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Insulin Glulisine

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Contents

Abstract

▲ Insulin glulisine is a rapid-acting human insulin analogue that has a faster onset of action and shorter duration of action than regular human insulin (RHI) in patients with type 1 or 2 diabetes mellitus and is efficacious in controlling prandial blood glucose levels in these patients.

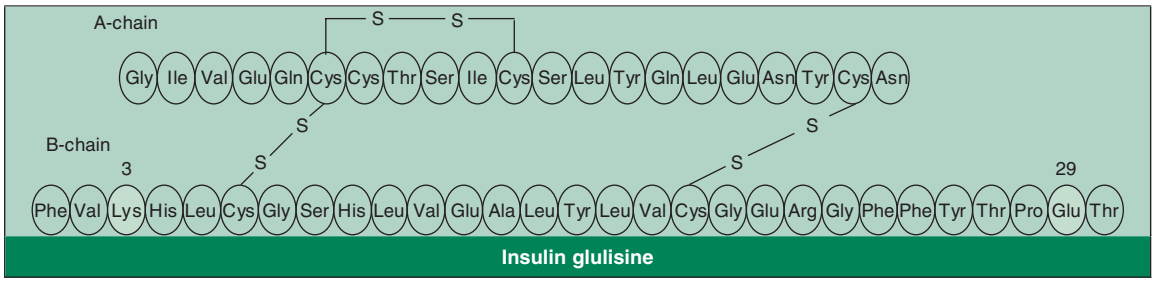
▲ In large, well designed trials in patients with type 1 diabetes, insulin glulisine demonstrated a similar degree of glycaemic control, as measured by glycosylated haemoglobin (HbA_{1c}) levels, to RHI after 12 weeks and insulin lispro after 26 weeks.

▲ Pre-meal insulin glulisine was also more effective than RHI at controlling 2-hour post-prandial glucose excursions in patients with type 1 or 2 diabetes over a period of 12 weeks.

▲ In patients with type 2 diabetes, insulin glulisine induced significantly greater reductions in HbA_{1c} levels and 2-hour post-breakfast and post-dinner blood glucose levels than RHI over a period of 26 weeks.

▲ Insulin glulisine was generally well tolerated by patients with type 1 or 2 diabetes and had a similar safety profile to insulin lispro or RHI. Severe hypoglycaemia was experienced by similar proportions of insulin glulisine or comparator insulin (insulin lispro or RHI) recipients with type 1 or type 2 diabetes.

Features and properties of insulin glulisine (Apidra®)	
Indications	
Control of prandial hyperglycaemia in adult patients with diabetes mellitus	
Mechanism of action	
Binds to and activates the insulin receptor	
Dosage and administration	
Dosage in clinical trials	Titrated to achieve a 2h postprandial blood glucose level of 6.7–8.9 mmol/L
Route of administration	Subcutaneous
Frequency of administration	Within 15 min before a meal or within 20 min after starting a meal
Pharmacokinetic profile (single subcutaneous abdominal injection of 0.15 IU/kg immediately prior to a meal in patients with type 1 diabetes)	
Peak plasma concentration	82 μIU/mL
Time to peak plasma concentration	55 min
Area under the plasma concentration-time curve from 0–6h	11 912 μIU • min/mL
Adverse events	
Most frequent serious adverse event	Hypoglycaemia



Worldwide, 3.2 million deaths annually are attributed to diabetes mellitus.[1] The disease increases the risk of cardiovascular disease[1] and is associated with microvascular complications (retinopathy, neuropathy, nephropathy), which can be prevented or delayed by close control of blood glucose levels.[2,3]

Patients with type 1 diabetes and some patients with type 2 diabetes require insulin replacement therapy to maintain adequate glucose control.[4] Recombinant DNA technology[5] enables the synthesis of regular human insulin (RHI) analogues that have a longer (e.g. insulin glargine[6]) or shorter (e.g. insulin glulisine, insulin aspart[7] and insulin lispro[8]) duration of action than RHI.[5] Insulin glulisine (Apidra®)[1] is a rapid-acting human insulin analogue, produced by recombinant DNA technology using a non-pathogenic laboratory strain of *Escherichia coli* (K12), that is equipotent to human insulin.[9]

This review examines the pharmacological properties, clinical efficacy and tolerability of insulin glulisine in patients with diabetes mellitus.

