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ORIGINAL RESEARCH

Insulin degludec versus insulin glargine U100 for patients with type 1 or type 2 diabetes in the US: a budget impact analysis with rebate tables

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ABSTRACT

Background and aims: Drug rebates are almost universally negotiated privately between the manufacturer and the payer in the US. The aim of the present study was to illustrate the use of a "rebate table" to improve the transparency and utility of published budget impact analyses in the US by modeling ranges of hypothetical rebates for two comparators. Worked examples were conducted to illustrate the budgetary implications of using insulin degludec (IDeg) relative to insulin glargine (IGlar) U100 in patients with type 1 or 2 diabetes.

Methods: A short-term (1-year) budget impact model was developed to evaluate the costs of switching to IDeg from IGlar in patients with type 1 or 2 diabetes on basal-bolus and basal-only insulin, respectively. The analysis used insulin dose and hypoglycemia data from recent randomized trials, data on the prevalence of diabetes, and estimates of the proportion of patients using each insulin regimen. The model was configured to run multiple rebate scenarios to generate a rebate table in a hypothetical 1 million member commercial plan.

Results: Relative to IGlar, IDeg resulted in reductions in non-severe and severe hypoglycemia incidence and costs both in patients with type 1 and patients with type 2 diabetes. Insulin acquisition costs were higher, and respective rebates of 7.3% and 10.6% were required for IDeg to break-even with IGlar at the full list price. Incremental per member per month IDeg costs without a rebate were USD 0.04 in type 1 diabetes and USD 0.80 in type 2 diabetes.

Conclusions: Using IDeg instead of IGlar at list price could result in a modest increase in costs when considering insulin and hypoglycemia costs alone, but modest incremental rebates with IDeg would result in cost neutrality relative to IGlar. In addition, IDeg would result in reduced incidence of severe and non-severe hypoglycemia.

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Introduction

There were an estimated 29.1 million patients with diabetes in the US in 2012, of which 1.25 million had type 1 diabetes and 27.85 million had type 2 diabetes, and 1.4 million Americans aged 20 years or older are newly diagnosed with diabetes each year[1]. The cost of treating all diabetes was USD 245 billion in 2012, including USD 176 billion of direct medical costs and USD 69 billion dollars of indirect costs, including reduced productivity[2]. A 2010 study of costs associated with type 1 diabetes estimated that medical and indirect costs attributable to type 1 diabetes were USD 13,452 per capita per annum (USD 6,288 medical and USD 7,164 indirect), amounting to USD 14.4 billion per annum in the US[3]. Given that the prevalence and cost of diabetes in the US is expected to continue to increase, making best use of the available healthcare budget is ever more important for healthcare payers[4].

Negotiations between payers and pharmaceutical companies commonly result in discounts being agreed relative to the "list price" of a given drug, as listed on the formulary. Such negotiations are almost universally confidential, as any published rebate or discount might affect future negotiations and may also ultimately influence the product list price in other reimbursement environments. In the UK, for example, negotiations between pharmaceutical companies are typically codified in Patient Access Schemes and Primary Care Rebate Schemes, and the Department of Health outlined the commitment to confidentiality around commercially sensitive data in the Pharmaceutical Price Regulation Scheme (PPRS) in 2014[5]. Similarly, in the US, maximum allowable costs (MACs) or maximum reimbursement amounts (MRAs) are typically kept confidential, and, while Medicaid best prices (the lowest manufacturer price paid for a given prescription drug by any purchaser) are reported to the Centers for Medicare & Medicaid Services and states, they are otherwise kept confidential[6].

Given the high prevalence of diabetes, the importance of using accurate pricing for the purposes of budget allocation is more acute than for less prevalent conditions. Scrutinizing expenditure on insulin is particularly important. Patients with

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type 1 diabetes are entirely dependent on exogenous insulin to maintain glycemic control and, while the armamentarium for type 2 diabetes has expanded in the past decade to include the glucagon-like peptide 1 (GLP-1) agonists and sodium-glucose cotransporter 2 (SGLT2) inhibitors, the progressive nature of type 2 diabetes leads to many patients becoming dependent on exogenous insulin to maintain glycemic control, once diet and exercise and oral agents such as metformin and sulfonylurea have failed[7]. Insulin, therefore, remains an important focus when considering overall diabetes treatment costs.

In patients with type 1 diabetes, a basal-bolus insulin regimen consisting of three to four injections per day of basal and prandial insulin is typically recommended to ensure glycemic control is maintained throughout the day and immediately after mealtimes. For both the basal and bolus components of a basal-bolus regimen, the American Diabetes Association (ADA) recommends starting patients with type 1 diabetes on insulin analogs such as insulin glargine (IGlar), detemir, or degludec (IDeg) as basal insulins, and insulin aspart, glulisine, or lispro as bolus insulins to reduce the risk of hypoglycemia relative to human insulin[7]. In type 2 diabetes patients initiating insulin, a basal-only regimen is usually recommended, in combination with metformin and possibly another non-insulin agent. Basal insulin is typically initiated at 10 IU or 0.1–0.2 IU/kg, depending on the extent of hyperglycemia, and the ADA recommends starting patients on NPH insulin, IGlar, insulin detemir, or IDeg[7].

