Injectable therapy in Diabetes Management

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Endocrinologist

24 / 7 / 1404


بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ
In The Name of ALLAH,

ADA

Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2025

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If injectable therapy is needed to reduce A1C[1]

Consider GLP-1 RA or dual GIP and GLP-1 RA in most individuals prior to insulin[2]

INITIATION: Initiate appropriate starting dose for agent selected (varies within class)
TITRATION: Titrate to maintenance dose (varies within class)

If already on GLP-1 RA or dual GIP/GLP-1 RA, or if these are not appropriate, or if insulin is preferred

If A1C is above goal

Considerations for adding basal insulin[3]

Choice of basal insulin should be based on person-specific considerations, including cost. Refer to **Table 9.4** for insulin cost information. Consider prescription of glucagon for emergent hypoglycemia.

Initiation and titration of basal analog or bedtime NPH insulin[4]

INITIATION: Start 10 units per day OR 0.1-0.2 units/kg per day
TITRATION:

- Set FPG goal (see Section 6, "Glycemic Goals and Hypoglycemia")
- Choose evidence-based titration algorithm, e.g., increase 2 units every 3 days to reach FPG goal without hypoglycemia
- For hypoglycemia: determine cause; if no clear reason, lower dose by 10-20%

Assess adequacy of insulin dose at every visit

Consider clinical signals to evaluate for overbasalization and need to consider adjunctive therapies (e.g., elevated bedtime-to-morning and/or postprandial-to-preprandial differential, hypoglycemia [aware or unaware], high glucose variability)

- If A1C is above goal and the individual is not already on a GLP-1 RA or dual GIP and GLP-1 RA, consider these classes in combination and with insulin (may use fixed-ratio product, if available and appropriate)
- If A1C remains above goal:

Initiation and titration of prandial insulin[5,6]

Usually one dose with the largest meal or meal with greatest PPG excursion; prandial insulin can be dosed individually or mixed with NPH as appropriate

INITIATION:

- 4 units per day or 10% of basal insulin dose
- If A1C <8% (<64 mmol/mol), consider lowering the basal dose by 4 units per day or 10% of basal dose

TITRATION:

- Increase dose by 1-2 units insulin dose or 10-15% twice weekly
- For hypoglycemia: determine cause; if no clear reason, lower corresponding dose by 10-20%

If A1C is above goal

If on bedtime NPH, consider converting to twice-daily NPH plan

Conversion based on individual needs and current glycemic management. The following is one possible approach:

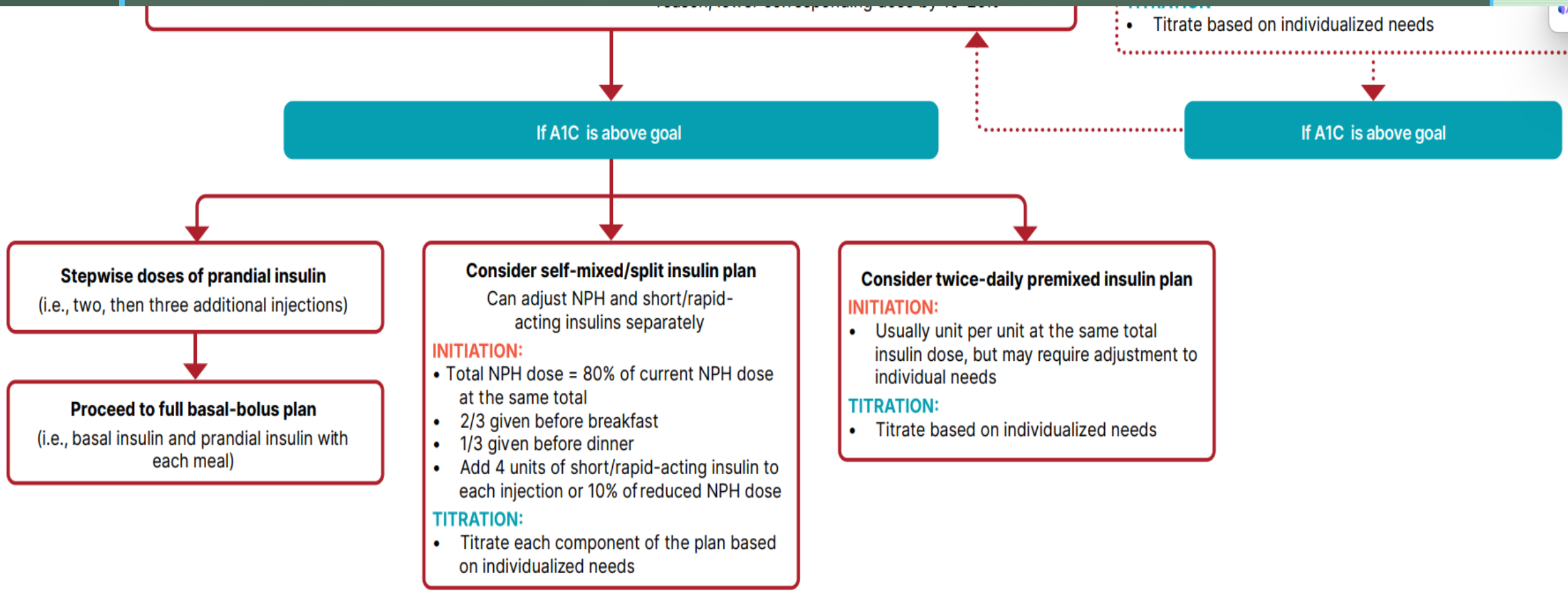
INITIATION:

- Total dose = 80% of current bedtime NPH dose
- 2/3 given in the morning
- 1/3 given at bedtime

TITRATION:

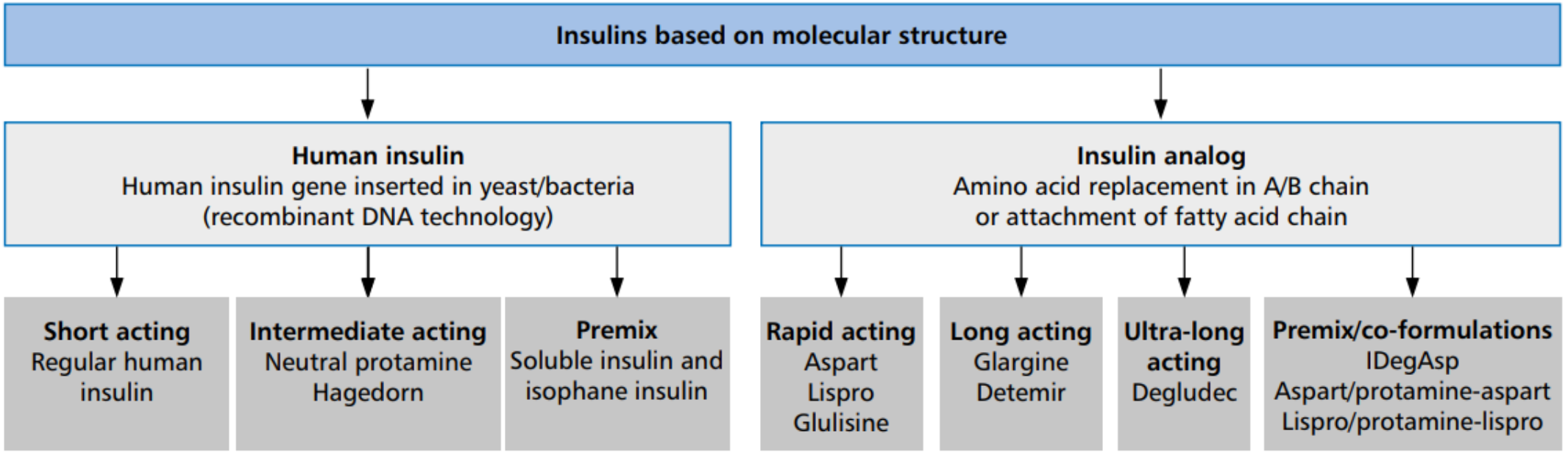
- Titrate based on individualized needs

If A1C is above goal



1. Consider insulin as the first injectable if symptoms of hyperglycemia are present, when A1C or blood glucose levels are very high (i.e., A1C >10% [>86 mmol/mol] or blood glucose ≥300 mg/dL [≥16.7 mmol/L]), or when a diagnosis of type 1 diabetes is a possibility.
2. When selecting GLP-1 RAs, consider individual preference, A1C lowering, weight-lowering effect, and frequency of injection. If CVD is present, consider GLP-1 RA with proven CVD benefit; oral or injectable GLP-1 RAs are appropriate.
3. For people on GLP-1 RA and basal Insulin combination, consider use of a fixed-ratio combination product (IDegLira or iGlarLixi).
4. Consider switching from evening NPH to a basal analog if the individual develops hypoglycemia and/or frequently forgets to administer NPH in the evening and would be better managed with a morning dose of a long-acting basal Insulin. Consider dosing NPH in the morning for steroid-induced hyperglycemia.
5. Prandial insulin options include injectable rapid- and ultra-rapid-acting analog insulins, injectable short-acting human insulin, or inhaled human insulin.