1. Pharmacodynamic Profile

- Insulin and insulin analogues regulate glucose metabolism through the stimulation of peripheral glucose uptake and the inhibition of hepatic glucose production.[9] In the insulin glulisine B-chain, glutamate substitution for lysine at position 29 and lysine substitution for asparagine at position 3[9] was expected to reduce self-association, improve monomer stability, increase the rate of absorption while retaining unaltered affinity for the insulin receptor.[5]

- No differences in insulin receptor association, dissociation or receptor binding affinity were observed in an *in vitro* study in rat-1 fibroblasts overexpressing the human insulin receptor isoform B.[10]

- Binding of insulin glulisine to the insulin-like growth factor-1 (IGF-1) receptor, which promotes mitogenic activity, is similar to that of RHI.[11] In a cell line expressing predominantly IGF-1 receptors and only marginal levels of insulin receptors (i.e. K6 rat heart myoblasts) binding and internalisation were similar with both ^{125}I-insulin glulisine and regular human ^{125}I-insulin; however, degradation of insulin glulisine was lower than that of RHI.[11]

- Compared with RHI, insulin glulisine did not promote excessive mitogenic activity, as a consequence of IGF-1 activation, in K6 myoblasts *in vitro* or in rat mammary glands *in vivo*.[11] It activated the adaptor protein Shc/mitogen-activated protein kinase cascade and stimulated DNA synthesis in myoblasts in a manner similar to that of RHI.

- Insulin glulisine does not appear to preferentially activate the insulin receptor substrate (IRS)-2 protein, which is crucial to pancreatic β-cell growth and survival,[12] over IRS-1 *in vivo*.[13] Early *in vitro* data suggested that insulin glulisine preferentially activated IRS-2 over IRS-1 in K6 rat heart myoblasts, adult rat cardiomyocytes, proliferating human skeletal muscle cells[11] and the rat insulinoma cell line INS-1.[12] However, recent *in vivo* data in mice indicate that insulin and insulin glulisine induce a similar degree of activation of the insulin receptor, IRS-1 and IRS-2.[13] Phosphatidylinositol 3-kinase

1 The use of trade names is for product identification purposes only and does not imply endorsement.

activation and downstream signalling events were also similar in liver, muscle and hypothalamus.[13]

- Apoptosis induced in INS-1 cells by cytokine or fatty-acid exposure was more strongly inhibited by 500nM insulin glulisine (55–60%) than by insulin aspart (35–40%) or RHI (20%).[12]
- The molar efficacy of insulin glulisine and RHI were equivalent, as evinced by a similar mean glucose infusion rate (GIR), area under the glucose infusion rate time-curve (GIR-AUC) at steady state and from time zero to clamp-end (GIR-AUC_{end}; representing total glucose disposal) during a 2-hour continuous infusion of insulin glulisine or RHI in a crossover study in 16 healthy volunteers.[14]
- Subcutaneous insulin glulisine has a glucose-lowering profile characterised by a more rapid onset (figure 1) and shorter duration of action than RHI in healthy volunteers[15] and in patients with either type 1 or type 2 diabetes.[16,17]
- The mean GIR-AUC_{end} was similar with subcutaneous insulin glulisine and RHI.[16,17] However, median times to 20% of total GIR-AUC (GIR-$AUC_{20\%}$; early glucose disposal) or 80% of total GIR-AUC (duration of bulk activity) values were shorter with insulin glulisine than RHI (121 vs 194 minutes and 350 vs 435 minutes; both $p < 0.05$).[17]