IDeg is a once-daily basal insulin analog with an ultra-long duration of action that was recently approved for use in the US for the improvement of glycemic control in patients with type 1 or type 2 diabetes. Evidence from two open-label, randomized, controlled, treat-to-target trials demonstrated that IDeg was non-inferior to IGlar U100 in terms of glycemic control, while significantly reducing the rate of nocturnal hypoglycemia in patients with type 1 diabetes[8–10]. In a *post-hoc* meta-analysis of the BEGIN trial program, Vora *et al.*[11] analyzed glycemic control, insulin dosing, and hypoglycemia in patients with type 1 diabetes on a basal-bolus regimen (and patients with type 2 diabetes on basal-only or basal-bolus regimens), finding that non-severe nocturnal hypoglycemia was significantly reduced with IDeg relative to IGlar U100 (rate ratio = 0.83, $p < .05$) with equivalent glycemic control. More recently, the SWITCH 1 and 2 trials have been conducted. The trials were double-blind, randomized, controlled, cross-over trials of insulin in patients with type 1 or type 2 diabetes, respectively. Over the full treatment period in SWITCH 1, IDeg resulted in significantly lower rates of severe or blood glucose-confirmed hypoglycemia (−6%), severe or blood glucose confirmed nocturnal hypoglycemia (−25%), and severe hypoglycemia (−26%) alone relative to IGlar U100 in patients with type 1 diabetes[12]. Over the full treatment period in SWITCH 2, patients with type 2 diabetes exhibited significantly lower rates of severe or blood glucose-confirmed hypoglycemia (−23%), severe or blood glucose-confirmed nocturnal hypoglycemia (−25%), and severe hypoglycemia alone (−51%)[13].

The present analysis used data from the SWITCH 1 and 2 trials, combined with a simple budget impact model to establish the effect of using IDeg in place of IGlar U100 on healthcare budgets in the US, with a particular view to using a "rebate table" to present the results in a format that would be applicable to payers with different negotiated discounts or rebates, without prior knowledge of the magnitude of such price reductions.

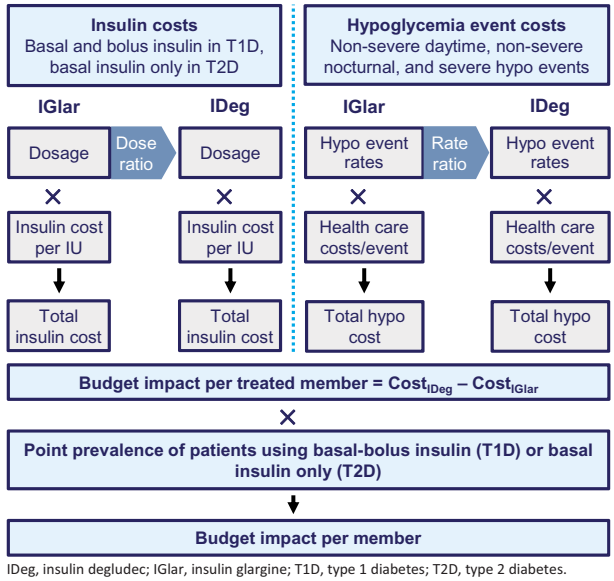
Methods

Model

A budget impact analysis was conducted using a budget impact model developed in Microsoft Excel (Microsoft Corporation, Redmond, WA) and validated in a JavaScript and HTML5 model (Figure 1). Two base case analyses were conducted to estimate the budget impact of IDeg and generate budget impact rebate tables for patients with type 1 or type 2 diabetes. Note that the model was designed to evaluate costs only, rather than cost-effectiveness or cost-utility.

The analysis in patients with type 1 diabetes captured the prevalence of type 1 diabetes in the US, the proportion of patients with type 1 diabetes using a basal-bolus insulin regimen (as opposed to a pump or biphasic insulin), average daily insulin dosing, and rates of non-severe daytime, non-severe nocturnal, and all severe hypoglycemia. The hypoglycemia categories were selected because of their mutual exclusivity, thereby avoiding any double counting. The analysis in patients with type 2 diabetes was similarly structured, but focusing on the basal insulin-using population rather than patients on a basal-bolus insulin regimen.

In both analyses, the model reported outcomes for the overall population, and on per-member per year and per-member per month bases. Support for discounting of future costs was built into the model, although outcomes were not discounted in the reference case, in line with budget impact modeling guidance from the International Society for Pharmacoeconomics and Outcomes Research (ISPOR)[14]. The model was also configured to run multiple analyses for each



IDeg, insulin degludec; IGlar, insulin glargine; T1D, type 1 diabetes; T2D, type 2 diabetes.

Figure 1. Budget impact model schematic. Abbreviations. IDeg, insulin degludec; IGlar, insulin glargine; T1D, type 1 diabetes; T2D, type 2 diabetes.

reference case, varying a hypothetical discount for each comparator in each arm and thereby generating a rebate table, a 2-dimensional representation of the incremental costs of the comparators across a range of rebates. For the present illustrative analyses, 20 rebate price points were selected for each comparator, resulting in 441 analyses in total (including 41 analyses with one or both comparators at full list price and 400 with levels of rebate varying from 0–100% for each comparator in 5% increments). A breakeven frontier was then plotted across the rebate table representing the rebate scenarios between which the incremental cost of the comparators was USD 0.

Hypoglycemia

Rates of non-severe daytime, non-severe nocturnal, and severe hypoglycemia in patients using IGlar were based on the observed rates in the SWITCH 1 and SWITCH 2 trials, 2 × 32-week randomized controlled trials (RCT) comparing once-daily IDeg with once-daily IGlar U100 in patients with type 1 diabetes (SWITCH 1, clinicaltrials.gov ID: NCT02034513) and once-daily IDeg with once-daily IGlar in patients with type 2 diabetes (SWITCH 2, clinicaltrials.gov ID: NCT02030600)[12,13]. Hypoglycemia rate ratios for IDeg were then derived from Poisson model analyses of the relative rates of non-severe daytime, non-severe nocturnal, and severe hypoglycemic events in SWITCH 1 and SWITCH 2 using treatment, period, sequence and dosing time as fixed effects, subject as a random effect, and a logarithm of the exposure time (100 years) as offset (Table 1). The deterministic rate estimates for each hypoglycemic event type with IDeg were ultimately derived from the IGlar base rate and the modeled relative rate with IDeg relative to IGlar.

