

Rationale for combining basal insulin with a GLP-1 RA

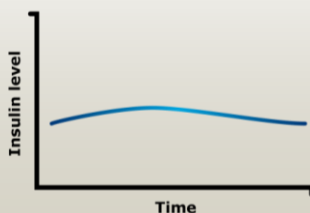
Glucagon-like peptide-1 receptor agonists (GLP-1 RAs)

People with type 2 diabetes who do not respond to oral anti-diabetic therapies, which are used to initially control blood glucose levels, may be offered basal insulin injections or treatments such as GLP-1 RAs if their blood glucose levels remain uncontrolled.¹

GLP-1 RAs are treatments for type 2 diabetes that mimic a hormone (GLP-1), a type of incretin. Incretins are released in the intestines and stimulate a reduction in blood glucose, which is reflected by measuring the HbA_{1c} in the long term.¹ Incretins also slow emptying of the stomach and the flow of nutrients in the body can create the sensation of fullness.

Basal insulin

Controls blood glucose levels in between meals (fasting glycaemic control)¹



Glucagon-like peptide-1 receptor agonist (GLP-1 RA)

Controls blood glucose levels during and in-between meals (postprandial and fasting glycaemic control)¹



Importance of preventing complications

Control of HbA_{1c} is a crucial target in diabetes management. In the United Kingdom (UK), the Quality and Outcomes Framework has set the HbA_{1c} target as 58mmol/mol or less ($\leq 7.5\%$).² Nearly three quarters of people with type 2 diabetes on basal insulin regimens in the UK fail to reach HbA_{1c} of 58mmol/mol or less ($\leq 7.5\%$) and are therefore at a greater risk of medical complications.³⁻⁶

A reduction in HbA_{1c} can provide both a huge personal benefit but also a significant cost saving through the reduction of diabetes-related complications. A one percentage point drop in HbA_{1c} can lead to a 37% reduction in microvascular complications, a 14% reduction in myocardial infarctions and a 21% reduction in overall diabetes-related mortality.⁵

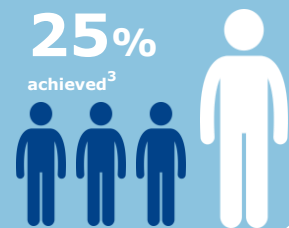
Target

$\leq 7.5\%$

HbA_{1c} level²

25%

achieved³



Another challenging complication is hypoglycaemia, which occurs when the concentration of glucose in the blood falls to an abnormally low level. Episodes can have a significant impact on a person living with diabetes as symptoms can range from trembling, sweating, poor sleep and nightmares⁷ to night-time convulsions and, in severe cases, coma and death.⁸

Insulin is an effective diabetes treatment, but it is often underutilised due to the risk or fear of hypoglycaemia - and also possible weight gain.⁹ These two factors can be a major barrier to insulin initiation and optimising the use of insulin.^{10,11}

Benefits for combining basal insulin with GLP-1 RA^{12,13}

There may be important benefits associated with using basal insulin with a GLP-1 RA:

- Improvements in blood glucose levels overall
- A lower risk of hypoglycaemia compared to taking a higher dose of insulin
- Using basal insulin and a GLP-1 RA together may lower insulin-associated weight gain and may achieve weight loss

Improves blood glucose levels overall^{12,13}



May lower risk of hypoglycaemia compared to a basal insulin alone^{12,13}



Lowers insulin-associated weight gain or even results in weight loss^{12,13}



References

1. Tibble C A, *et al.* Longer Acting GLP-1 Receptor Agonists and the Potential for Improved Cardiovascular Outcomes. *Expert Rev Endocrinol Metab.* 2013;8(3):247-259.
2. doctors.net.uk. Diabetes NICE Clinical Guidelines 2012:Locally Adapted Guidelines http://www.doctors.net.uk/_datastore/ecme/mod1101/Diabetes_NICE_clinical_guidelines_v02.pdf. Accessed 07 August 2014.
3. Novo Nordisk data on file.
4. International Diabetes Federation. *Diabetes Atlas 2013*. Available at: <http://www.idf.org/diabetesatlas>. Accessed: 15 July 2014.
5. Stratton I, *et al.* Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000;321(7258):405-412.
6. Bethel, M and M Feinglos, Basal Insulin Therapy in Type 2 Diabetes. *J. Am. Board Fam. Med.* 2005;18(3):199-204.
7. NHS Choices 'Hypoglycaemia – symptoms' <http://www.nhs.uk/conditions/hypoglycaemia/Pages/Symptoms.aspx>. Accessed 15 July 2014.
8. Cryer P, Hypoglycemia, functional brain failure, and brain death *J. Clin. Invest.* 2007;117(4):868–870.
9. Khunti K, *et al.* Clinical Inertia in People with Type 2 Diabetes. *Diabetes Care.* 2013;36:3411-17.
10. Rakei R, Improving patient acceptance and adherence in diabetes management: a focus on insulin therapy. *Adv Ther.* 2009;26:838–846.
11. Peyrot M, *et al.* Insulin adherence behaviours and barriers in the multinational Global Attitudes of Patients and Physicians in Insulin Therapy study. *Diabet Med.* 2012;29:682–689.
12. Mathieu C, *et al.* A comparison of adding liraglutide versus a single daily dose of insulin aspart to insulin degludec in subjects with Type 2 diabetes (BEGIN: VICTOZA ADD-ON). *Diabetes, Obesity and Metabolism.* 2014
13. Buse J B, *et al.* Liraglutide contributes significantly to glycaemic control achieved in IDegLira: a double blind phase 3 trial in type 2 Diabetes. *Oral presentation IDF world congress 2013.*