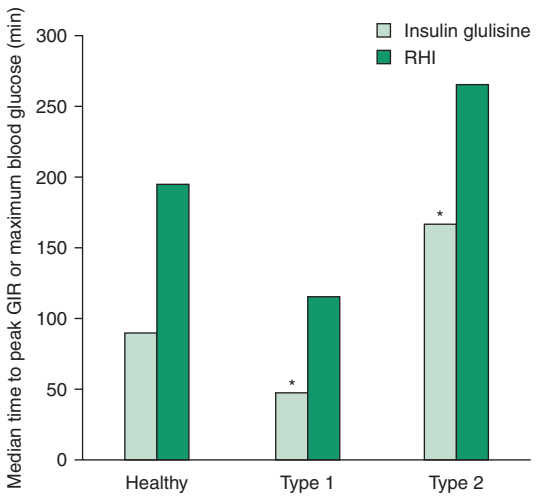


Fig. 1. Time to maximum effect of insulin glulisine and regular human insulin (RHI). Median time to peak glucose infusion rate (GIR) during euglycaemic clamp[15,17] or maximum blood glucose following a standardised meal[16] with glulisine insulin or RHI. Healthy volunteers (n = 16)[15] received a 0.3 IU/kg subcutaneous dose of insulin glulisine or RHI, while patients with type 1 (n = 20)[16] or type 2 (n = 24)[17] diabetes mellitus received a 0.15[16] or 0.20 IU/kg[17] dose of either insulin. Statistical analysis not reported in one study.[15] * $p < 0.05$ vs RHI.

2. Pharmacokinetic Profile

- In euglycaemic-clamp studies in healthy volunteers,[15] or patients with type 1[16] or type 2[17] diabetes, mean maximum plasma concentrations (C_{max}) were higher with subcutaneous insulin glulisine than with the same doses of RHI, while median times to C_{max} (t_{max}) and mean residence times (MRT) were shorter (figure 2).
- Insulin glulisine absorption was more rapid than RHI but total systemic availability did not differ in patients with type 1 or type 2 diabetes.[16,17] In patients with type 1 diabetes receiving a 0.15 IU/kg dose of subcutaneous insulin glulisine or RHI 0.15 IU/kg, values of geometric mean insulin AUC from from time zero to 2 hours (AUC_2) with insulin glulisine or RHI were 7278 versus 4258 μIU • min/mL ($p < 0.05$), whereas the geometric mean insulin AUC from time zero to 6 hours (AUC_6) did not differ between treatment groups (11 912 vs 11 550 μIU • min/mL).[16]
- Likewise, in patients with type 2 diabetes receiving insulin glulisine or RHI 0.20 IU/kg, the geometric mean insulin AUC_2 was significantly higher in insulin glulisine recipients (7661 vs 4221 μIU • min/mL; $p < 0.05$), but by clamp end (after 10 hours) total insulin AUC values did not differ between treatment groups (18 408 vs 19 731 μIU • min/mL).[17]
- The pharmacokinetics of subcutaneous insulin glulisine 0.15 IU/kg administered immediately prior to a meal or 15 minutes after a meal were similar.[16] Geometric mean C_{max} (82 vs 79 μIU/mL), AUC_6 (11 912 vs 11 897 μIU • min/mL) and t_{max} (55 vs 57 minutes) values were independent of time in relation to meals.
- Absorption was similar after injection of insulin glulisine 0.1 IU/kg into several subcutaneous sites.[20] Median t_{max} values were 44, 58 or 66 minutes after injection into the abdominal, deltoid or