Resource use

Average daily basal insulin doses were based on the doses observed at the end of the SWITCH 1 and SWITCH 2 RCTs. In the type 1 diabetes analysis, the mean IGlar U100 dose was taken to be 40.58 IUs, and a dose ratio of 0.97 was applied to derive the dose for IDeg, yielding a deterministic mean daily basal dose of 39.36 IUs per patient (Table 2). No significant differences were observed in bolus insulin dosing in SWITCH 1, and the bolus doses were, therefore, assumed to be 31.93 IUs/day in both model arms. In the type 2 analysis, average daily doses of 82.7 IUs for IGlar and 79.4 IUs for IDeg were assumed in the base case analysis, based on the IGlar dose at the end of SWITCH 2 and the IDeg dose ratio of 0.96 (Table 2).

Costs

Drug cost data were taken from the Medi-Span Price Rx database, with costs per unit of USD 0.25 and USD 0.2959 for IGlar U100 and IDeg, respectively[15]. Insulin aspart was selected as the bolus insulin, at a cost of USD 0.29 per unit, also in line with the Medi-Span Price Rx database[15]. Costs associated with each non-severe hypoglycemic event were taken to be USD 11, based on a US-focused study of hypoglycemic resource use by Foos *et al.*[16].

Costs associated with severe hypoglycemia were weighted based on three possible treatment settings: domestic/family, community healthcare professional, and hospital healthcare professional. The weighting between the three treatment settings were based on UK data from a 2009 study by Hammer *et al.*[17], and were modeled differently for type 1 and type 2 diabetes (Table 3). Costs in each setting were based on two recent US studies of costs associated with additional self-monitoring of blood glucose (SMBG) tests, glucagon, GP visits, outpatient, inpatient and emergency department admissions[18,19]. It was assumed that all patients treated outside of the hospital setting would perform an average of 3.9 additional SMBG tests after each event[20]. For patients treated in the domestic/family setting, it was further assumed that 7.2% of patients with type 1 diabetes and 2.1% of patients with type 2 diabetes would receive glucagon at a cost of USD 215, based on the Medi-Span Price Rx database[21]. All patients treated by a community healthcare professional were assumed to receive glucagon and incur a cost of USD 177.60 for a GP visit[15,22]. Hospital admission was divided into outpatient, emergency department, and inpatient admissions, costing USD 181, USD 1,129, and USD 16,297, respectively[23]. Combining the group and hospital admissions weightings with the unit costs yielded a mean cost per severe hypoglycemic event of USD 844.47 in patients with type 1 diabetes, and USD 2,397.10 in patients with type 2 diabetes (Table 3).

Population and analyses

The proportions of patients with type 1 and type 2 diabetes were derived from national estimates from the

Table 1. Hypoglycemia rates in patients with type 1 or type 2 diabetes in the reference case analyses expressed in events per 100 patient years.

	Non-severe daytime	Non-severe nocturnal	Severe
Hypoglycemia in the type 1 basal-bolus population			
Glargine base rate	1,718.1	345.1	104.8
Degludec rate ratio	1.00 (0.98 NS)	0.76	0.74
Derived degludec rate	1,718.1	261.6	77.9
Hypoglycemia in the type 2 basal-only population			
Glargine base rate	179.4	86.3	9.4
Degludec rate ratio	0.80	0.76	0.49
Derived degludec rate	143.2	65.4	4.6

Abbreviation. NS, not significant.

Table 2. Basal and bolus insulin doses and costs associated with insulin glargine and insulin degludec in the type 1 and type analyses.

	Insulin glargine	Insulin degludec
Insulin dosing in the type 1 basal-bolus population		
Basal insulin dose (IUs/day)	40.58	39.36 (dose ratio 0.97)
Basal insulin cost per IU (USD)	0.250	0.296
Basal insulin cost per day (USD)	10.15	11.65
Bolus insulin dose (IUs/day)	31.93	31.93 (ratio not significant)
Bolus cost per IU (USD)	0.290	0.290
Bolus insulin cost per day (USD)	9.26	9.26
Insulin dosing in the type 2 basal-only population		
Basal insulin dose (IUs/day)	82.7	79.4 (dose ratio 0.96)
Basal insulin cost per IU (USD)	0.250	0.296
Basal insulin cost per day (USD)	20.67	23.48

Table 3. Severe hypoglycemia cost estimates for patients with type 1 or type 2 diabetes in the US.

	Cost (USD)	Insulin dosing in the type 1 basal-bolus population			Insulin dosing in the type 2 basal-only population		
		Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
Proportion of patients in group		76.9%	11.6%	11.6%	47.5%	18.4%	34.2%
Additional SMBG	3.90	100%	100%	0%	100%	100%	0%
Glucagon injection	215.00	7.2%	100%	0%	2.1%	100%	0%
GP visit	177.60	0%	100%	0%	0%	100%	0%
Outpatient admission	181.00	0%	0%	32.8%	0%	0%	32.8%
Emergency department	1,129.00	0%	0%	27.9%	0%	0%	27.9%
Inpatient admission	16,297.00	0%	0%	39.3%	0%	0%	39.3%
Cost in group (USD)	–	19.381	396.50	6,785.92	8.42	396.50	6,785.92
Weighted cost in group (USD)	–	14.90	45.80	783.77	4.00	73.30	2,320.11
Total weighted cost (USD)	–	844.47			2,397.10		

Group 1, community (family/domestic); group 2, community (healthcare professional); group 3, hospital.