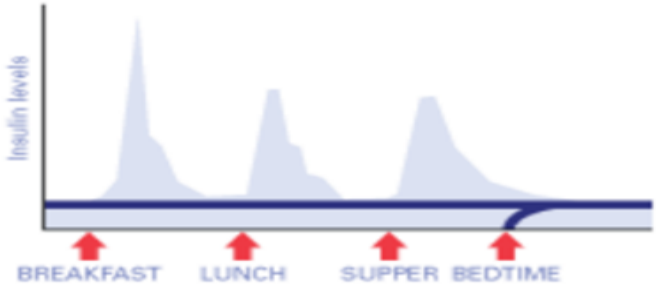
Classification of Insulins



Schematic diagram of insulin onset and time action profiles

BASAL (Lantus®)

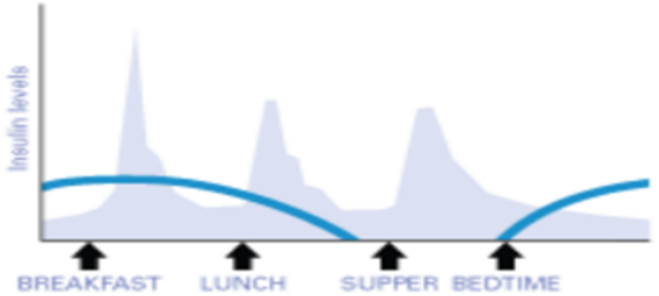
LONG-ACTING INSULIN



Onset
2-4 hours

Duration
24 hours

INTERMEDIATE-ACTING INSULIN (NPH)



Onset
0.5-1 hours

Duration
10-16 hours

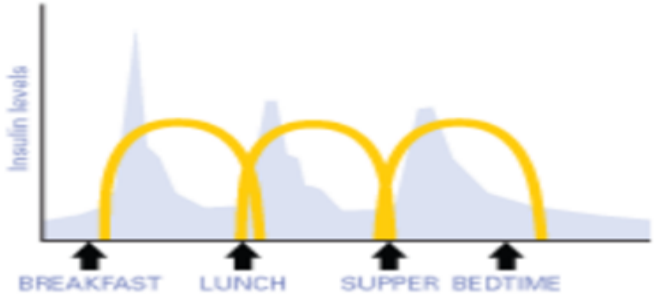
PRANDIAL

RAPID-ACTING INSULIN

Onset
~5 minutes

Duration
4-5 hours

SHORT-ACTING INSULIN (RHI)

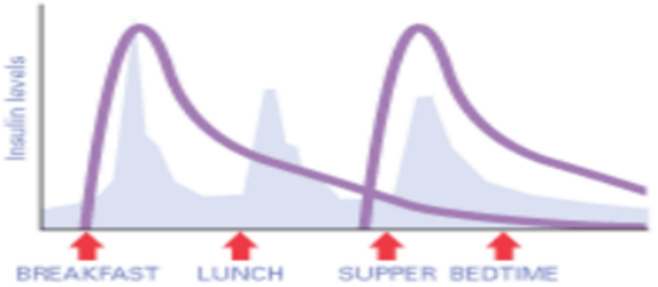


Onset
30 minutes

Duration
Up to 6 hours

PREMIX

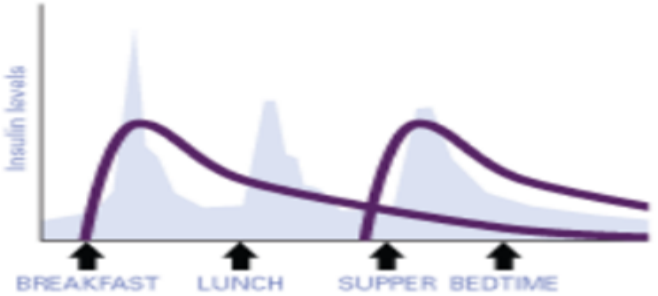
PREMIXED INSULIN (ANALOG)



Onset
5-15 minutes

Duration
10-16 hours

PREMIXED INSULIN (HUMAN)



Onset
5-15 minutes

Duration
10-16 hours

Different types of Human Insulins

Human insulin types	Onset	Peak	Duration	Examples
Short-acting (regular) [19]	30–60 minutes	2–4 hours	5–8 hours	Humulin® R Insuman® R Actrapid®
Intermediate-acting [19]	2–4 hours	4–12 hours	12–24 hours	NPH
Premix human insulins [20]	30 minutes	2–8 hours	Up to 24 hours	Mixtures of regular and NPH insulin in 25/75, 30/70, and 50/50 proportions

NPH — neutral protamine Hagedorn

Different Types of Analog Insulins

Analog insulin type	Onset	Peak	Duration
Ultra-rapid-acting insulin (faster aspart) [19]	10–20 minutes	1–3 hours	3–5 hours
Ultra-rapid-acting insulin lispro [21]	15–18 minutes	1–2 hours	~ 4 hours
Rapid-acting analog (RAA) insulin (Insulin aspart, insulin glulisine, insulin lispro) [19]	15–35 minutes	1–3 hours	3–5 hours
Long-acting analogs (LAA)			
Glargine [19]	2–4 hours	8–12 hours	22–24 hours
Detemir [19]	1–2 hours	4–7 hours	20–24 hours
Ultra-long-acting analogs (ULAA)			
Glargine U300 [19]	2–6 hours	Minimal peak	30–36 hours
Degludec [19]	30–90 minutes	Minimal peak	> 42 hours
Pre-mix analog preparations			
Biphasic IAsp [21]	10–20 minutes	1–4 hours	Up to 24 hours
70% aspart protamine, 30% aspart			
50% aspart protamine, 50% aspart			
Biphasic lispro [21]	15–30 minutes	1–3 hours	12–24 hours
75% lispro protamine, 25% lispro			
50% lispro protamine, 50% lispro			
IDegAsp co-formulation [21]	10–20 minutes	1–2 hours	> 24 hours
70% degludec, 30% aspart			

IDegAsp — insulin degludec + insulin aspart

Insulin Regimens: Advantages and Disadvantages

Types of insulin regimen	Advantages	Disadvantages
Basal insulin	Effective and safe It is simple and easy for early facilitation of insulin Potentially less weight gain Low risk of hypoglycemia Useful for symptom relief if tight control is not a major issue	Some individuals may not achieve glycemic targets The regimen doesn't offer optimum control of post-prandial hyperglycemia
Premix/co--formulation	Better PPG control It is more effective in lowering HbA1c when compared to basal insulin alone Simple for the person to understand than BBR	Less flexibility (i.e., a person is unable to adjust the bolus or basal component of the insulin independently) Fixed daily routine about lifestyle, CHO content, and meal timing is required There is a time delay of injection with conventional mixture (need to inject 20–30 minutes before a meal)
Basal plus	Better flexibility It is comparable to other conventional approaches in terms of glycemic control It offers the additional advantages of fewer hypoglycemic events Personalization of therapy, and a simple self-management algorithm for titration	Weight gain Some may need progression to BBR Careful patient evaluation and scheduling is necessary due to the complicated nature of this regimen
Basal-bolus	Potential for better metabolic control if used optimally Closely mimics normal physiology Potential for the better control of FPG and PPG Potential for a better lifestyle choice Offers optimum flexibility in terms of diet and activity	Requires multiple insulin injections More complicated to support and teach Needs CHO counting Risk of hypoglycemia and weight gain Needs better patient cooperation Requires more frequent glucose monitoring

BBR — basal-bolus regimen; CHO — carbohydrate; FPG — fasting plasma glucose; HbA1c — glycated hemoglobin; PPG — postprandial plasma glucose

Concentrated Insulins

Several concentrated insulin preparations are available, each offering distinct advantages:

1. *U-500 Regular Insulin:* Five times more concentrated than U-100 regular insulin, suitable for individuals needing large doses. Typically administered in two to three daily injections due to its pharmacokinetics.

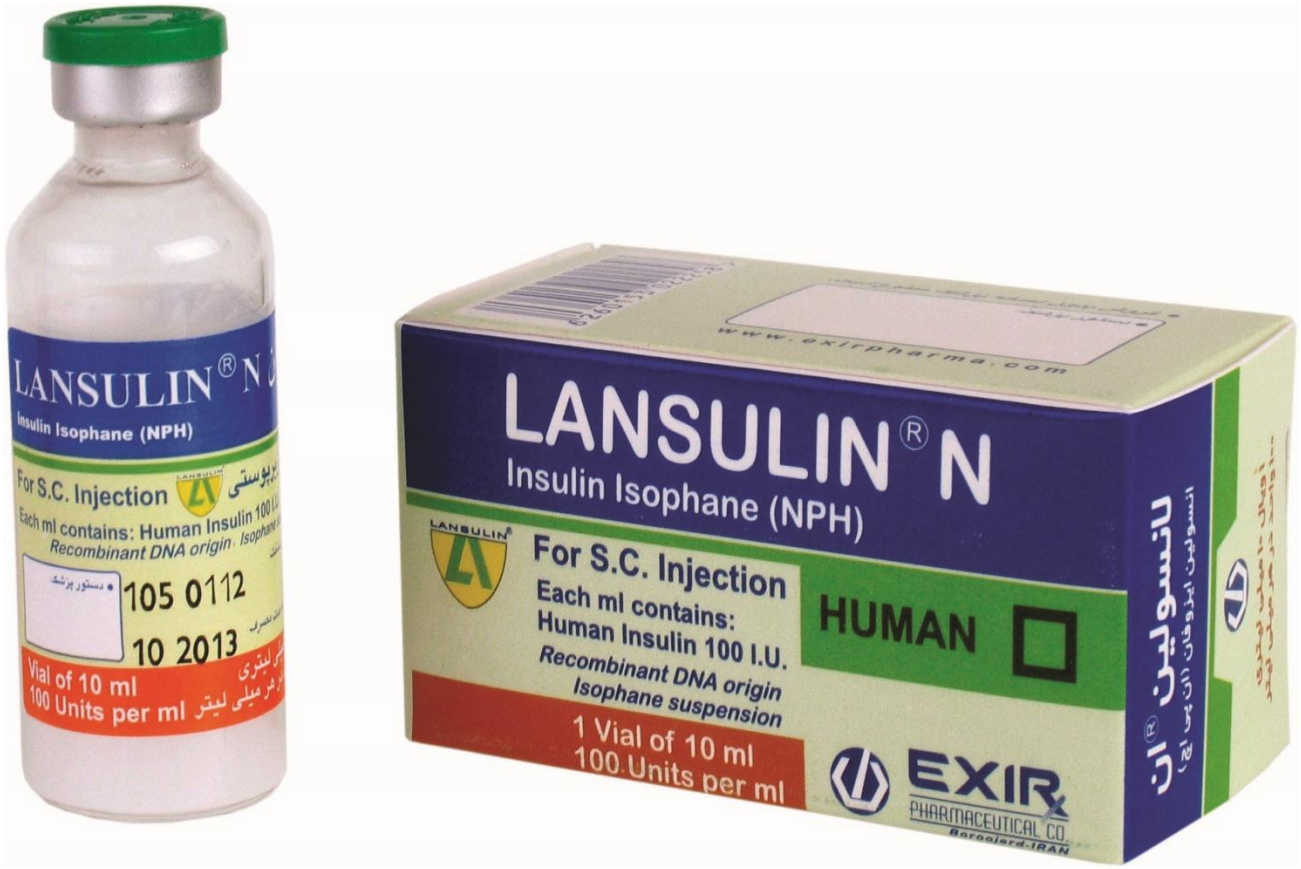
2. U-300 Glargine: Three times more concentrated than U-100 glargine. Allows for higher doses of basal insulin with less volume, reducing the number of injections.