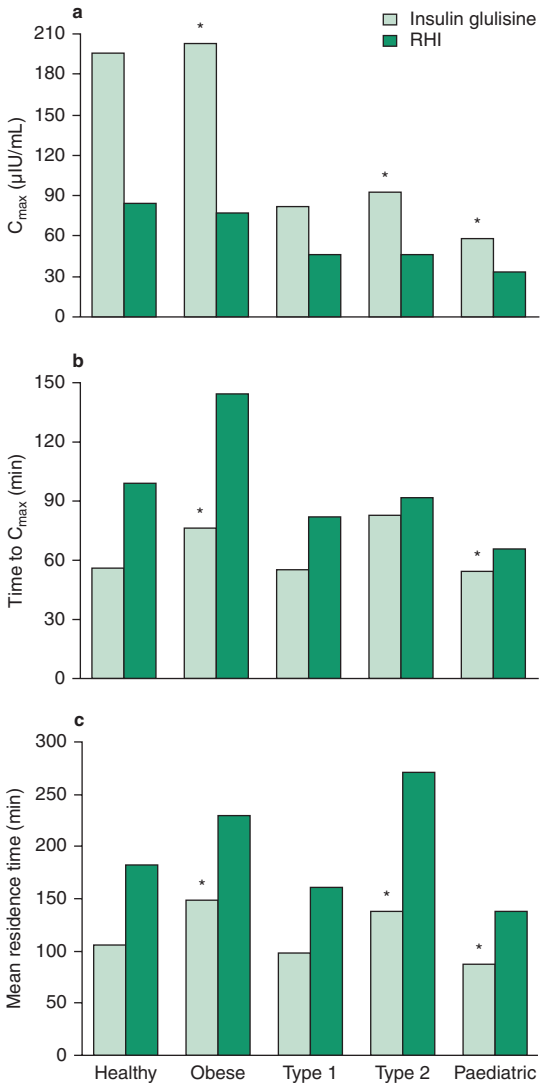


Fig. 2. Pharmacokinetics of insulin glulisine versus regular human insulin (RHI). (**a**) Mean maximum plasma concentration (C_{max}), (**b**) time to C_{max} and (**c**) mean residence time after subcutaneous injection of insulin glulisine or RHI. Healthy (n = 16),[15] and obese volunteers without diabetes mellitus (n = 18),[18] received a 0.30 IU/kg dose of subcutaneous insulin glulisine or RHI,[15,18] adult (n = 20)[16] or paediatric (aged 5–17 years) [n = 20][19] patients with type 1 diabetes received a 0.15 IU/kg dose of either insulin and adult patients with type 2 diabetes (n = 24)[17] received a 0.20 IU/kg dose. Statistical analyses not reported in healthy volunteers[15] and patients with type 1 diabetes.[16] * $p < 0.05$ vs RHI.

femoral areas in 16 healthy male volunteers aged 19–28 years, while MRT was 89, 103 or 114 minutes and absolute bioavailability did not differ between injection sites (68–73%).

- Whereas after intravenous administration the apparent half-lives of insulin glulisine and RHI were 13 and 17 minutes, after subcutaneous administration apparent half-lives were 42 and 86 minutes.[21]
- Volumes of distribution of insulin glulisine and RHI after intravenous administration were 13L and 21L.[21]
- Premixing insulin glulisine 0.1 IU/kg and neutral protamine hagedorn (NPH) insulin 0.2 IU/kg in the syringe did not affect the total bioavailability of insulin glulisine in 32 healthy volunteers.[22] Premixing reduced the mean insulin glulisine C_{max} value relative to that following separate simultaneous subcutaneous injections (51 vs 70 μIU/mL; $p < 0.05$); however, mean AUC_{end} and median t_{max} values were not affected (8251 vs 9262 μIU • min/mL and 50 vs 47 minutes).