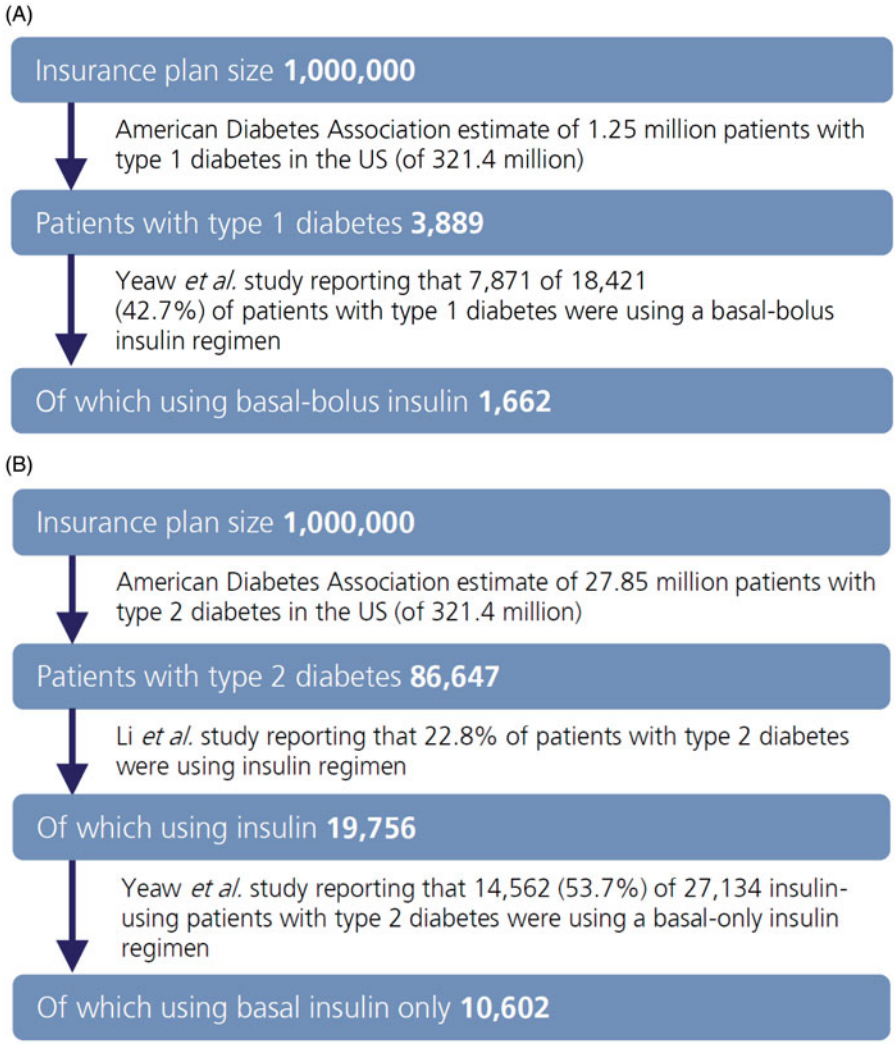


Figure 2. Estimate of the number of (A) basal-bolus insulin users with type 1 diabetes and (B) basal-only insulin users with type 2 diabetes in 1,000,000 member health insurance plans.

American Diabetes Association (ADA), which placed type 1 diabetes prevalence at 1.25 million in 2012, leaving 27.85 million patients with type 2 diabetes. This corresponds to 4.3% of all patients with diabetes or ~0.39% of the US population with type 1 diabetes and 95.7% of patients or ~8.66% of the US population with type 2 diabetes. Of the patients with type 1 diabetes, the base case assumption was that 7,871 of 18,421 (42.7%) patients would be using a basal-bolus insulin regimen (Figure 2A)[24]. In patients with type 2 diabetes, the reference case assumption was that 12.2% of patients were using a basal-only insulin regimen, based on two studies reporting that 22.8% of patients with type 2 diabetes use insulin, and that 14,562 patients of 27,134 insulin-using patients with type 2 diabetes were using a basal-only insulin regimen (Figure 2B)[24,25].

Table 4. Breakdown of treatment costs in the reference case analysis.

	Type 1 basal-bolus			Type 2 basal-only		
	Insulin degludec cost (USD)	Insulin glargine cost (USD)	Difference (USD)	Insulin degludec cost (USD)	Insulin glargine cost (USD)	Difference (USD)
Basal insulin cost (USD)	3,705.46	4,254.21	+548.75	7,547.89	8,576.34	+1,028.45
Bolus insulin cost (USD)	3,382.11	3,382.11	0.00	0.00	0.00	0.00
Non-severe daytime hypoglycemia cost (USD)	188.99	188.99	0.00	19.73	15.75	−3.98
Non-severe nocturnal hypoglycemia cost (USD)	37.96	28.77	−9.19	9.49	7.20	−2.30
Severe hypoglycemia cost (USD)	885.17	657.74	−227.44	225.09	110.41	−114.68
Total cost (USD)	8,199.69	8,511.81	+312.12	7,802.20	8,709.69	+907.49

Table 5. Per treated member per year and per member per month costs of insulin degludec relative to insulin glargine.