3. U-200 Degludec: Twice as concentrated as U-100 degludec. Also facilitates higher doses with less volume.

These concentrated insulins are particularly useful for patients with insulin resistance requiring large doses. For U-500 insulin, it is crucial to use U-500 syringes to avoid dosing errors.


Regular
Insulin
10 ml

Basal insulins/ NPH




LANSULIN® 70/30
Insulin Biphasic Isophane
تزریق زیرپوستی
Each mL contains:
70 units human insulin isophane
30 units human insulin injection
(Recombinant DNA Origin)
024 1011
04 2013
Vial of 10 ml
100 IU/ml
LANSULIN® 70/30
Insulin Biphasic Isophane
S.C. Injection
HUMAN
Each mL contains:
70 units human insulin isophane suspension (NPH)
30 units human insulin injection (Regular)
(Recombinant DNA Origin)
1 Vial of 10 ml
100 IU/ml
EXIR
PHARMACEUTICAL CO
Boroujerd-IRAN
لانسولین ۷۰/۳۰


Insulin aspart I.P
NovoRapid® FlexPen®


100 U/ml
Insulin aspart I.P.
NovoRapid®* Penfill®
Solution for injection for s.c. use, monocomponent, biosynthetic r-DNA insulin
Penfill® cartridges for use with Novo Nordisk insulin devices only.
Store between 2°C - 8°C in a refrigerator.
Do not freeze. Protect from light.
See package insert for Usage, Dosage and Storage.
Penfill® cartridge is for use by one person only.
Keep out of the reach and sight of children.
During use, NovoRapid®* Penfill® may be kept at room temperature below 30°C for up to 4 weeks.
Destroy Penfill® after use.
Ask for NovoFine® needles.
NovoRapid®* Penfill® is designed to be used with NovoPen® and NovoFine® needles.
Single patient use only
novo nordisk®

5×3 ml
100 U/ml
NovoRapid®
FlexPen®
100 U/ml
Solution for injection in pre-filled pen
Insulin aspart
Subcutaneous or intravenous use
Designed to be used with NovoFine® or NovoTwist® disposable needles up to a length of 8 mm
Needles are not included
1 ml contains 100 U (3.5 mg) of insulin aspart, glycerol, phenol, metacresol, zinc chloride, disodium phosphate dihydrate, sodium chloride, hydrochloric acid, sodium hydroxide for pH adjustment and water for injections
Keep out of the reach and sight of children
Read the package leaflet before use
Use only clear and colourless solution
Single patient use only
Store in a refrigerator (2°C – 8°C)
Do not freeze
Keep the cap on in order to protect from light
After first opening: use within 4 weeks
Do not refrigerate.
Store below 30°C
Discard the needle after each injection
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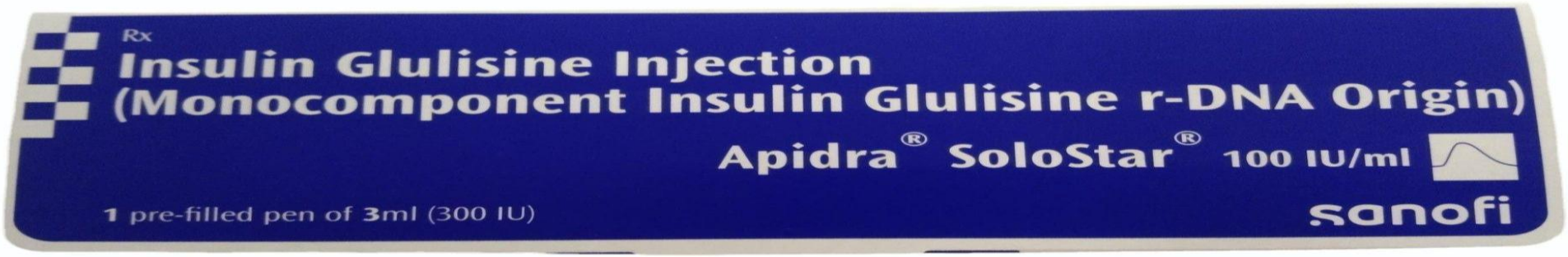
Marketing authorisation holder:
Novo Nordisk Pharma (Private) Limited
113 Shahrah-e-Iran Clifton, Karachi, Pakistan.
Manufactured by:
Novo Nordisk Production SAS
45 Avenue d'Orléans
F-28002 Chartres, France
novo nordisk®
NovoRapid®
FlexPen®


5×3 ml
NovoMix® 30
FlexPen®
100 U/ml
Suspension for injection
in a pre-filled pen
30% soluble insulin aspart and
70% insulin aspart crystallised
with protamine
Subcutaneous use
Designed to be used with NovoFine®
or NovoTwist® disposable needles
up to a length of 8 mm
Needles are not included
novo nordisk®
NovoMix® 30
FlexPen®


Rx
Insulin Glulisine Injection
(Monocomponent Insulin Glulisine r-DNA Origin)
Apidra® SoloStar® 100 IU/ml
1 pre-filled pen of 3ml (300 IU)
sanofi


100 units/ml
solution for injection in a
pre-filled pen
insulin glulisine
SANOFI
6 years.
Travel
Before travelling
need to talk about:
– the availability of
100 Unités/ml - 100 Units/ml
Solution injectable en stylo prérempli
Solution for injection in a pre-filled pen
insuline glulisine / insulin glulisine
EXP. 2023.04.30
Apidra SoloStar
100 Unités/ml - 100 Units/ml
Solution injectable en stylo prérempli
Apidra SoloStar
100 Unités/ml - 100 Units/ml
Solution injectable en stylo prérempli
Solution for injection in a pre-filled pen
insuline glulisine / insulin glulisine

Humalog mix 75/25 KwikPen

insulin lispro protamine and
insulin lispro injectable suspension
100 units/mL

Humalog Junior KwikPen

insulin lispro injection
100 units/mL

Humalog KwikPen

insulin lispro injection
100 units/mL


Diabetes
DDG
Lantus SoloStar
100 Einheiten/ml Injektionslösu
Insulin glARGin
Toujeo® 300 Ein
SoloStar® Injektion
Insulin glARGin


Rapidsulin
به زودی قلم رپیدسولین (انسولین آسپارت)
همیشه در تمام شرایط در کنار بیماران
Rapidsulin
Basalin


Basalin
Insulin Glargine 100 I.U/mL
Recombinant Insulin Glargine 100 I.U/mL
3ml Solution for Injection in pre-filled pen for Subcutaneous Injection
Each box contains 5 Pens.
Basalin


ABASAGLAR®
KwikPen®
100 unidades/ml
inyectable

ABASAGLAR®
KwikPen™
100 U/mL


TRESIBA
(insulin degludec)
injection
100 units/mL (U-100)
For subcutaneous use only
Rx Only
One 10 mL vial


FlexTouch
(insulin degludec) injection
For Single Patient Use Only
100 units/mL (U-100)


Tresiba
100
80
Tresiba
200
160

Insulin therapy in people with T1D

A. For individuals with T1D, BBR of basal and prandial insulin or CSII has proven to be an effective and safe therapy.

B. BBR insulin therapy is considered as the standard regimen for the management of T1D.

C. Basal insulin dosage is estimated based on weight and is normally initiated at 0.1 to 0.2 units/kg body weight/day and then up-titrated based on glycemic value, with typical doses ranging from 0.2 to 1.0 units/kg body weight/day.

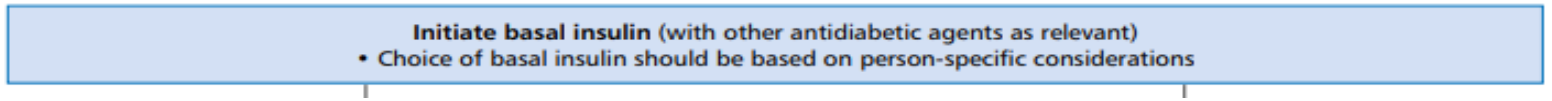
D. Short-acting insulins to be added for PPG control.

Pooyesh Darou

Insulin therapy in people with T2DM

A. Either basal insulin or premix insulin can be considered as an initial insulin regimen in people with T2D. When FPG is high, consider initiating insulin therapy with basal insulin. When both FPG and PPG are high, one may consider initiating insulin therapy with premix insulin.

B. BBR is the initial insulin regimen in acutely unwell and hospitalized people with T2D, women with T2D planning pregnancy when other regimens do not achieve optimal glycemic control, and in people with challenging lifestyles.

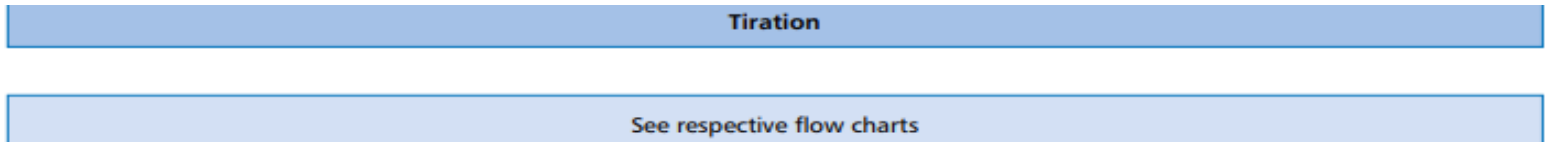


Choice of Insulin Regimen at Initiation

Recommendations of Iran consensus

- Choice of insulin regimen needs to be individualized based on needs of the patient. The following parameters may be considered while choosing between basal and premix regimens.

