דצמבר 2023

# Suliqua 100/50 Suliqua 100/33

Suliqua 100/50

Each pre-filled pen contains 300 units of insulin glargine and 150 micrograms lixisenatide in 3 ml solution.
Each ml contains 100 units of insulin glargine and 50 micrograms lixisenatide.
Each dose step contains 1 unit of insulin glargine and 0.5 micrograms of lixisenatide

Suliqua 100/33

Each pre-filled pen contains 300 units of insulin glargine and 100 micrograms Lixisenatide in 3 ml solution.
Each ml contains 100 units of insulin glargine and 33 micrograms lixisenatide.
Each dose step contains 1 unit of insulin glargine and 0.33 micrograms of lixisenatide

## חברת סאנופי ישראל מבקשת להודיע על עדכון ההתוויה ומשטר המינון של התכשירים שבנדון וכן על עדכון העלון לרופא והעלונים לצרכן בנובמבר 2023.

**ההתוויה העדכנית המאושרת:**

Suliqua is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise in addition to metformin with or without sodium-glucose co-transporter-2 (SGLT-2) inhibitors.

העדכונים **העיקריים** בעלונים הינם:

**בעלון לרופא**:

### 4.1 Therapeutic indications

~~Suliqua is indicated in combination with metformin for the treatment of adults with type 2 diabetes mellitus to improve glycaemic control when this has not been provided by metformin alone or metformin combined with another oral glucose lowering medicinal product or with basal insulin (see section 4.4 and 5.1 for available data on the different combinations).~~

Suliqua is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise in addition to metformin with or without sodium-glucose co-transporter-2 (SGLT-2) inhibitors.
(For study results with respect to effect on glycaemic control, and the populations studied, see section 4.4 and 5.1).

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## 4.2 Posology and method of administration

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*Starting dose*

Therapy with basal insulin or glucagon-like peptide-1 (GLP-1) receptor agonist or oral glucose lowering medicinal product other than metformin and SGLT-2 inhibitors should be discontinued prior to initiation of Suliqua.

The starting dose of Suliqua is based on previous anti-diabetic treatment, and in order not to exceed the recommended lixisenatide starting dose of 10 mcg:

| | | **Previous therapy** | | |
|---|---|---|---|---|
| | | **Insulin naïve patients (~~O~~oral anti-diabetic treatment or GLP-1 receptor agonist) ~~(insulin naïve patients)~~** | **Insulin glargine (100 units/ml)** ≥20 to <30 units** | **Insulin glargine (100 units/ml)** ≥30 to ≤60 units** |
| **Starting dose and pen** | **Suliqua (10-40) pen** | 10 dose steps (10 units/5 mcg)* | 20 dose steps (20 units/10 mcg)* | |
| | **Suliqua (30-60) pen** | | | 30 dose steps (30 units/10 mcg)* |

* Units insulin glargine (100 units/ml)/mcg lixisenatide

**** If a different basal insulin was used:**

- For twice daily basal insulin or insulin glargine (300 units/ml), the total daily dose previously used should be reduced by 20% to choose the Suliqua starting dose.
- For any other basal insulin, the same rule as for insulin glargine (100 units/ml) should be applied

The maximum daily dose is 60 units insulin glargine and 20 mcg lixisenatide corresponding to 60 dose steps.

Suliqua should be injected once a day within one hour prior to a meal. It is preferable that the prandial injection is performed before the same meal every day, when the most convenient meal has been chosen.

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*Special population*

*Elderly (≥65 years old)*
Suliqua can be used in elderly patients. The dose should be adjusted on an individual basis, based on glucose monitoring. In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements. For lixisenatide no dose adjustment is required based on age. The therapeutic experience of Suliqua in patients ≥75 years of age is limited.

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## 4.8 Undesirable effects

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**Table 2: Documented symptomatic or severe hypoglycaemic adverse reactions**

| | Insulin naïve patients | | | Switch from basal insulin | | Switch from GLP-1 receptor agonist*** | |
|---|---|---|---|---|---|---|---|
| | Suliqua | Insulin glargine | Lixisenatide | Suliqua | Insulin glargine | Suliqua | GLP-1 receptor agonist*** |
| **N** | 469 | 467 | 233 | 365 | 365 | 255 | 256 |
| **Documented symptomatic hypoglycaemia*** | | | | | | | |
| Patients with event, n (%) | 120 (25.6%) | 110 (23.6%) | 15 (6.4%) | 146 (40.0%) | 155 (42.5%) | 71 (27.8%) | 6 (2.3%) |
| Events per patient-year, n | 1.44 | 1.22 | 0.34 | 3.03 | 4.22 | 1.54 | 0.08 |
| **Severe hypoglycaemia**** | | | | | | | |
| Events per patient-year, n | 0 | <0.01 | 0 | 0.02 | <0.01 | <0.01 | 0 |

* Documented symptomatic hypoglycaemia was an event during which typical symptoms of hypoglycaemia were accompanied by a measured plasma glucose concentration of ≤3.9 mmol/L.
** Severe symptomatic hypoglycaemia was an event requiring assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions.
*** Liraglutide, exenatide BID (twice in a day) or extended release, dulaglutide or albiglutide