	Insulin glargine per member per month cost (USD)	Insulin degludec per member per month cost (USD)	Incremental per member per month cost (USD)
Type 1 basal-bolus	1.14	1.18	+0.04
Type 2 basal-only	6.89	7.70	+0.80
	Insulin glargine per treated member per year cost (USD)	Insulin degludec per member per year cost (USD)	Incremental per member per year cost (USD)
Type 1 basal-bolus	8,200	8,512	+312
Type 2 basal-only	7,802	8,710	+907

Results

The reference case analysis of costs per patient with type 1 diabetes showed total costs of USD 8,200 per treated member per year with IGlar U100 vs USD 8,512 per treated member per year with IDeg, for an incremental increase in costs of USD 312 over 1 year (Table 4). Despite slightly lower dosing with IDeg, incremental costs were driven primarily by insulin, with bolus insulin costs of USD 3,382 per treated member per year in both arms, and basal insulin costs of USD 4,254 with IDeg and USD 3,705 with IGlar U100. However, the increase in costs with IDeg was partially offset by reductions in the costs associated with hypoglycemia, particularly severe hypoglycemia, which resulted in savings of USD 227 per treated member per year.

Based on a hypothetical 1,000,000 patient insurance plan, there would be an estimated 3,889 patients with type 1 diabetes, of whom 1,662 would be using a basal-bolus insulin regimen. In this patient group, overall annual costs would be USD 14.14m with IDeg vs USD 13.63m with IGlar U100, corresponding to a cost per treated member per month (PTMPM) of USD 709.32 with IDeg vs USD 683.31 with IGlar U100, an increase of USD 26.01 per treated member per month. Over the whole plan, costs were USD 14.14 per member per year (PMPY) or USD 1.18 per member per month (PMPM) with IDeg vs USD 13.63 PMPY or USD 1.14 PMPM with IGlar U100 (Table 5).

There would be an estimated 86,647 patients with type 2 diabetes in the same hypothetical plan, of whom 19,756 would be using insulin and 10,602 would be using a basal-only insulin regimen. In this patient group, overall costs would be USD 92.34m with IDeg vs USD 82.72m with IGlar, corresponding to a cost per treated member per month (PTMPM) of USD 725.81 with IDeg vs USD 650.18 with IGlar, an increase in costs of USD 75.62 per treated member per month. Over the whole plan, costs were USD 92.34 per member per year (PMPY) or USD 7.70 per member per month (PMPM) with IDeg vs USD 82.72 PMPY or USD 6.89 PMPM with IGlar, corresponding to an increase in PMPM costs of USD 0.80 (Table 5).

The break-even frontier on the rebate table for type 1 diabetes showed a 7.3% rebate would be required with IDeg to break-even with IGlar at the full IGlar list price (Figure 3). When omitting drug costs entirely (i.e. with 100% rebates for both arms), IDeg reduced costs by USD 0.03 per member per month, driven by reductions in hypoglycemia incidence. The corresponding values for type 2 diabetes were a 10.6% required rebate and a PMPM cost reduction of USD 0.11 when drug costs were omitted entirely (Figure 4).

Discussion

The model developed as part of the present analysis included a proposed approach to addressing the confidential nature of drug price negotiations in published budget impact analyses. The specific analysis showed an increase in overall costs with IDeg of USD 907 per treated member per year driven primarily by the higher insulin unit cost. As with any increase in healthcare expenditure, the budgetary consequences should be balanced by improvements in life expectancy, quality-adjusted life expectancy, or other tangible health outcomes. A country-specific cost-effectiveness or cost-utility analysis would be required to address the question of the incremental cost-effectiveness of IDeg relative to IGlar. While this was not the focus of the present analysis, previous studies have demonstrated that IDeg is cost-effective relative to IGlar. A 2014 study in the UK reported an incremental cost-effectiveness ratio (ICER) of GBP 15,795 per QALY gained (USD 19,800 per QALY gained at 1.25 USD:GBP[26]), falling below an estimated willingness-to-pay threshold of GBP 23,000 (USD 18,400) per QALY gained in the UK setting[27,28]. Similarly, a short-term analysis of IDeg in Sweden found the ICER to be SEK 10,082 per QALY gained (USD 1,100 per QALY gained at 0.11 USD:SEK[29]), falling well