Favor Premix	Parameter	Favor Basal
>8.5%	HbA1c	<8.5%
>200 mg/dl	PPG	<200 mg/dl
>54 mg/dl	PPG increment	<54 mg/dl
Predictable	Lifestyle (meal pattern)	Unpredictable
High Carb load	Diet	Low carb load
Without comorbidities	Elderly	With comorbidities



Initiate basal plus insulin

Recommendation on titration of basal insulin

FPG (mg/dL)	Dose adjustments (units)
80–130	0
131–160	+ 2
161–200	+ 4
≥ 201	+ 6

Recommendation on titration of prandial insulin

PPG (mg/dL)	Dose adjustments (units)
≤ 180 mg/dL	0
181–200	+ 1 to 2
201–220	+ 2 to 3
≥ 221	+ 3 to 4

Basal-bolus regimen

A. It is recommended to calculate the total insulin dose as 0.5 units/kg body weight for people with T1D and 0.2–0.3 units/kg body weight for people with T2D.

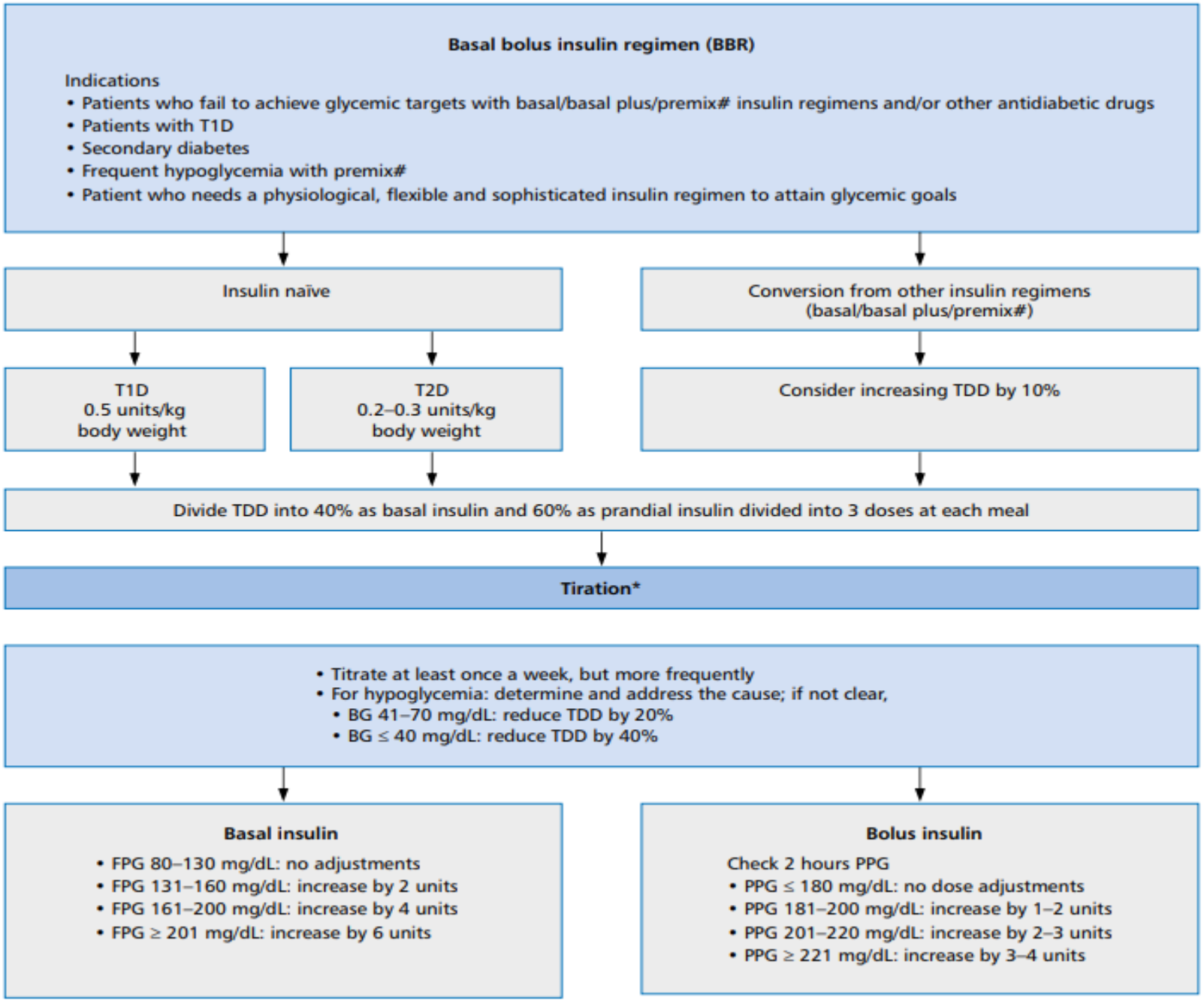
B. B. 40% of the TDD to be given as basal insulin as a single dose usually at bedtime.

C. C. 60% of the TDD to be given as prandial insulin divided as 3 doses at each meal.

D. D. The recommended target for titration of basal component is a FPG value of 80–130 mg/dL.

E. E. The recommended target for titration of the prandial component is a 2-hour PPG value of ≤ 180 mg/dL.

Initiate basal bolus insulin

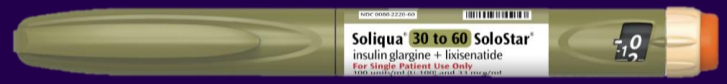


Soliqua pen

Fixed Ratio Combination (FRC)


SOLIQUA
Peach 10-40 Pen
SOLIQUA® SoloStar® 3 ml
100 units/ml + 50 mcg/ml
10
SOLIQUA® SoloStar® 3 ml
100 units/ml + 33 mcg/ml
10
SOLIQUA
Olive 30-60 Pen

iGlarLixi is available in two pens

	 **Soliqua® (10–40) pen**	 **Soliqua® (30–60) pen**
Composition	Soliqua SoloStar® 100 units/mL + 50 µg/mL 300 units of insulin glargine and **150** µg lixisenatide in 3 mL solution	Soliqua SoloStar® 100 units/mL + 33 µg/mL 300 units of insulin glargine and **100** µg lixisenatide in 3 mL solution
Lixisenatide concentration	50 µg/mL	33 µg/mL
Ratio Glargine: lixisenatide	2 IU : 1 µg	3 IU : 1 µg
Dose range	10 IU to 40 IU	30 IU to 60 IU
Color	**Peach**	**Olive**

Highlights from the EU SmPC are provided here; please refer to the SmPC for more detailed information. Available at Soliqua, INN - insulin glargine + lixisenatide (europa.eu)

Two fixed-ratios available for individual needs

- The dose is **adjusted** according to **insulin glargine** requirement and
- the lixisenatide dose follows the insulin glargine dose

10–40 pen
(2 U:1 µg ratio)*

30–60 pen
(3 U:1 µg ratio)*

***The single-dose unit displayed on both pens corresponds to the dose of insulin glargine only**

IR-SA-SLQ-25-09-130

Soliqua EU SmPC. Available at: https://www.ema.europa.eu/en

When a patient is **Insulin Naive**….

Start with 10 units

Highlights from the EU SmPC are provided here; please refer to the SmPC for more detailed information.
Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002445/WC500140401.pdf (Last accessed: Nov 2018)

iGlarLixi Starting Dose

		Previous therapy		
		Insulin naïve (Oral anti-diabetic treatment or GLP-1RA)	Insulin glargine (U100)* **<20 U**	Insulin glargine (U100)* ≥20 to **<30** U
Starting dose	**iGlarLixi 10-40 Pen**	**10** dose steps (10 U/5 µg)		**20** dose steps (20 U/10 µg)

The starting dose of iGlarLixi should not exceed the recommended lixisenatide starting dose of 10 mcg.

*If a different basal insulin was taken:
- For twice daily basal insulin or Gla-300, the total daily dose previously taken should be reduced by 20% to choose the iGlarLixi starting dose.
- For any other basal insulin, the same rule as for insulin glargine (U100) should be applied.

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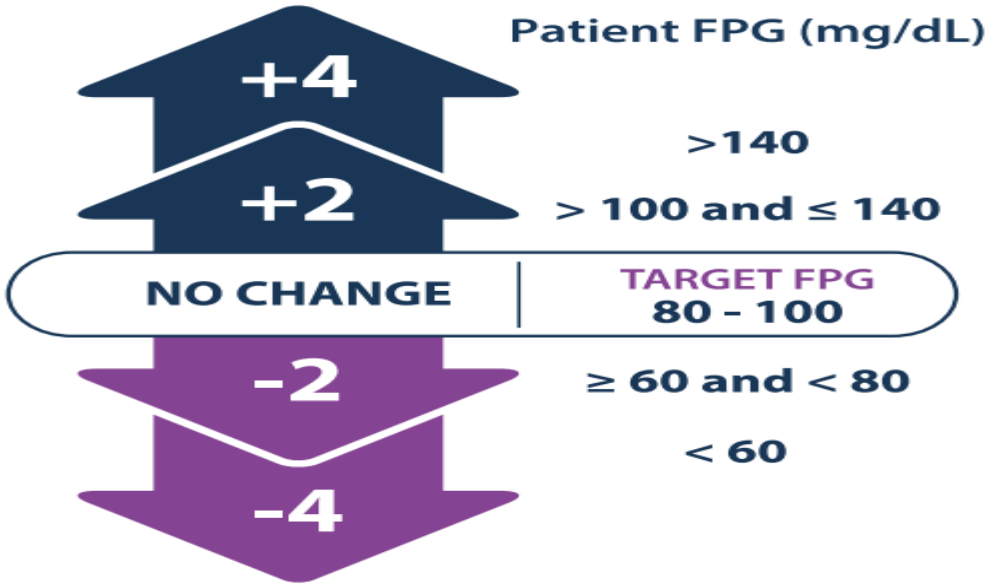
Adapted from Soliqua® SoloStar® PI.pdf (sanofi.in) Last accessed online on 16° April, 2024 at 12:54PM