Special Populations

- The rapid-acting properties of insulin glulisine are maintained in paediatric patients (aged 5–17 years) with type 1 diabetes (figure 2).[19] The relative differences in pharmacokinetics between a 0.15 IU/kg dose of subcutaneous insulin glulisine or RHI were similar to those in healthy adult volunteers and adults with type 1 diabetes (figure 2).
- Obesity had no effect on the rapid absorption and elimination of insulin glulisine (figure 2) and the rapid onset and duration of action in obese (body mass index 30–40 kg/m^2) non-diabetic volunteers.[18]
- Non-diabetic volunteers with moderate (creatinine clearance 30–50 mL/min) or severe (<30 mL/min) renal impairment had values for the pharmacokinetic parameters characterising the absorption of insulin glulisine (C_{max}, t_{max} and AUC_2) that were similar to those in volunteers with normal renal function (>80 mL/min) [n = 8 in each group].[23] Weak, but statistically significant correlations, were found between renal impairment and parameters of insulin glulisine characteristic of total exposure and relative total clearance (AUC_5 and AUC_{end}), which were increased by 29–47%. Careful

monitoring of glucose and insulin dose adjustments may be necessary in patients with renal dysfunction.[9]

Drug Interactions

- As with other insulin analogues, close monitoring and dose adjustment may be required for compounds that have not been specifically tested with insulin glulisine, but that have an effect on glucose metabolism. Substances that usually reduce the blood-glucose-lowering effect of insulin include corticosteroids, hormonal steroids, antihypoglycaemics, diuretics, sympathomimetics, phenothiazines, thyroid hormones, protease inhibitors, atypical antipsychotics, isoniazid and somatropin, while those that increase insulin effects include oral antidiabetic products, ACE inhibitors, fibrates, monoamine oxidase inhibitors, salicylates, sulphonamide antibiotics, disopyramide, fluoxetine, pentoxifylline and dextropropoxyphene.[9]
- Hypoglycaemia, sometimes followed by hyperglycaemia, may be elicited by pentamidine, while other substances may either enhance or depress the blood-glucose-lowering effect of insulin (e.g. β-adrenoceptor antagonists, lithium salts, clonidine and alcohol). Sympatholytic medicinal products (e.g. β-adrenoceptor antagonists, clonidine, guanethidine and reserpine) may reduce or obscure signs of hypoglycaemia.[9]

3. Therapeutic Efficacy

The therapeutic efficacy of subcutaneous insulin glulisine has been evaluated in comparison with insulin lispro[24] or RHI[21,25,26] in four large, randomised, nonblind, multicentre, 12-[25] or 26-week[21,24,26] trials, including one unpublished trial (trial 3005),[21] in patients with type 1[24,25] or type 2[21,26] diabetes. Two studies[24,26] included a 26-week extension phase to evaluate the safety of insulin glulisine over a 52-week period.[21] Some data have been extracted from US FDA review documents.[21,27]

Patients were at least 18 years of age, with glycosylated haemoglobin (HbA_{1c}) levels ranging from >6% to ≤11%.[21,24-26] In trial 3005, type 1 diabetes was defined as onset before the age of 40 years and requiring insulin therapy since the time of diagnosis, whereas type 2 diabetes was defined as a medical history of diabetes not requiring continuous insulin therapy since diagnosis.[21]

In general, demographic and disease characteristics were well balanced between treatment groups; pooled demographics indicated that >90% of patients were Caucasian and while patients with type 1 diabetes averaged 40 years of age, patients with type 2 diabetes averaged 59 years of age.[21]

Patients were maintained on a basal insulin regimen of insulin glargine once daily[24,25] or NPH insulin twice daily.[21,26] Insulin glulisine was administered 0–15 minutes before meals,[21,24-26] or within 20 minutes after starting a meal,[25] whereas insulin lispro was administered 0–15 minutes before meals,[24] and RHI was administered 30–45 minutes before meals.[21,25,26] Doses were adjusted to achieve 2-hour postprandial blood glucose levels of 6.7–8.9 mmol/L, whereas basal insulin therapy was titrated to achieve preprandial blood glucose levels of 5.0–6.7 mmol/L.[21,25,26] In two trials in patients with type 2 diabetes,[21,26] randomisation was stratified according to oral antidiabetic agent use and their continued use was permitted.