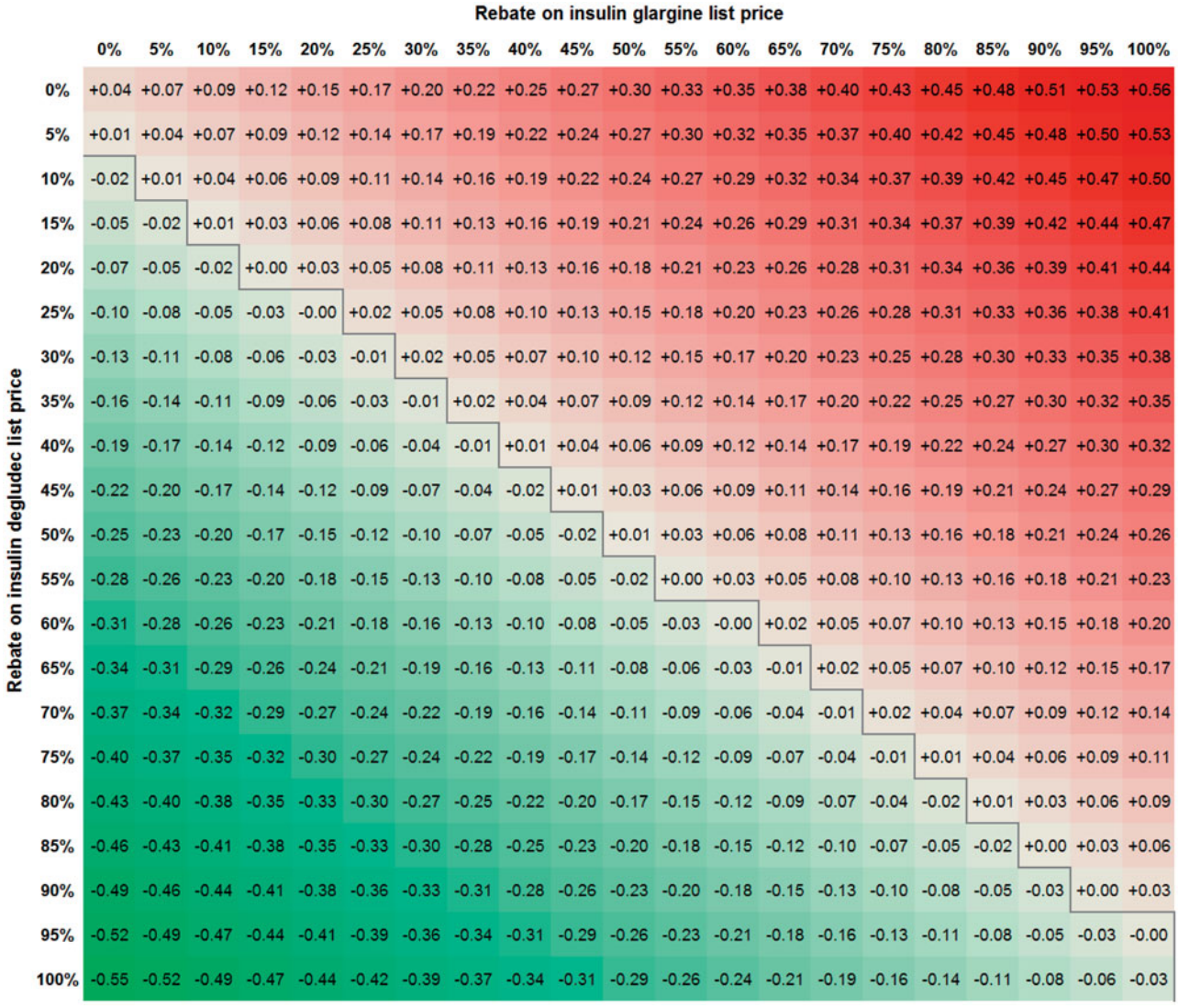


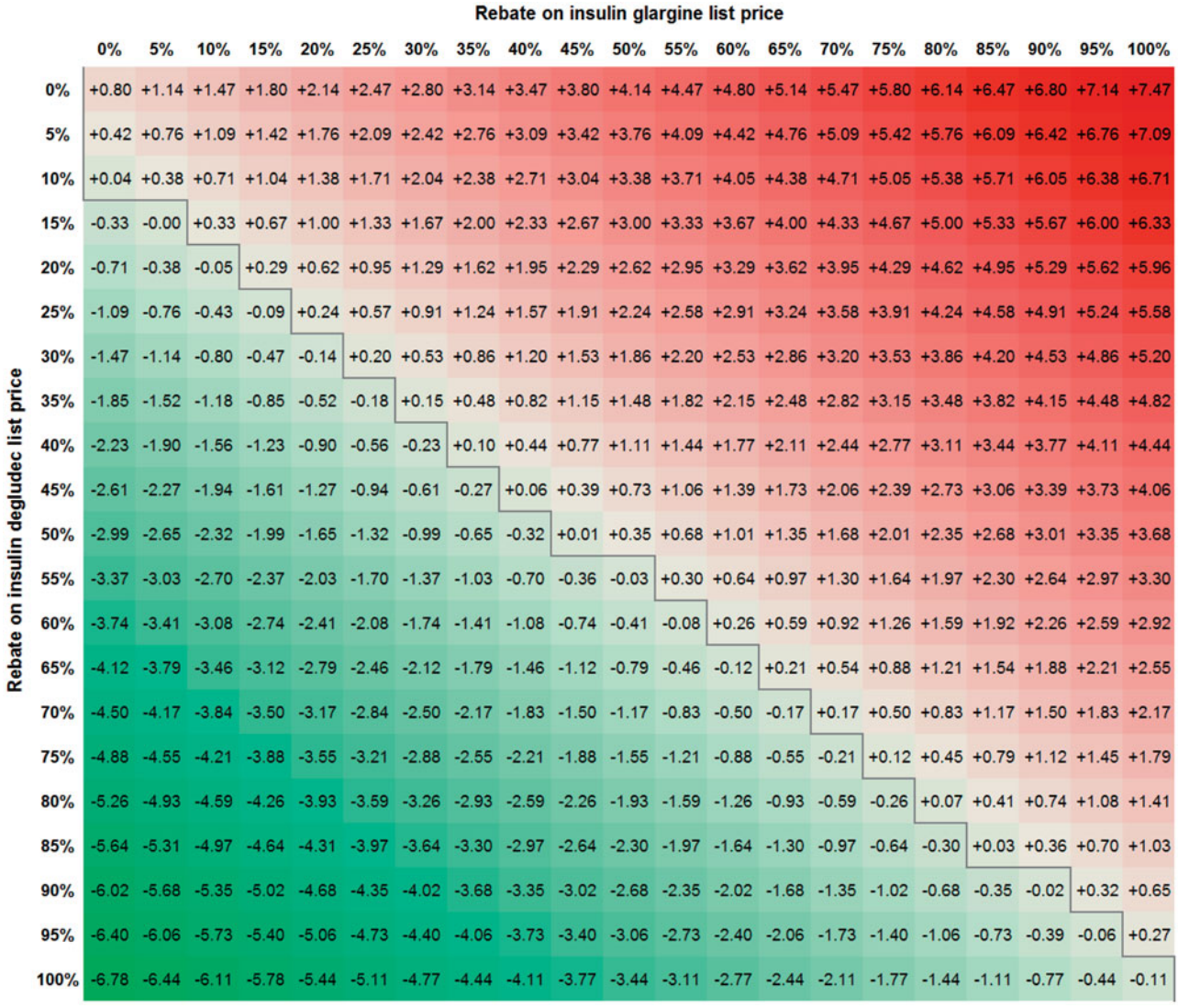
Figure 3. Per member per month incremental cost of insulin degludec relative to insulin glargine in patients with type 1 diabetes in the US (USD).