Simple titration

THEN TITRATE BY 2-4 UNITS WEEKLY [2-6]

Simple titration



- Titrate by 2–4 dose steps every week until target fasting plasma glucose (FPG) is reached. [2-4]
- The dose must be individualised based on clinical response and is titrated based on the patient's need for insulin.[2]

Rosenstock J,Aonson R, GrunbergerG et al. Diabetes care 2016.
Yuon X, Guo X, Zhang J,et al. Diabetes Obes Metab.2022

iGlarLixi in insulin-naïve T2DM patients (OAD medication only)

Initiation

10

Starting dose*

10 U
11
12
13
14
15
16
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18
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40

10-40 Pen

is required, move to

30-60 Pen

When **>40 U**

30 U
31
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60

IR-SA-SLQ-25-09-130

Highlights from the EU SmPC are provided here; please refer to the SmPC for more detailed information.
Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002445/WC500140401.pdf (Last access: Nov 2019)

Dose titration with iGlarLixi

Dosing should be **titrated based on FPG** in accordance with individual patient needs

If the patient starts with the iGlarLixi (10–40) pen, the dose may be **titrated up to 40** dose steps with this pen

For doses >40 dose steps/day, titration must be continued with the iGlarLixi (30–60) pen

If the patient starts with the iGlarLixi (30–60) pen, the dose may be **titrated up to 60** dose steps with this pen

For total daily doses >60 dose steps/day, iGlarLixi must not be used

Highlights from the EU SmPC are provided here; please refer to the SmPC for more detailed information.
Available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002445/WC500140401.pdf (Last accessed: Nov 2018)

Dose calculation: When a patient is on basal insulin…

What is the previous basal insulin dose?

If ≥20 and <30 units*

▼

Start with 20 dose steps ("U")†

▼

If ≥30 and ≤60 units*

▼

Start with 30 dose steps ("U")‡

▼

***Starting doses are based on previous insulin glargine 100 U/mL dose.**

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 Soliqua starting dose. For any other basal insulin, the same rule as for insulin glargine (100 units/mL) should be applied; †Each dose step contains 1 unit of insulin glargine and 0.50 micrograms of lixisenatide; ‡Each dose step contains 1 unit of insulin glargine and 0.33 micrograms of lixisenatide.

Therapy with basal insulin or GLP-1 RA or oral glucose-lowering medicinal product other than metformin and SGLT-2 inhibitors should be discontinued prior to initiation of Soliqua.

Consult prescribing information in your country of practice as information and availability of specific pens shown on this page may vary.

GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT-2, sodium-glucose cotransporter-2.

Adapted from: Rosenstock J, et al. Diabetes Care 2016;39:2026–35; Soliqua SmPC Available at: Soliqua, INN - insulin glargine + lixisenatide (europa.eu)

Dose calculation: iGlarLixi dosing based on previous basal insulin dose* (in patients receiving ≥20, <30 U per day)

Initiation

20 dose steps†

Starting dose*

10 U
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40

10–40 Pen
Each dose step contains 1 unit of insulin glargine and 0.5 micrograms of lixisenatide

When **>40 U**

is required, move to

30–60 Pen
Each dose step contains 1 unit of insulin glargine and 0.33 micrograms of lixisenatide.

30 U
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

*__Therapy with basal insulin or GLP-1 RA or OAD other than metformin and SGLT-2 inhibitors should be discontinued prior to initiation of Soliqua__. Starting doses are based on previous insulin glargine 100 U/mL dose. Subsequent dose adjustments are based on FPG. 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 Soliqua starting dose. For any other basal insulin, the same rule as for insulin glargine 100 units/mL should be applied; †Each dose step contains 1 unit of insulin glargine and 0.5 micrograms of lixisenatide for the 10–40 pen. For the 30–60 pen, each dose step contains 1 unit of insulin glargine and 0.33 micrograms of lixisenatide. The maximum daily dose is 60 units insulin glargine and 20 mcg lixisenatide corresponding to 60 dose steps. Consult prescribing information in your country as information and availability of the pens shown on the slide may vary.

GLP-1RA, glucagon-like peptide-1 receptor agonist; OAD, oral antidiabetic drug; SGLT-2, sodium-glucose cotransporter-2.

Adapted from: Rosenstock J, et al. Diabetes Care 2016;39:2026–35; Soliqua SmPC available at:

Dose calculation: iGlarLixi dosing **based on previous basal insulin dose*** (in patients receiving ≥30 and ≤60 U per day)

30
Dose steps†

Starting dose* →

30–60 Pen

30 U
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Consult prescribing information in your country as information and availability of the pens shown on the slide may vary.

Adapted from: Aroda V, et al. Diabetes Care 2016;39:1972–80; Soliqua SmPC Available at: Soliqua, INN - insulin glargine + lixisenatide (europa.eu)

Shelf life and storage

- Shelf life is 3 years
- Shelf life after first use of the pen is 28 days

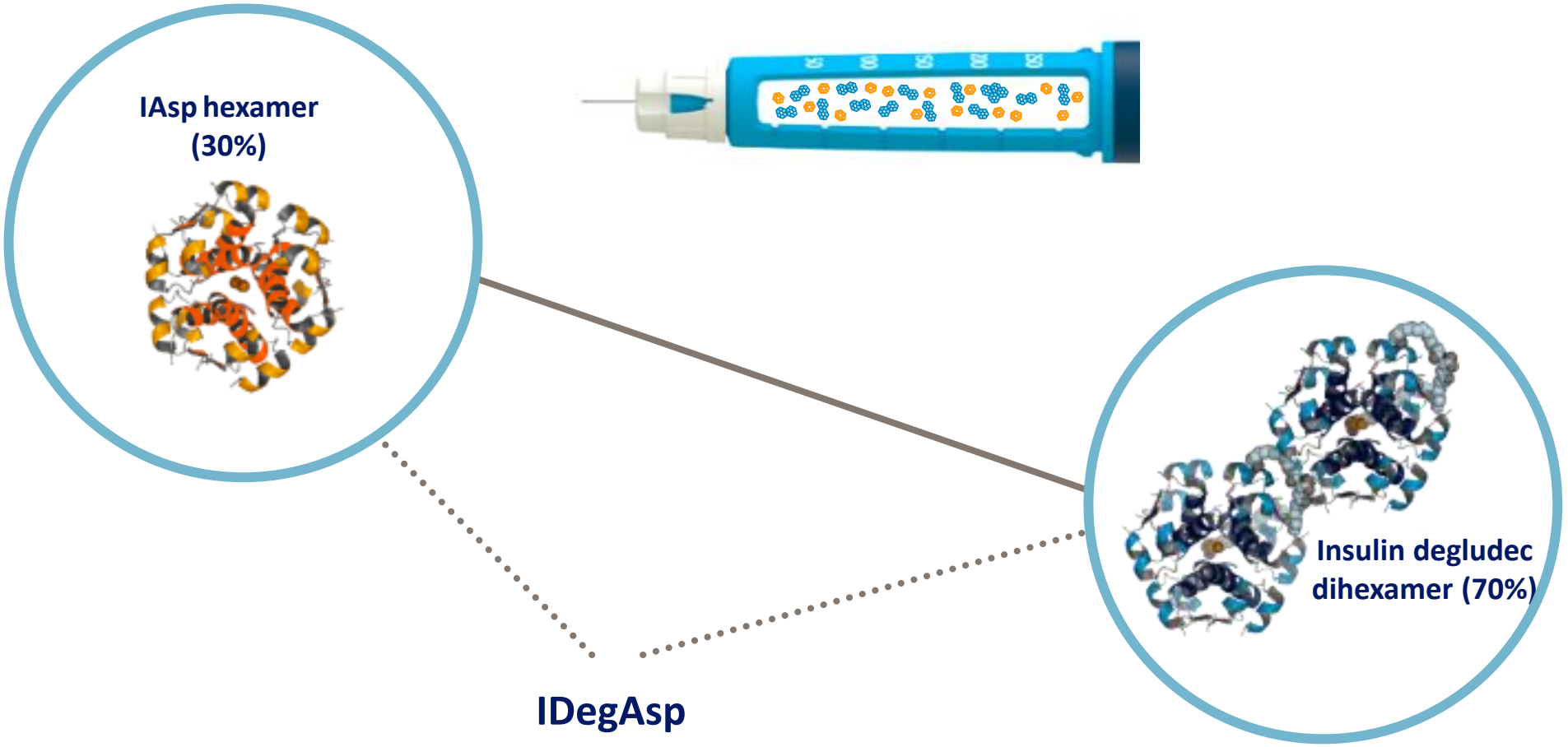
Storage	In-use pens	Not-in-use pens
Temperature	Store below **25°C** **Do not refrigerate** **Do not freeze**	Store in a refrigerator (2°C–8°C) Do not freeze
Needle	Do not store with attached needle	
Storage conditions	Store away from direct heat/light	Keep pen in outer carton to protect from light
Cap	Put pen cap back on after each injection	

