19:1289–90.

Guo JY, Chen HH, Yang YC, Wu PY, Chang MP, Chen CC. The association of dipeptidyl peptidase IV inhibitors and other risk factors with bullous pemphigoid in patients with type 2 diabetes mellitus: a retrospective cohort study. J Diabetes Complications 2020;34:107515.

Kridin K, Bergman R. Association of bullous pemphigoid with dipeptidyl-peptidase 4 inhibitors in patients with diabetes: estimating the risk of the new agents and characterizing the patients. JAMA Dermatol 2018;154:1152–8.

Lee H, Chung HJ, Pawar A, Patorno E, Kim DH. Evaluation of risk of bullous pemphigoid with initiation of dipeptidylpeptidase–4 inhibitor vs second-generation sulfonylurea. JAMA Dermatol 2020;156:1107–14.

Liu SD, Chen WT, Chi CC. Association between medication use and bullous pemphigoid: a systematic review and meta-analysis. JAMA Dermatol 2020;156:891–900.

Nishie W, Tasanen K. Gliptin-associated bullous pemphigoid: a valuable model of the mechanism of breakdown of immune tolerance against BP180. J Invest Dermatol 2019;139:755–6.

Phan K, Charlton O, Smith SD. Dipeptidyl peptidase-4 inhibitors and bullous pemphigoid: a systematic review and adjusted meta-analysis. Australas J Dermatol 2020;61:e15–21.

Plaquevent M, Tétart F, Fardet L, Ingen-Housz-Oro S, Valeyrie-Allanore L, Bernard P, et al. Higher frequency of dipeptidyl peptidase-4 inhibitor intake in bullous pemphigoid patients than in the French general population. J Invest Dermatol 2019;139:835–41.

Reolid A, Muñoz-Aceituno E, Rodríguez-Jiménez P, González-Rojano E, Llamas-Velasco M, Fraga J, et al. Bullous pemphigoid associated with dipeptidyl peptidase-4 inhibitors. a case series and analysis of cases reported in the Spanish pharmacovigilance database. Int J Dermatol 2020;59:197–206.

Silverii GA, Dicembrini I, Nreu B, Montereggi C, Mannucci E, Monami M. Bullous pemphigoid and dipeptidyl peptidase-4 inhibitors: a meta-analysis of randomized controlled trials. Endocrine 2020;69:504–7.

Varpuluoma O, Försti AK, Jokelainen J, Turpeinen M, Timonen M, Huilaja L, et al. Vildagliptin significantly increases the risk of bullous pemphigoid: a Finnish nationwide registry study. J Invest Dermatol 2018a;138:1659–61.

Varpuluoma O, Försti AK, Jokelainen J, Turpeinen M, Timonen M, Tasanen K, et al. Oral diabetes medications other than dipeptidyl peptidase 4 inhibitors are not associated with bullous pemphigoid: a Finnish nationwide case-control study. J Am Acad Dermatol 2018b;79:1034–1038.e5.

Wu CY, Wu CY, Li CP, Chou YJ, Lin YH, Chang YT. Association between dipeptidyl peptidase-4 inhibitors and risk of bullous pemphigoid in patients with type 2 diabetes: a population-based cohort study. Diabetes Res Clin Pract 2021;171:108546.

Supplementary Table S1. Diabetes Drugs Included in this Study and Dates of Approval in Finland Obtained from the Finnish Medicines Agency Database

Diabetes Drug	Date of Approval
Metformin	15 March 1967
Glipizide	16 July 1975
Glimepiride	07 July 1997
Metformin and rosiglitazone	20 October 2003
Metformin and pioglitazone	28 July 2006
Metformin and sitagliptin	16 July 2008
Metformin and vildagliptin	14 November 2007
Metformin and linagliptin	20 July 2012
Metformin and dapagliflozin	16 January 2014
Metformin and empagliflozin	27 May 2015
Rosiglitazone	11 July 2000
Pioglitazone	11 October 2000
Sitagliptin	21 March 2007
Vildagliptin	26 September 2007
Saxagliptin	01 October 2009
Linagliptin	28 April 2011
Exenatide	20 November 2006
Liraglutide	30 June 2009
Dulaglutide	21 November 2014
Lixisenatide	01 February 2013
Dapagliflozin	12 November 2012
Empagliflozin	22 May 2014
Guar gum	22 September 1982
Repaglinide	17 August 1998