The primary efficacy outcome in the four pivotal trials[21,24-26] was the mean change from baseline HbA_{1c} levels at the end of treatment. Changes in HbA_{1c} from baseline to endpoint induced by insulin glulisine and RHI[21,25,26] or insulin lispro[24] were compared by non-inferiority analysis, which was considered to be demonstrated in the intention-to-treat[21,24-26] and per-protocol populations[21,24] if the upper limit of the 95%[21,24,26] or 98.33%[25] confidence interval (CI) for the mean difference between insulin glulisine and comparator was ≤0.4%.

Secondary efficacy variables included changes in preprandial and 2-hour postprandial self-monitored blood glucose (SMBG) profiles, insulin dose changes and the incidence of hypoglycaemic episodes (see section 4).[21,24-26]

In Patients with Type 1 Diabetes Mellitus

- Insulin glulisine was noninferior to RHI and insulin lispro in reducing HbA_{1c} levels in patients with type 1 diabetes.[24,25]
- In the 12-week trial, pre-meal insulin glulisine (n = 286), post-meal insulin glulisine (n = 296) and pre-meal RHI (n = 278) all significantly reduced HbA_{1c} levels from baseline by 0.26–0.11% ($p < 0.05$).[25] The baseline-to-endpoint adjusted mean change in HbA_{1c} induced by post-meal insulin glulisine (−0.11%) was noninferior to that induced by pre-meal insulin glulisine (−0.26%) or pre-meal RHI (−0.13%).
- A subsequent superiority analysis indicated that the reduction in HbA_{1c} was greater in pre-meal insulin glulisine recipients than in post-meal insulin glulisine recipients ($p = 0.006$) or pre-meal RHI recipients ($p = 0.02$).[25]
- In the 26-week trial, insulin glulisine (n = 339) and insulin lispro (n = 333) induced the same adjusted mean changes from baseline in HbA_{1c} levels (−0.14% in both groups).[24] The proportions of patients reaching target levels of HbA_{1c} were also similar between treatment groups; 35.6% of insulin glulisine and 34.5% of insulin lispro recipients had a HbA_{1c} level ≤7.0%, and 75.2% of insulin glulisine and 75.5% of insulin lispro recipients had a HbA_{1c} level ≤8.0% at endpoint.
- During the 26-week extension of this trial,[21] the initial reductions in HbA_{1c} were lost in both insulin glulisine and insulin lispro recipients (change from baseline at 52 weeks −0.02% vs 0.00%).
- The SMBG profile and 2-hour postprandial glucose levels with pre-meal insulin glulisine were better than those with post-meal insulin glulisine or RHI and similar to those with insulin lispro during the 26-week trial.[24,25] Pre-meal insulin glulisine induced a significantly lower mean 2-hour post-breakfast blood glucose level than post-meal insulin glulisine (7.83 vs 8.57 mmol/L; $p = 0.0017$) or pre-meal RHI (9.10 mmol/L; $p = 0.0001$), as well as a lower 2-hour post-dinner blood glucose level (8.12 vs 8.77 and 9.23 mmol/L; $p = 0.0137$ and $p = 0.0001$).[25] No significant differences in SMBG profile and 2-hour postprandial glucose levels were observed between pre-meal insulin glulisine and insulin lispro either during the initial 26-week trial[24] or during the 26-week extension.[21]
- No between-group differences in the baseline-to-endpoint change in mean daily insulin lispro or insulin glulisine dose were noted during the 26-week trial, whereas the mean dose of long-acting insulin glargine was increased to a significantly greater extent with insulin lispro than insulin glulisine (1.82 vs 0.12IU; $p < 0.05$).[24] In the 12-week trial, the dose of RHI increased by 1.75IU, whereas the dose of pre- or post-meal insulin glulisine declined (by 0.88IU or 0.47IU; $p = 0.0001$ or $p = 0.0012$ vs RHI).[25]