Soliqua SmPC – Summary of product characteristics updated 14-Nov-2024

FlexTouch Ryzodeg

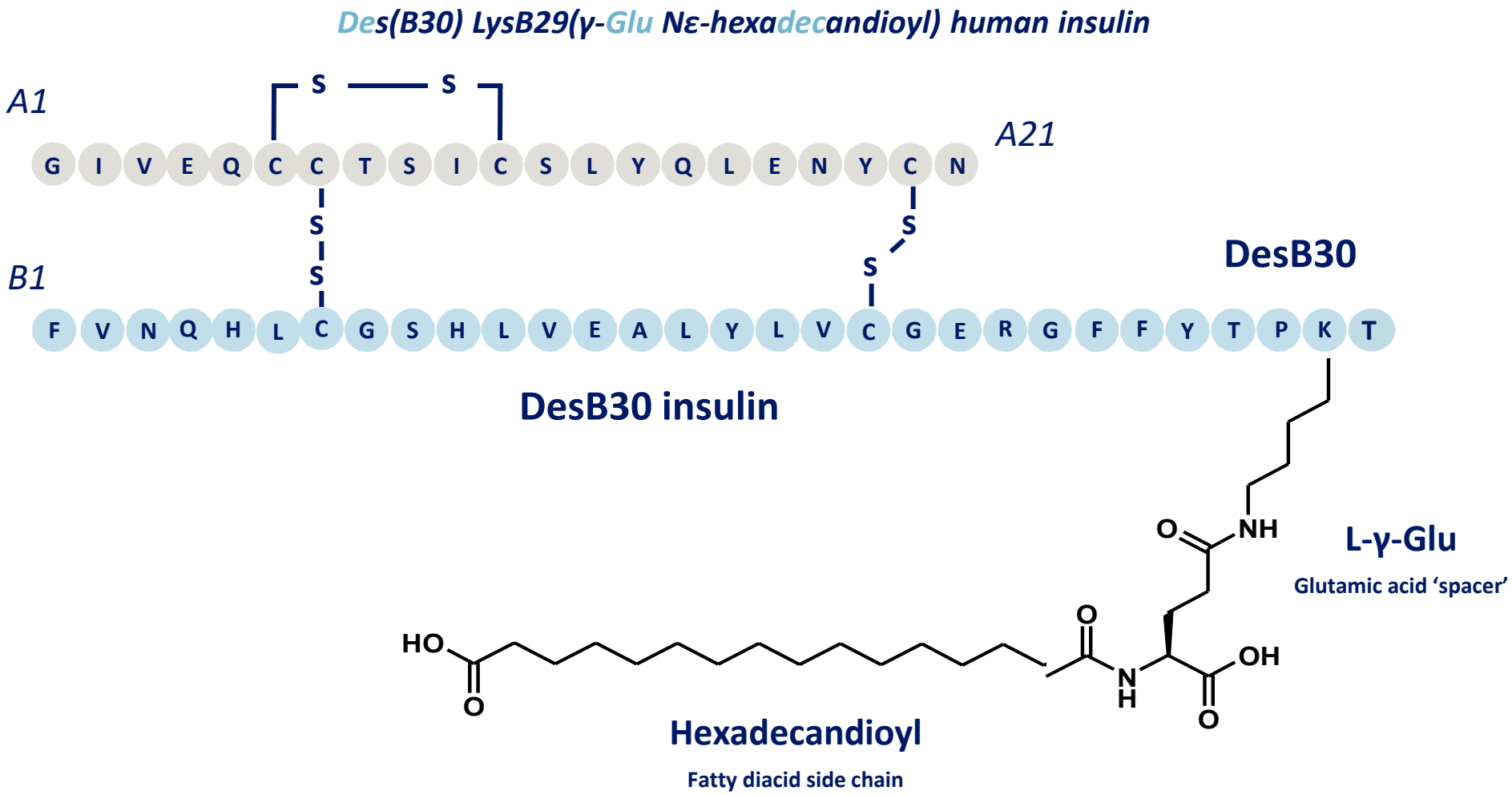
The IDegAsp co-formulation

Co-formulation of insulin degludec with insulin aspart (IAsp)



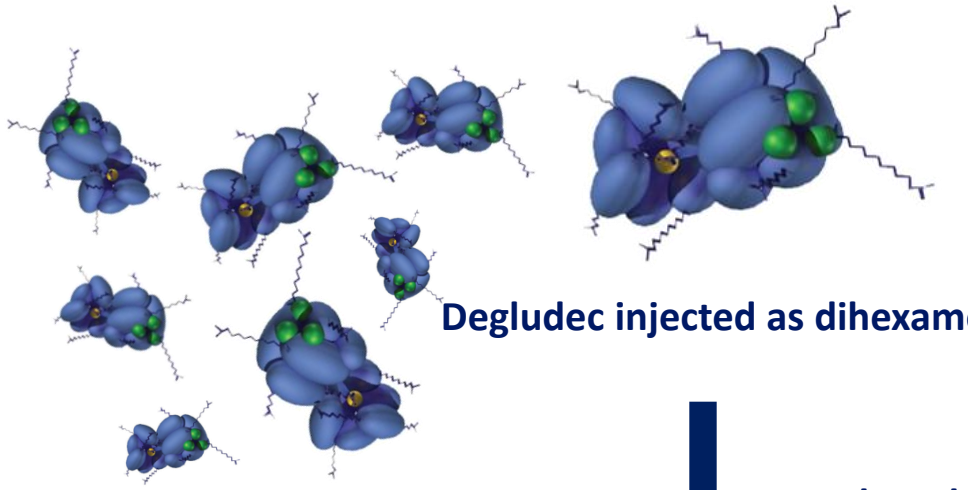
IAsp, insulin aspart; IDegAsp, insulin degludec/insulin aspart

Degludec: rationally designed, beyond sequence modification



Jonassen *et al. Pharm Res* 2012;29:2104–14

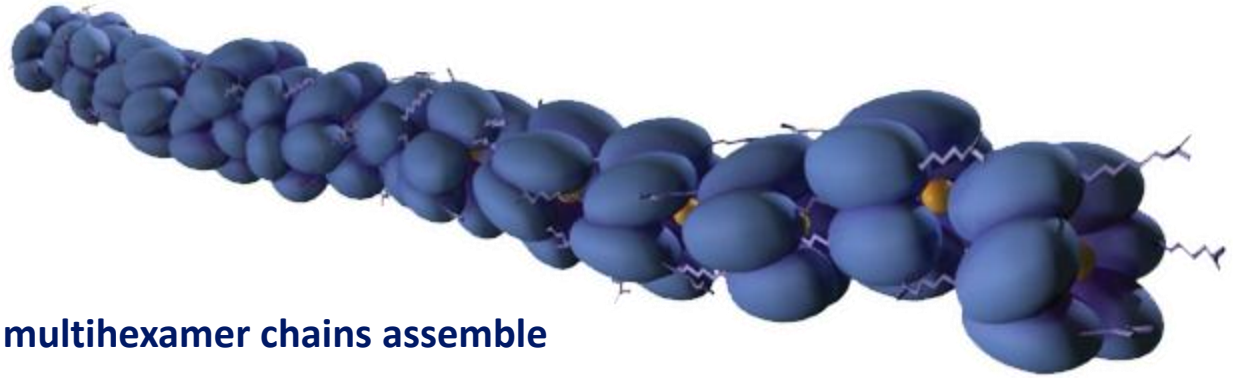
Degludec: immediately after injection



Degludec injected as dihexamers

Phenol; [Zn^{2+}]

Phenol from the vehicle diffuses quickly, and insulin degludec links up via single side-chain contacts



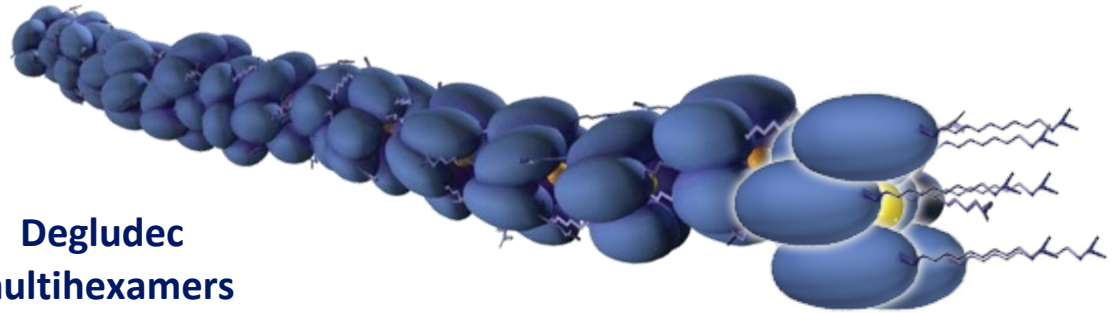
Long multihexamer chains assemble

Jonassen *et al. Pharm Res* 2012;29:2104–14

Degludec: slow release following injection

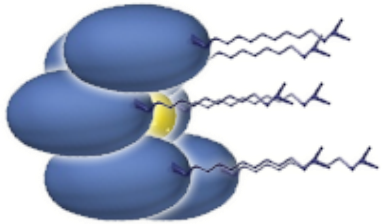
Subcutaneous depot

[Zn^{2+}]

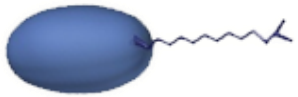


Degludec multihexamers

Zinc diffuses slowly causing individual hexamers to disassemble, releasing monomers



Monomers are absorbed from the depot into the circulation

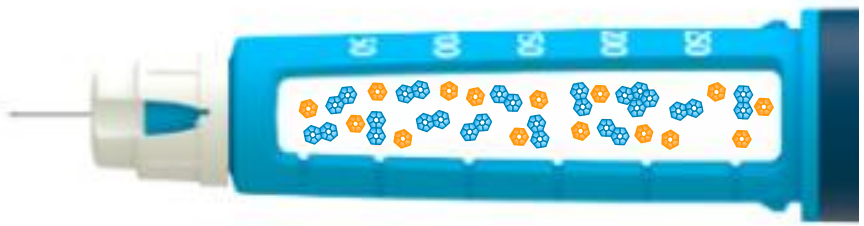


Jonassen *et al. Pharm Res* 2012;29:2104–14

Co-formulation of insulin degludec with rapid-acting insulin possible because of stable dihexamers in solution

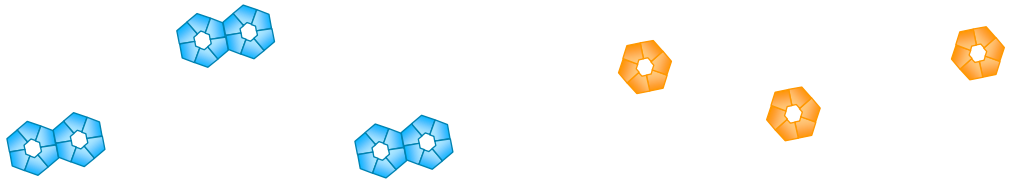
In the formulation

IDegAsp = Insulin degludec (70%) + IAsp (30%) existing separately in one formulation