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## 5.1 Pharmacodynamic properties

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Clinical efficacy and safety

The safety and effectiveness of Suliqua on glycaemic control were evaluated in three~~two~~ randomised clinical studies in patients with type 2 diabetes mellitus:

- Add-on to metformin [ Insulin Naïve ]
- Switch from basal insulin
- Switch from GLP-1 receptor agonist

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Switch from GLP-1 receptor agonist

*Clinical study in patients with Type 2 diabetes insufficiently controlled on GLP-1 receptor agonist*

The efficacy and safety of Suliqua compared to unchanged pre-trial GLP-1 receptor agonist treatment were studied in a 26-week, randomised, open-label trial. The trial included 514 patients with type 2 diabetes mellitus inadequately controlled (HbA1c level of 7% to 9% both inclusive) while treated for at least 4 months with liraglutide or exenatide or for at least 6 months with dulaglutide, albiglutide or exenatide extended release, all at maximal tolerated dose, and metformin alone or in combination with pioglitazone, a SGLT-2 inhibitor or both. Eligible patients were randomised to either receive Suliqua or to continue their previous GLP-1 receptor agonist both on top of their previous oral anti-diabetic treatment.

At screening, 59.7% of the subjects received a once or twice-daily GLP-1 receptor agonist and 40.3% received a once weekly GLP-1 receptor agonist. At screening, 6.6% of the subjects received pioglitazone, and 10.1% a SGLT-2 inhibitor in combination with metformin. The study population had the following characteristics: mean age was 59.6 years, 52.5% of the subjects were male. The mean duration of diabetes was 11 years, the mean duration of previous GLP-1 receptor agonist treatment was 1.9 years,

the mean BMI was approximately 32.9 kg/m$^2$, mean eGFR was 87.3 ml/min/1.73 m$^2$ and 90.7% of patients had an eGFR ≥60 ml/min.

At week 26, Suliqua provided statistically significant improvement in HbA1c (p <0.0001). A pre-specified analysis by GLP-1 receptor agonist subtype (once/twice daily or weekly formulation) used at screening showed that HbA1c change at week 26 was similar for each subgroup and consistent with the primary analysis for the overall population. The mean daily dose of Suliqua at Week 26 was 43.5 dose steps.

See table and figure below for the other endpoints in the study.

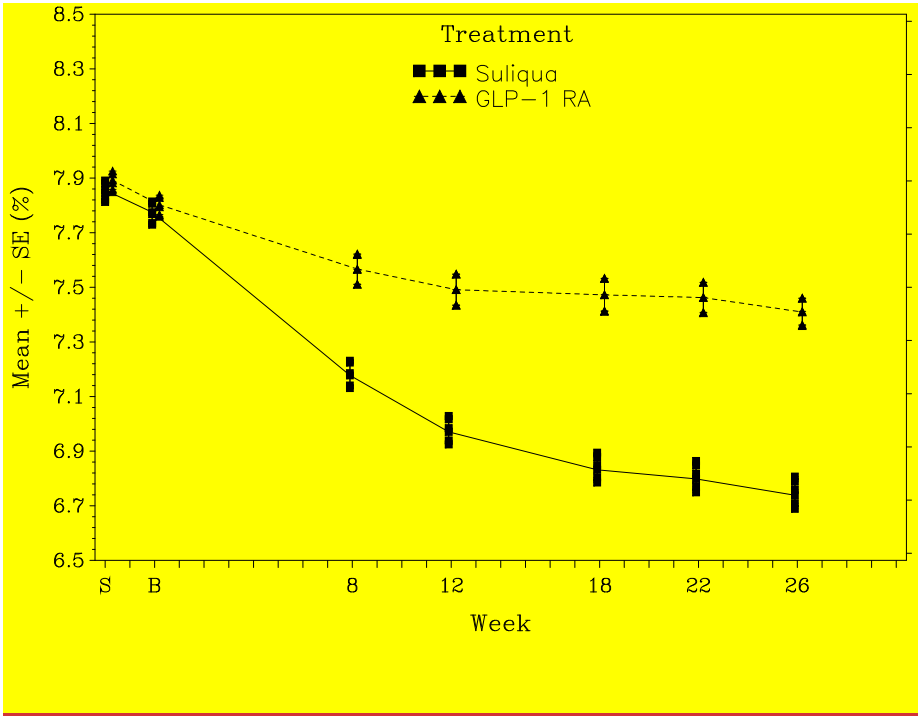
**Table 5: Results at 26 weeks - Study Type 2 diabetes uncontrolled on GLP-1 receptor agonist mITT population**