below a suggested willingness-to-pay threshold of SEK 500,000 (USD 55,000) in the Swedish setting[30], and the authors concluded that IDeg would be cost-effective relative to IGlar[31].

The most significant limitation of the present study was the exclusive focus on insulin and hypoglycemia costs, limiting the applicability to budget holders interested exclusively in drug costs and the cost of hypoglycemia-related healthcare expenditure such as healthcare professional (HCP) contacts, hospitalization, and increased self-monitoring of blood glucose testing. Costs associated with other HCP contact, longer-term complications of diabetes, or reduced productivity, were all omitted from the analysis. The omission of differences in efficacy is in part due to the treat-to-target nature of the RCTs of IDeg. Treat-to-target trials greatly reduce the relevance of differentiating between different insulin analogs on the basis of glycemic control, as patients failing to reach HbA1c targets are titrated to higher doses until the specified target is met. Clinical differentiation is, therefore, restricted to incidence of hypoglycemia, the dose of insulin required to reach the HbA1c target, and other risk factors for complications of diabetes (such as bodyweight), which typically only differ significantly between different therapeutic classes rather than between specific insulin analogs.

One final limitation is in the calculation of the number of patients with type 2 diabetes treated with basal insulin. A key factor in making a realistic assessment of the cost of treating diabetes is the proportion of patients who adhere to and persist with their prescribed regimen. For instance, a 2009 study on adherence to IGlar and exenatide reported that the average medication possession ratio (MPR) was 57.9%, resulting in an over-estimation of medication usage of 72.7% if adherence is not captured in the analysis[32]. A full analysis of patients with type 1 diabetes, and patients with type 2 diabetes on more complex insulin regimens, would need to be conducted to establish the overall budgetary implications of the replacement of IGlar with IDeg.

The primary objective of the present analysis was to highlight the need to acknowledge and address privately-negotiated discounts and rebates when conducting and publishing budget impact analyses. Whilst the ISPOR guidelines recommend incorporating such factors into budget impact models,



