Focus on....

Soliqua®

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Introduction

Guidelines recommend a target haemoglobin A1C (HbA_{1c}) of < 7.0% for most non-pregnant adults with type 2 diabetes.[1,2] Most current guidelines also advocate a step-wise introduction of pharmacotherapy for individuals with type 2 diabetes not achieving their glycaemic targets.[1,2]

Until recently, patients not achieving their individualised glycaemic targets with a regimen that includes basal insulin had four options:[3]

- Adding rapid-acting insulin to the existing basal insulin regimen
- Switching to multiple daily premix insulin doses (basal and prandial insulin co-formulation)
- Adding a daily or weekly glucagon-like peptide-1 receptor agonist (GLP-1 RA) to an existing basal insulin regimen
- Switching to a once-daily fixed-ratio combination of basal insulin and GLP-1 RA

Titratable fixed-ratio combinations of basal insulin and a GLP-1 RA provide a novel alternative therapy advancement option to premix insulin; basal insulin primarily reduces fasting plasma glucose (FPG), while the GLP-1 RA targets postprandial glucose.[3]

Indication

SOLIQUA® is indicated for the treatment of adult patients with type 2 diabetes mellitus to improve glycaemic control when oral glucose-lowering medicines alone or combined with basal insulin, or basal insulin alone, do not provide adequate glycaemic control.[4]

Mechanism of action

SOLIQUA® contains insulin glargine and the GLP-1 RA, lixisenatide (iGlarLixi).[4] It is a titratable, fixed-ratio combination of insulin glargine and lixisenatide delivered via a single, daily injection.[5]

- Insulin glargine lowers blood glucose by stimulating peripheral glucose uptake, especially by skeletal muscle and fat, by inhibiting hepatic glucose production.[4] Insulin glargine inhibits lipolysis and proteolysis and enhances protein synthesis.[4]
- After a meal, lixisenatide enhances insulin secretion by beta cells, slows gastric emptying and suppresses glucagon secretion by alpha cells.[4]

In other words, the combination of a basal insulin with a GLP-1 RA has complementary effects:[5]

- Basal insulin therapy improves fasting plasma glucose and nocturnal hypoglycaemia, whereas GLP-1 RAs have a significant effect on postprandial plasma glucose.[5]
- When combined with basal insulin, GLP-1 RAs do not increase the risks of hypoglycaemia and can mitigate the weight gain associated with insulin therapy.[5]

Dosing

SOLIQUA® is titratable and available in two pens, providing different dosing options.[4] The differentiation between the pen strengths is based on the dose range of the pen:[4]

SOLIQUA® 50/100 (10-40 pen):

- 1 unit of SOLIQUA® contains 1 unit of insulin glargine and 0.5 µg lixisenatide
- Allows daily doses between 10 and 40 units of SOLIQUA® (10 to 40 units of insulin glargine and 5.0 to 20.0 µg lixisenatide)

SOLIQUA® 33/100 (30-60 pen):

- 1 unit of SOLIQUA® contains 1 unit of insulin glargine and 0.33 µg lixisenatide
- Allows daily doses between 30 and 60 units of SOLIQUA® (30 to 60 units of insulin glargine and 10.0 to 20.0 µg lixisenatide)

The maximum daily dose of SOLIQUA® is 60 units (60 units of insulin glargine and 20.0 µg lixisenatide).[4]

To avoid errors, make sure the correct SOLIQUA® pen: 10-40 pen or 30-60 pen is stated on the prescription.[4]

- The starting dose of SOLIQUA® is selected based on previous antidiabetic treatment and should not exceed the recommended lixisenatide dose of 10 µg daily.[4] For further information on selecting an appropriate starting dose, please refer to the manufacturer's professional information.
- The dose of SOLIQUA® must be individualised based on clinical response and is titrated based on the patient's need for insulin.
- The lixisenatide dose is increased or decreased along with the insulin glargine dose and also depends on which pen is used.
- Patients adjusting the amount or timing of dosing should only do so under medical guidance with appropriate glucose monitoring.