In Patients with Type 2 Diabetes

- Similar or greater reductions from baseline in HbA_{1c} levels were observed in patients with type 2 diabetes receiving insulin glulisine compared with those receiving RHI.[21,26] In the published 26-week trial, insulin glulisine (n = 435) was noninferior to RHI (n = 441) in reducing mean HbA_{1c} levels by 0.46% versus 0.30%; a superiority test indicated that the difference between groups was significant ($p = 0.0029$) [figure 3].[26] In the 26-week extension phase of this trial, HbA_{1c} levels in both treatment groups rose, so that by 52 weeks the changes from baseline levels were −0.23% and −0.13% for insulin glulisine and RHI (statistical analysis not reported).[21]
- In the unpublished 26-week study (trial 3005),[21] the reduction in mean HbA_{1c} level induced by insulin glulisine (n = 448) was non-inferior the RHI (n = 442) induced reduction (0.32% vs 0.35%).[27]
- In the published trial, insulin glulisine therapy induced greater reductions in SMBG values than RHI,[21,26] which persisted throughout the 26-week extension period.[21] For example, significantly ($p < 0.05$) greater reductions were observed in 2-hour post-breakfast (8.66 vs 9.02 mmol/L) and post-dinner (8.54 vs 9.05 mmol/L) blood glucose levels with insulin glulisine than with RHI.[26]
- Insulin glulisine and RHI doses increased to a similar extent during both trials (3.7 vs 5.0 IU/day[26] and 2.95 vs 4.47 IU/day[21]), as did doses of

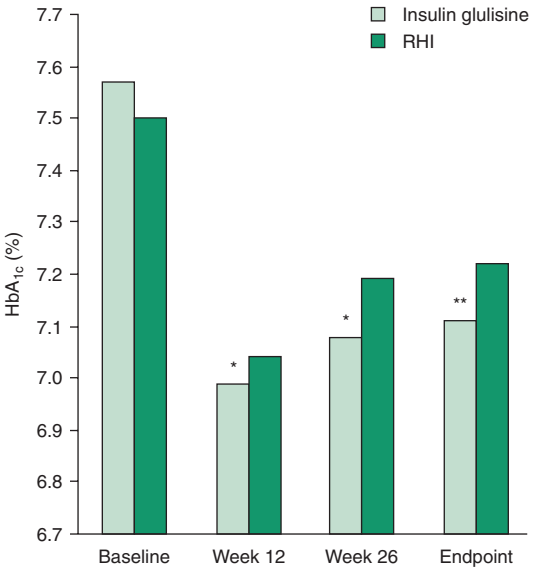


Fig. 3. Reduction in glycosylated haemoglobin (HbA_{1c}) levels with insulin glulisine in patients with type 2 diabetes mellitus. HbA_{1c} levels in patients receiving subcutaneous insulin glulisine (n = 435) 0–15 minutes before meals or regular human insulin (RHI) (n = 441) 30–45 minutes before meals.[26] Doses were adjusted to achieve a 2-hour postprandial blood glucose level of 6.7–8.9 mmol/L. * $p < 0.05$, ** $p < 0.01$ vs RHI.

long-acting NPH insulin (5.7 vs 6.0 IU/day[26] and 4.54 vs 4.81 IU/day[21]).

4. Tolerability

The tolerability profile of insulin glulisine discussed in this section is primarily based on a pooled analysis of safety data in the FDA review[21] (n = 1833 for insulin glulisine and n = 1524 for comparator insulin [insulin lispro and RHI] recipients). The pooled analysis is based on data from the four pivotal trials[21,24-26] and the two 26-week safety extensions[24,26] discussed in section 3, and a 12-week safety evaluation of insulin glulisine in continuous subcutaneous insulin infusion (CSII) in patients with type 1 diabetes.[28]