Rebate on insulin degludec list price	0%	5%	10%	15%	20%	25%	30%	35%	40%	45%	50%	55%	60%	65%	70%	75%	80%	85%	90%	95%	100%
0%	+0.80	+1.14	+1.47	+1.80	+2.14	+2.47	+2.80	+3.14	+3.47	+3.80	+4.14	+4.47	+4.80	+5.14	+5.47	+5.80	+6.14	+6.47	+6.80	+7.14	+7.47
5%	+0.42	+0.76	+1.09	+1.42	+1.76	+2.09	+2.42	+2.76	+3.09	+3.42	+3.76	+4.09	+4.42	+4.76	+5.09	+5.42	+5.76	+6.09	+6.42	+6.76	+7.09
10%	+0.04	+0.38	+0.71	+1.04	+1.38	+1.71	+2.04	+2.38	+2.71	+3.04	+3.38	+3.71	+4.05	+4.38	+4.71	+5.05	+5.38	+5.71	+6.05	+6.38	+6.71
15%	-0.33	-0.00	+0.33	+0.67	+1.00	+1.33	+1.67	+2.00	+2.33	+2.67	+3.00	+3.33	+3.67	+4.00	+4.33	+4.67	+5.00	+5.33	+5.67	+6.00	+6.33
20%	-0.71	-0.38	-0.05	+0.29	+0.62	+0.95	+1.29	+1.62	+1.95	+2.29	+2.62	+2.95	+3.29	+3.62	+3.95	+4.29	+4.62	+4.95	+5.29	+5.62	+5.96
25%	-1.09	-0.76	-0.43	-0.09	+0.24	+0.57	+0.91	+1.24	+1.57	+1.91	+2.24	+2.58	+2.91	+3.24	+3.58	+3.91	+4.24	+4.58	+4.91	+5.24	+5.58
30%	-1.47	-1.14	-0.80	-0.47	-0.14	+0.20	+0.53	+0.86	+1.20	+1.53	+1.86	+2.20	+2.53	+2.86	+3.20	+3.53	+3.86	+4.20	+4.53	+4.86	+5.20
35%	-1.85	-1.52	-1.18	-0.85	-0.52	-0.18	+0.15	+0.48	+0.82	+1.15	+1.48	+1.82	+2.15	+2.48	+2.82	+3.15	+3.48	+3.82	+4.15	+4.48	+4.82
40%	-2.23	-1.90	-1.56	-1.23	-0.90	-0.56	-0.23	+0.10	+0.44	+0.77	+1.11	+1.44	+1.77	+2.11	+2.44	+2.77	+3.11	+3.44	+3.77	+4.11	+4.44
45%	-2.61	-2.27	-1.94	-1.61	-1.27	-0.94	-0.61	-0.27	+0.06	+0.39	+0.73	+1.06	+1.39	+1.73	+2.06	+2.39	+2.73	+3.06	+3.39	+3.73	+4.06
50%	-2.99	-2.65	-2.32	-1.99	-1.65	-1.32	-0.99	-0.65	-0.32	+0.01	+0.35	+0.68	+1.01	+1.35	+1.68	+2.01	+2.35	+2.68	+3.01	+3.35	+3.68
55%	-3.37	-3.03	-2.70	-2.37	-2.03	-1.70	-1.37	-1.03	-0.70	-0.36	-0.03	+0.30	+0.64	+0.97	+1.30	+1.64	+1.97	+2.30	+2.64	+2.97	+3.30
60%	-3.74	-3.41	-3.08	-2.74	-2.41	-2.08	-1.74	-1.41	-1.08	-0.74	-0.41	-0.08	+0.26	+0.59	+0.92	+1.26	+1.59	+1.92	+2.26	+2.59	+2.92
65%	-4.12	-3.79	-3.46	-3.12	-2.79	-2.46	-2.12	-1.79	-1.46	-1.12	-0.79	-0.46	-0.12	+0.21	+0.54	+0.88	+1.21	+1.54	+1.88	+2.21	+2.55
70%	-4.50	-4.17	-3.84	-3.50	-3.17	-2.84	-2.50	-2.17	-1.83	-1.50	-1.17	-0.83	-0.50	-0.17	+0.17	+0.50	+0.83	+1.17	+1.50	+1.83	+2.17
75%	-4.88	-4.55	-4.21	-3.88	-3.55	-3.21	-2.88	-2.55	-2.21	-1.88	-1.55	-1.21	-0.88	-0.55	-0.21	+0.12	+0.45	+0.79	+1.12	+1.45	+1.79
80%	-5.26	-4.93	-4.59	-4.26	-3.93	-3.59	-3.26	-2.93	-2.59	-2.26	-1.93	-1.59	-1.26	-0.93	-0.59	-0.26	+0.07	+0.41	+0.74	+1.08	+1.41
85%	-5.64	-5.31	-4.97	-4.64	-4.31	-3.97	-3.64	-3.30	-2.97	-2.64	-2.30	-1.97	-1.64	-1.30	-0.97	-0.64	-0.30	+0.03	+0.36	+0.70	+1.03
90%	-6.02	-5.68	-5.35	-5.02	-4.68	-4.35	-4.02	-3.68	-3.35	-3.02	-2.68	-2.35	-2.02	-1.68	-1.35	-1.02	-0.68	-0.35	-0.02	+0.32	+0.65
95%	-6.40	-6.06	-5.73	-5.40	-5.06	-4.73	-4.40	-4.06	-3.73	-3.40	-3.06	-2.73	-2.40	-2.06	-1.73	-1.40	-1.06	-0.73	-0.39	-0.06	+0.27
100%	-6.78	-6.44	-6.11	-5.78	-5.44	-5.11	-4.77	-4.44	-4.11	-3.77	-3.44	-3.11	-2.77	-2.44	-2.11	-1.77	-1.44	-1.11	-0.77	-0.44	-0.11

Figure 4. Per member per month incremental cost of insulin degludec relative to insulin glargine in patients with type 2 diabetes in the US (USD).

the commercially sensitive nature of the exact discounts negotiated result in published budget impact models that over-estimate the costs borne by healthcare payers and may draw conclusions on the incremental budget impact that runs contrary to the reality as negotiated by the payer. The rebate table approach is one way in which this could be addressed in future publications of budget impact analyses. The worked examples in this instance showed that, at full IGlar list price, a rebate of 7.3% would be required to break-even with IDeg relative to IGlar in patients with type 1 diabetes using basal-bolus insulin regimens, while a rebate of 10.6% would be required in patients with type 2 diabetes using basal-only insulin. These break-even values and incremental costs would then ideally be combined with an estimate of the cost-effectiveness of the new intervention, a practice that is becoming increasingly common in the US[33]. The proposed technique of presenting a wide range of rebate scenarios could easily be extended to cost-effectiveness and cost-utility studies, in which a rebate table could be constructed to show incremental cost-utility ratios in place of incremental costs, and added to other more established measures of uncertainty such as one-way and probabilistic sensitivity analysis.

Conclusion

While using IDeg instead of IGlar at list price could result in a modest increase in costs when considering insulin and hypoglycemia costs alone, IDeg would result in reduced incidence of severe and non-severe hypoglycemia. At the full IGlar list price, IDeg would be cost neutral overall, with a 7.3% rebate in patients with type 1 diabetes, while a 10.6% rebate would be required to be cost neutral in patients with type 2 diabetes. The use of rebate tables to illustrate the findings of the present analysis should increase the longevity and utility of the results to healthcare payers.

Transparency

Declaration of funding

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Declaration of financial/other relationships

WSL has served on speaker and advisory panels for Novo Nordisk A/S and Insulet Corp and as an author for Novo Nordisk A/S; she has received research funding from Novo Nordisk A/S, Insulet Corp, and Eli Lilly and Company. JW is a full-time employee of Novo Nordisk, Inc. JG is a full-time employee of Nov Nordisk A/S, which manufactures and holds the marketing authorization for insulin degludec and other anti-diabetic agents. RFP is a full-time employee of Ossian Health Economics and Communications GmbH, which received consultancy fees from Novo Nordisk, Inc. to conduct the analysis and prepare the manuscript. JME peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

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