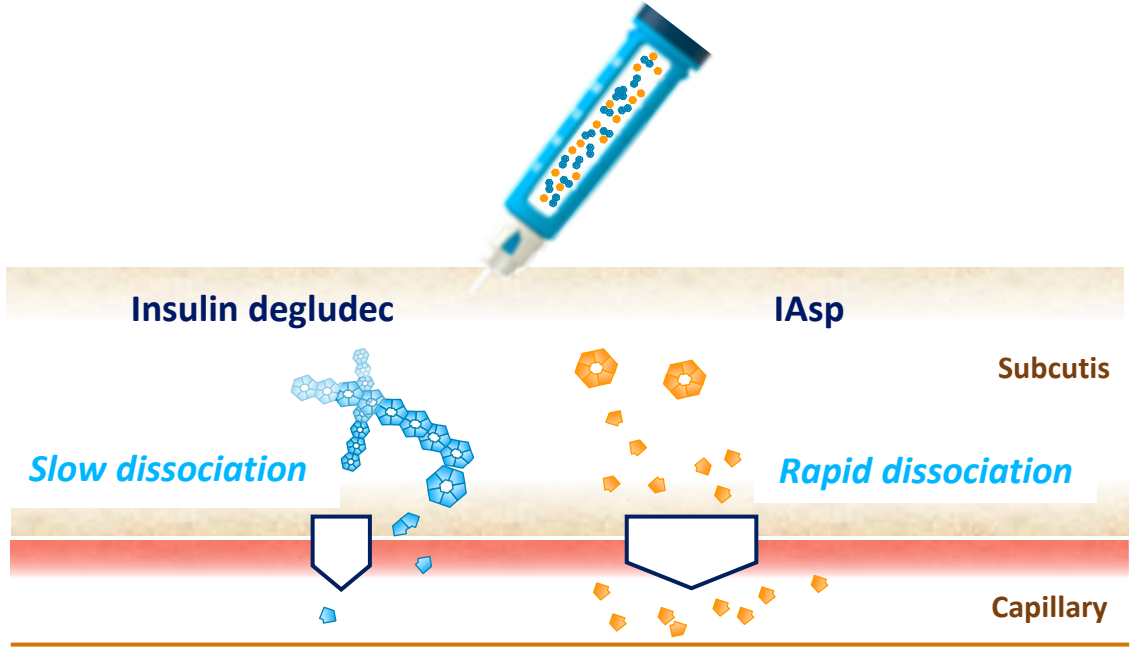


Insulin degludec dihexamers

IAsp hexamers



In the subcutaneous depot



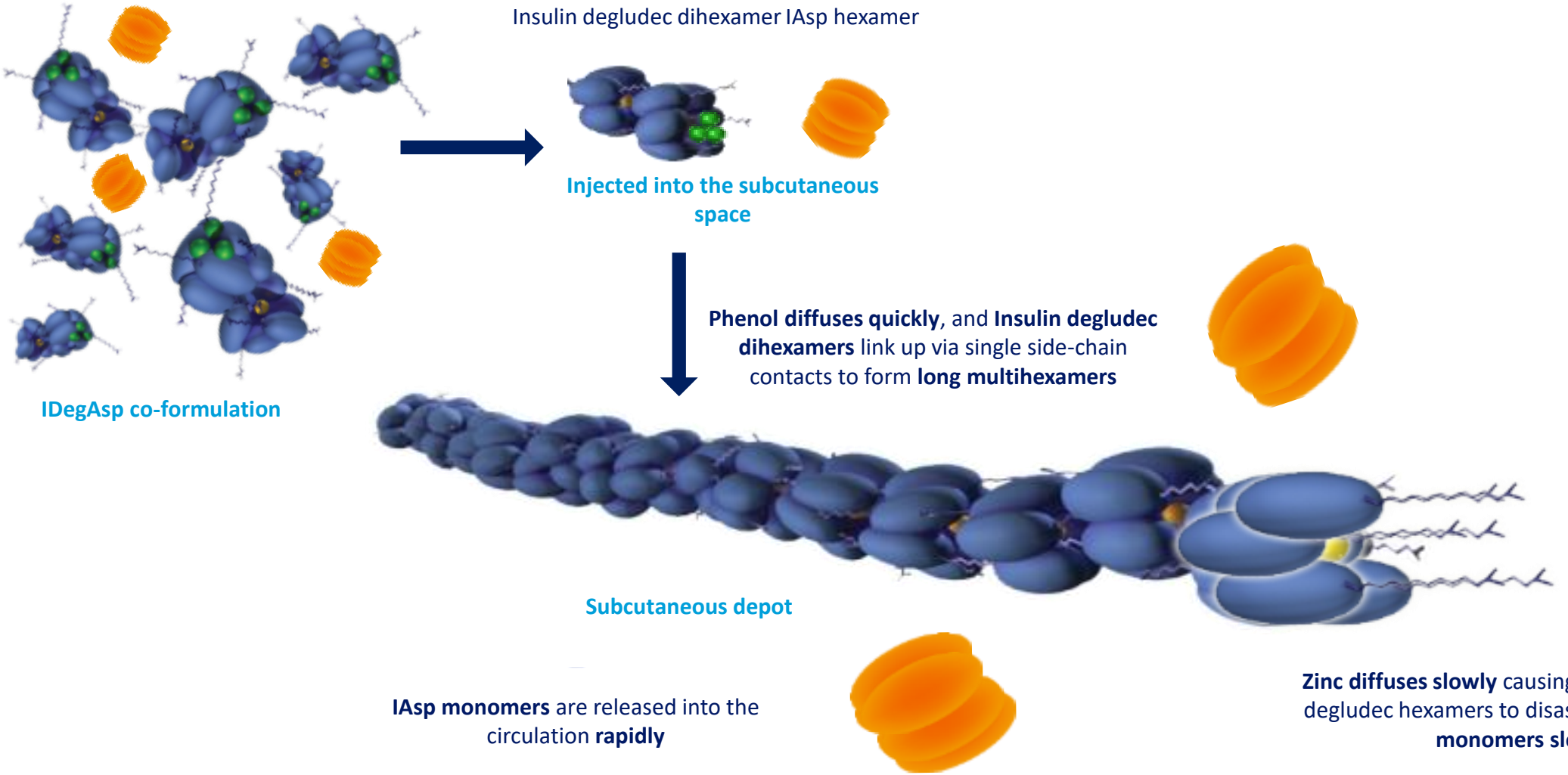
IAsp, insulin aspart; IDegAsp, insulin degludec/insulin aspart

Havelund *et al. Pharm Res.* 2015;32:2250–8

IDegAsp

Mode of protraction at steady state

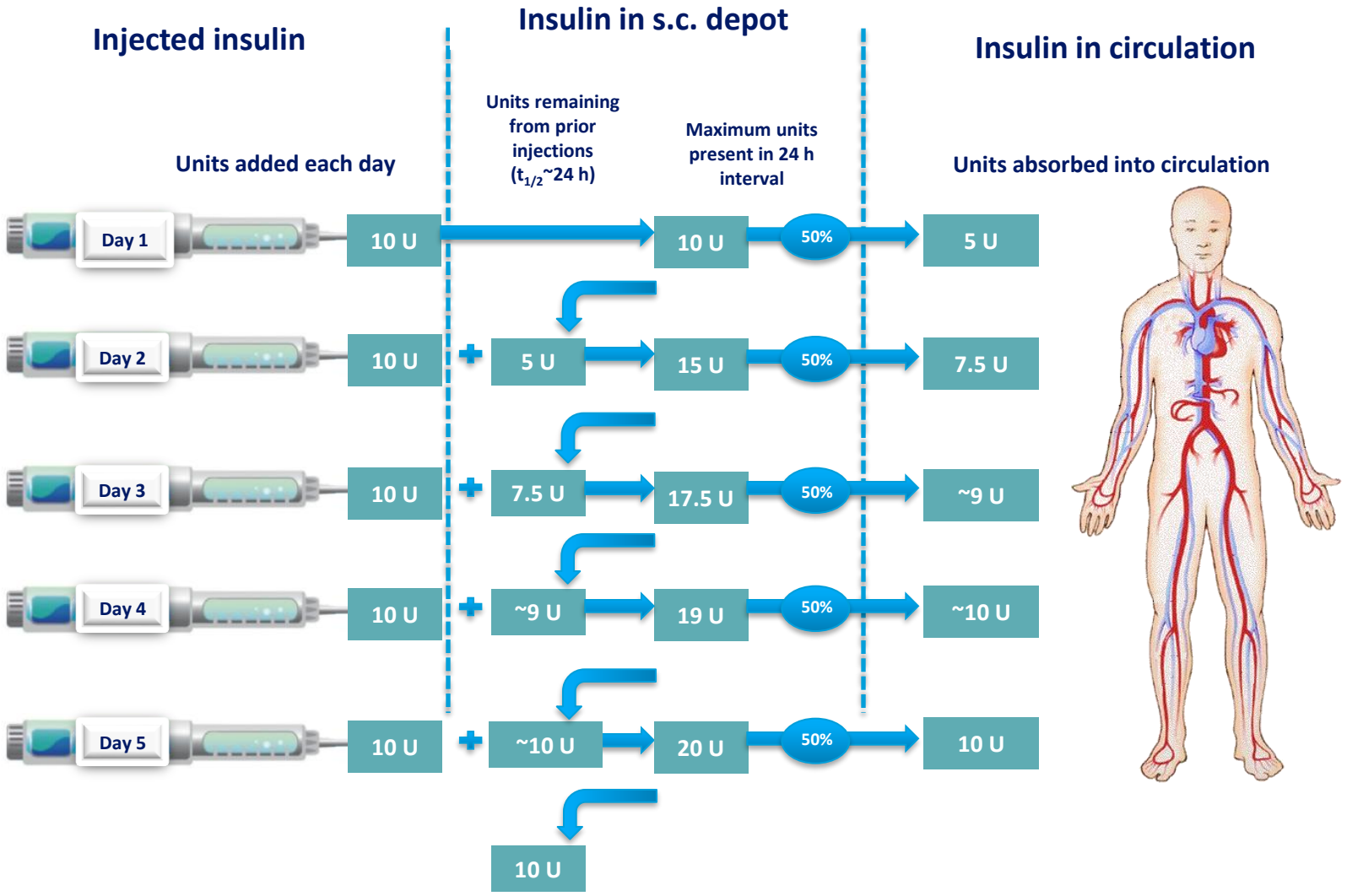
Phenol; Zn^{2+}]