| | **Suliqua** | **GLP-1 receptor agonist*** |
|---|---|---|
| **Number of subjects (mITT)** | 252 | 253 |
| **HbA1c (%)** | | |
| Baseline (mean; post run-in phase) | 7.8 | 7.8 |
| End of treatment (mean) | 6.7 | 7.4 |
| LS change from baseline (mean) | -1.0 | -0.4 |
| Difference versus GLP-1 receptor agonist [95% confidence interval] (p-value) | -0.6 [-0.8, -0.5] (<0.0001) | |
| **Patients [n (%)] reaching HbA1c <7% at week 26** | 156 (61.9%) | 65 (25.7%) |
| Proportion difference (95% confidence interval) vs GLP-1 receptor agonist | 36.1% (28.1% to 44%) | |
| p-value | <.0001 | |
| **Fasting plasma glucose (mmol/L)** | | |
| Baseline (mean) | 9.06 | 9.45 |
| End of study (mean) | 6.86 | 8.66 |
| LS change from baseline (mean) | -2.28 | -0.60 |
| Difference versus GLP-1 receptor agonist [95% confidence interval] (p-value) | -1.67 (-2.00 to -1.34) (<0.0001) | |
| **2 hour PPG (mmol/L)**** | | |
| Baseline (mean) | 13.60 | 13.78 |
| End of study (mean) | 9.68 | 12.59 |
| LS change from baseline (mean) | -4.0 | -1.11 |
| LS difference versus GLP-1 receptor agonist (mean) [95% confidence interval] (p-value) | -2.9 (-3.42 to -2.28) (<0.0001) | |

| | | |
|---|---|---|
| **Mean body weight (kg)** | | |
| Baseline (mean) | 93.01 | 95.49 |
| LS change from baseline (mean) | 1.89 | -1.14 |
| Comparison versus GLP-1 receptor agonist [95% confidence interval] (p-value) | -3.03 (2.417 to 3.643) (<0.0001) | |

* Liraglutide, exenatide BID or extended release, dulaglutide or albiglutide
**2 hour PPG minus the pre-meal glucose value

**Figure 3: Mean HbA1c (%) by visit during 26-week randomised treatment period-mITT population**




*Concomitant use of Suliqua with SGLT-2 inhibitors (SGLT2i)*

The concomitant use of Suliqua with SGLT2i is supported by subgroup analyses from three phase 3 randomised clinical studies (119 patients on the insulin glargine/lixisenatide fixed ratio combination (FRC) who also received SGLT2i).

One study conducted in Europe and North America included data from 26 patients (10.1%) who concomitantly received insulin glargine/lixisenatide FRC, metformin and an SGLT2i. Two more phase 3 studies from the dedicated Japanese clinical development program performed in patients not reaching sufficient glycaemic control on OADs provided data for 59 patients (22.7%) and 34 patients (21.1%), respectively, who concomitantly received SGLT2i and insulin glargine/lixisenatide FRC.

The data from these 3 studies show that initiation of Suliqua in patients inadequately controlled with a treatment including SGLT2i leads to improved change in HbA1c versus the comparators (insulin glargine, lixisenatide, liraglutide, exenatide BID or extended release, dulaglutide or albiglutide). There was no increased risk of hypoglycaemia and no relevant differences in the overall safety profile in SGLT2i users compared to non-users.

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**בעלונים לצרכן**:

## 1. למה מיועדת התרופה?

סוליקווה מיועדת ~~בשילוב עם מטפורמין~~ לטיפול במבוגרים עם סוכרת מסוג 2, ~~ככדי לעזור לשלוט ב~~לשיפור ~~ויסות~~ רמות הסוכר בדם כאשר הן גבוהות מדי, כתוספת לדיאטה ואימון גופני. היא ניתנת עם ~~ויסות זה אינו מושג על ידי טיפול במטפורמין בלבד או על ידי טיפול ב~~מטפורמין עם או ללא עם או ללא מעכבי SGLT2 (sodium-glucose co-transporter 2), כאשר תרופות אחרות אינן מספיקות בעצמן כדי לשלוט על רמות הסוכר בדם שלך. ~~בשילוב עם תרופות אחרות לטיפול בסוכרת במתן דרך הפה, או בשילוב עם אינסולין בזאל~~י.

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## 3. כיצד תשתמש בתרופה?

יש להשתמש בתכשיר תמיד בהתאם להוראות הרופא. המינון ואופן הטיפול יקבעו על ידי הרופא בלבד. רופאך עשוי להנחות אותך ליטול מינון שונה של סוליקווה ~~ב~~השוואה ~~ל~~עומת ~~ל~~מינון האינסולין או לתרופה אחרת להורדת גלוקוז, שהשתמשת ~~בה~~בו קודם. עליך לבדוק עם הרופא, האחות, או הרוקח אם אינך בטוח בנוגע למינון ואופן הטיפול בתכשיר.
**אין לעבור על המנה המומלצת.**

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העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים על ידי פנייה לבעל הרישום- סאנופי ישראל בע"מ, Greenwork Park, מתחם העסקים בקיבוץ יקום, בניין E (קומה 1), 6097600, יקום או בטלפון: 09-8633081.

להלן הקישור לאתר משרד הבריאות:
https://israeldrugs.health.gov.il/#!/byDrug

בברכה,

חברת סאנופי ישראל בע"מ