Administration

SOLIQUA® should be administered subcutaneously once a day within **one** hour prior to any meal.[4] Before use, the pen must be stored at room temperature for **one** to **two** hours.[4]

Administration is a subcutaneous injection in either the abdomen, deltoid or thigh.[4] The injection site should be rotated within the same region (abdomen, deltoid or thigh) from one injection to the next to reduce the risk of lipodystrophy.[4]

SOLIQUA® must not be mixed with any other insulin or diluted.[4] Mixing or diluting can change the time/action profile and mixing can also cause precipitation.[4]

Efficacy

Randomised controlled clinical studies have been carried out to assess the efficacy and safety of iGlarLixi.

The Lixilan-O trial compared iGlarLixi with insulin glargine (iGlar) or lixisenatide (Lixi) in patients with type 2 diabetes who had inadequate glycaemic control during metformin alone or in combination with a second oral antidiabetic drug (OAD).[6] The primary efficacy outcome was the change in HbA_{1c} at 30 weeks.[6]

- Greater reductions in HbA_{1c} from baseline (8.1%) were achieved with iGlarLixi compared with iGlar and Lixi (-1.6%, -1.3% and -0.9%, respectively), reaching mean final HbA_{1c} levels of 6.5%, 6.8% and 7.3% for iGlarLixi, iGlar and Lixi, respectively.[6]
- iGlarLixi improved postprandial glycaemic control versus iGlar and demonstrated fewer nausea and vomiting events than Lixi.[6]

The Lixilan-L trial compared the efficacy and safety of iGlarLixi with iGlar in patients inadequately controlled on basal insulin, with or without treatment with two OADs.[5] The primary efficacy outcome was the change in HbA_{1c} at 30 weeks.[6]

- iGlarLixi showed greater reductions in HbA_{1c} from baseline compared with iGlar (-1.1% versus -0.6%), reaching a mean final HbA_{1c} of 6.9 % with iGlarLixi compared with 7.5% with iGlar.[5]
- Mean body weight decreased by 0.7 kg with iGlarLixi and increased by 0.7 kg with iGlar.[5]

In the Lixilan-G study, switching to iGlarLixi improved glucose control for patients with type 2 diabetes inadequately controlled on a maximum tolerated dose of a GLP-1 RA plus oral antihypoglycaemic agents.[7]

The Solimix study compared the efficacy and safety of iGlarLixi with a premix insulin analogue (biphasic insulin aspart 30, BIAsp30) in patients with type 2 diabetes advancing from basal insulin plus one or two OADs.[3] Primary efficacy endpoints were non-inferiority in HbA_{1c} reduction or superiority in bodyweight change.[3]

- Both primary efficacy endpoints were met: after 26 weeks, baseline HbA_{1c} (8.6%) was reduced by 1.3% with iGlarLixi and 1.1% with BIAsp 30, meeting non-inferiority.[3]
- iGlarLixi was superior to BIAsp 30 for bodyweight change; mean difference -1.9 kg.[3]

In summary

The available data indicate that iGlarLixi is effective and well-tolerated in patients with type 2 diabetes who need further glycaemic control, with a safety profile that is comparable to or better than that of its separate components.[8] Due to its simple administration schedule, and low incidence of adverse events, iGlarLixi may enhance adherence, which in turn will maximise therapeutic outcomes.[8] Moreover, by exploiting complementary mechanisms of action, the fixed-ratio combination therapy may target multiple pathogenetic type 2 diabetes defects, while reducing the complexity and burden of treatment for the patient.[8]

Therefore, an appropriate clinical context for considering the iGlarLixi fixed-ratio combination is that of patients who are unable to achieve adequate control on OADs and are taking neither basal insulin nor a GLP-1 RA.[8] Rather than introducing a basal insulin or a GLP-1 RA first and then adding the other type of agent, patients may be initiated on iGlarLixi as soon as the need for intensification has been identified, especially if they will require robust glucose-lowering.[8]

SOLIQUA® is marketed by Sanofi-Aventis South Africa and was launched in June 2021.

References

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