- In patients with type 1 or 2 diabetes, insulin glulisine was as well tolerated as insulin lispro or RHI; no significant between treatment differences in adverse event profiles were observed.[21,24-26] In patients with type 1 diabetes, one or more adverse events were experienced by 66.2% of insulin glulisine recipients and 66.0% of comparator insulin recipients.[21] In patients with type 2 diabetes, adverse events were experienced by 82.3% of insulin glulisine and 79.6% of RHI recipients.[21,26]
- The incidence of serious adverse events did not differ significantly between treatments in the overall analysis (14.9% of insulin glulisine-treated patients vs 14.8% of comparator-treated patients) or when patients were assessed according to diabetes type (all ≈15%).[21]
- The most common serious adverse event in patients who received insulin therapy was severe hypoglycaemia (requiring assistance from another person), which was experienced by similar proportions of insulin glulisine and comparator insulin (insulin lispro or RHI) recipients with type 1 (10.4% vs 10.8%) or type 2 (3.1% vs 3.2%) diabetes.[21]
- In patients with type 1 diabetes, serious non-hypoglycaemic adverse events occurred in 4.7% of insulin glulisine and 4.5% of comparator insulin recipients, and comprised cardiac disorders (1.5% vs 0.5%), ketoacidosis (0.5% vs 0.5%), injection-site reactions (4.2% vs 5.0%) and systemic hypersensitivity reactions (2.1% vs 1.7%).[21]
- Serious non-hypoglycaemic adverse events occurred in 12.8% of patients with type 2 diabetes receiving insulin glulisine and 12.1% of patients receiving RHI.[21] There were no between-group differences in the incidences of potential cardiac disorders (5.5% vs 6.6%), ketoacidosis (0.0% vs 0.1%), systemic hypersensitivity (6.7% vs 5.3%) or injection-site reactions (2.3% vs 2.6%).[21]
- Changes in the concentrations of cross-reactive insulin antibodies were small in all treatment groups and did not correlate with changes in HbA_{1c} levels or insulin doses, or the incidence of symptomatic or severe hypoglycaemia.[21]
- A comparison of insulin glulisine and insulin aspart in CSII indicated no significant between-group differences in the number of patients who experienced any (14 vs 20 patients [48% vs 67%]) or serious (5 vs 4 patients [17% vs 13.3%]) adverse events.[21] There was a similar low rate of catheter occlusion in both treatment arms (0.08 vs 0.15 occlusions/month).[28] No significant difference be-

tween treatments was apparent in the incidence of unexplained hyperglycaemic (blood glucose >19.4 mmol/L) events (20.7% vs 40.0%) in either the presence or absence of overt pump occlusion.

- In the clinical trial programme as a whole, 10 deaths occurred (none considered related to trial treatment), 5 were in patients receiving insulin glulisine and 5 were in other treatment arms.[21]

5. Dosage and Administration

Insulin glulisine should be given within 15 minutes before a meal or within 20 minutes after starting a meal by subcutaneous injection in the abdominal wall, the thigh or the deltoid, or by continuous subcutaneous infusion in the abdominal wall.[9] Insulin glulisine should be used in conjunction with longer-acting insulin or by insulin infusion pump therapy to maintain adequate glucose control. The specific dosage of insulin glulisine should be individualised according to patient needs.

Insulin glulisine is contraindicated during episodes of hypoglycaemia and in patients hypersensitive to insulin glulisine or one of its excipients.[9] Local prescribing information should be consulted for dosage reduction guidelines in patients experiencing toxicity, dosage recommendations in special populations, contraindications and precautions.

6. Insulin Glulisine: Current Status

Insulin glulisine is approved for use in the US[29] and Europe[30] for the treatment of type 1 and type 2 diabetes mellitus in adult patients. It has favourable tolerability, similar to that of insulin lispro and RHI, with few adverse events of more than moderate severity. Used in combination with basal insulin therapy, insulin glulisine has demonstrated good efficacy in controlling prandial blood glucose levels.

Disclosure

During the peer review process, the manufacturer of the agent under review was offered an opportunity to comment on this article; changes based on any comments received were made on the basis of scientific and editorial merit.

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