IAsp, insulin aspart; IDegAsp, insulin degludec/insulin aspart; Zn, zinc

Jonassen *et al. Pharm Res* 2012;29:2104–14

Degludec once-daily administration without accumulation



Elimination of any insulin follows first order kinetics. Therefore there is no stacking.

s.c., subcutaneous

Figure adapted from Heise and Meneghini. Endocr Pract 2014;20:75–83

Switching to IDegAsp from other treatment regimens

Recommended if glycemia is insufficiently controlled, despite a threshold of 36–40U or 0.5 U/kg/day of basal insulin

Switching from basal insulin

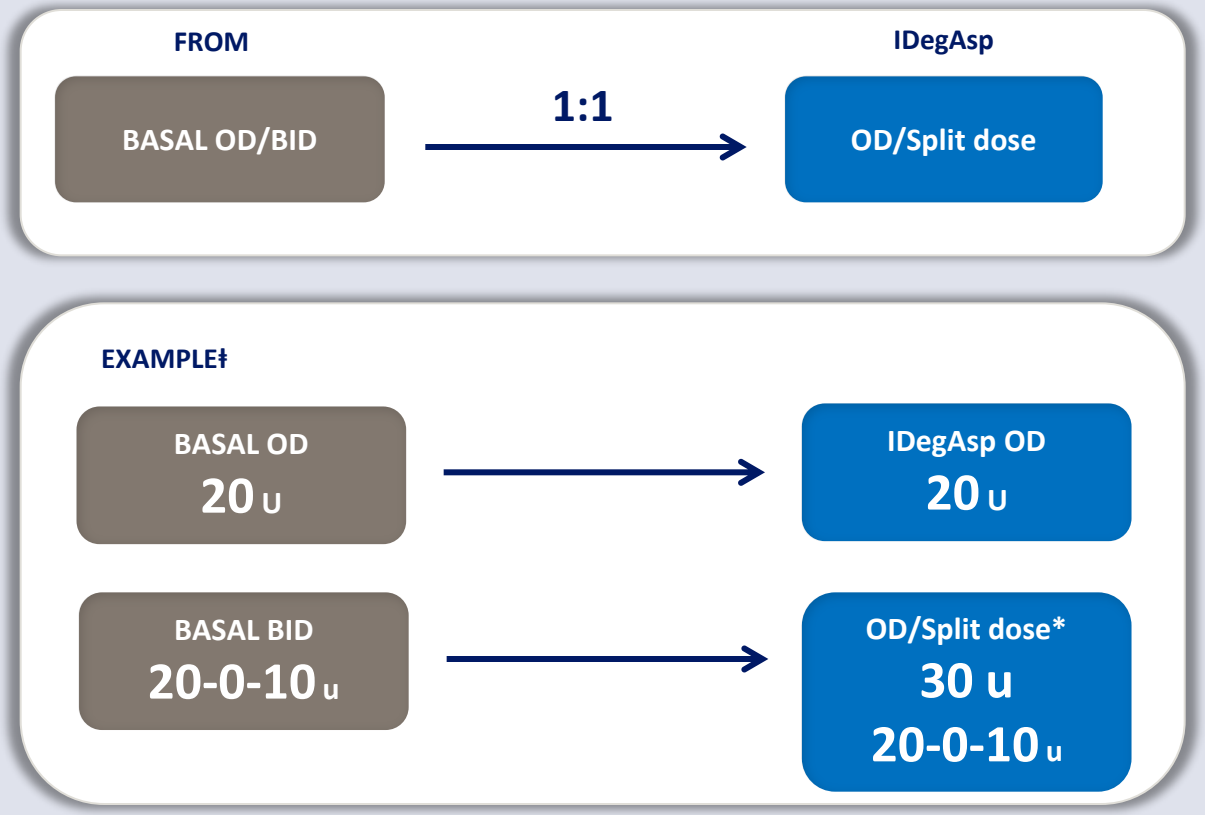
Unit-for-unit conversion when switching from basal insulin

Reduce dose for those experiencing hypoglycaemia or previously on insulin **glargine 300U/mL**

IDegAsp, insulin degludec/insulin aspart; U, unit.
Mehta R, et al. *Diabetes Obes Metab*. 2020;10.1111/dom.14128.

Practical recommendation switching from Basal to IDegAsp

GUIDANCE – Switching from Basal[1-3]



Practical Consideration switching from basal insulin to IDegAsp [1-2]

- Basal OD → IDegAsp OD or BID (equal or unequal)
- Basal BID → IDegAsp BID or OD

If **HbA1c is raised**:

- Maybe higher dose than total

If **HbA1c is not raised** or **high-dose basal**:

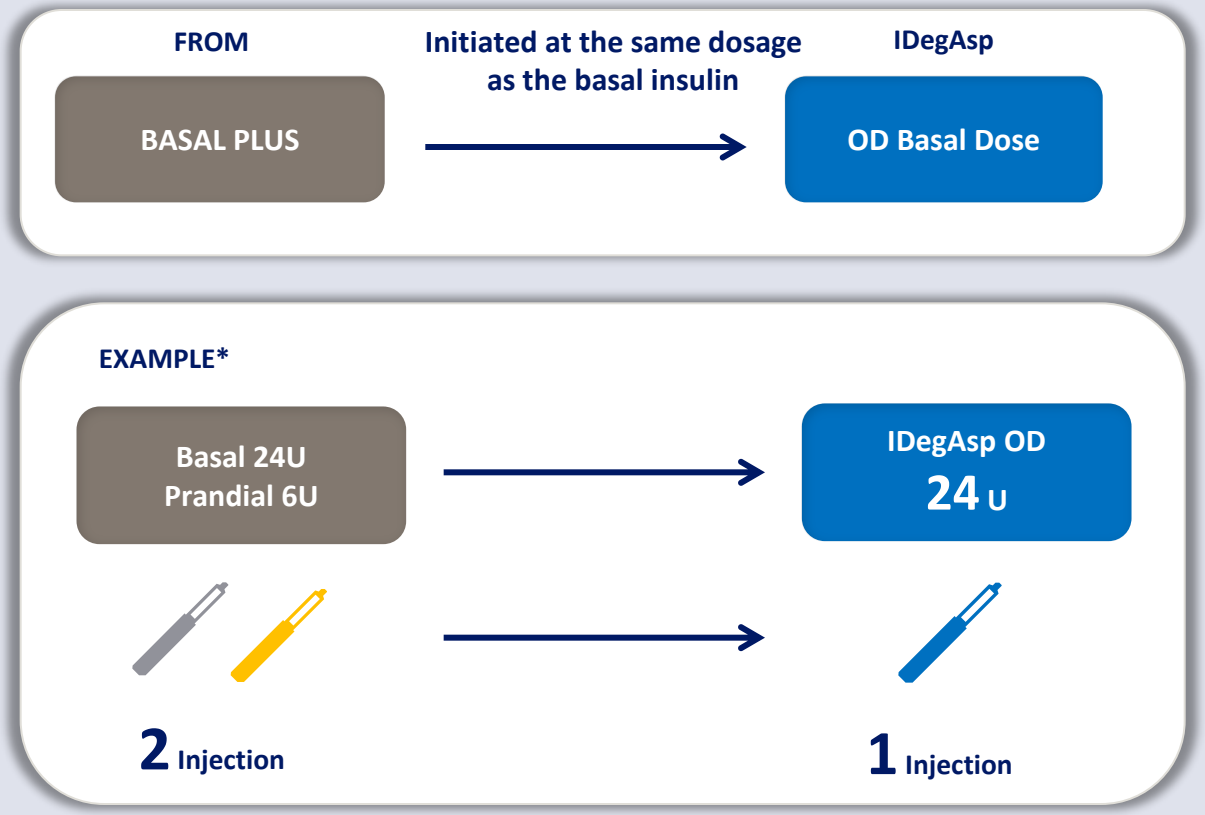
- ↓ 20% dose

*: Splitting dose not necessarily 50:50, assuming largest meal is in the morning. Titration needed to achieved desire glycaemic control ‡IDegAsp is given with the largest meals

References: 1. Sarah Galtras et al. J Clin Med 2020. 2. Roopa M et al. Diabetes Obes Metab. 2020;1-15

Practical recommendation switching from Basal Plus to IDegAsp

GUIDANCE – Switching from Basal Plus[1-2]



Practical Consideration switching from basal plus to IDegAsp [1-2]

- People with T2DM **not achieving glycaemic** control on basal-plus
- People require **simplification** of complex regimen

PRACTICAL RECOMMENDATION[1-2]

- Switching from basal plus require **individualisation** according to glycaemic profile.
- Following **switching** from basal plus, IDegAsp may be given OD
- **Titrate** to achieve optimal FPG.

***:** Individual needs, IDegAsp is given with the largest meals, titrate to achieve desired glycaemic control **Recommend a max OD dose 30-40 units.

References: 1. Sarah Galtras et al. J Clin Med 2020. 2. Roopa M et al. Diabetes Obes Metab. 2020;1-15

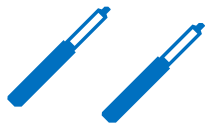
Practical recommendation switching from Basal-Bolus to IDegAsp

GUIDANCE – Switching from Basal Bolus[1-2]

FROM	Initiated at the same dosage as the basal insulin	IDegAsp
Basal-Bolus	→	Split dose

EXAMPLE*

Basal 15u Prandial 0-5-5 u	Iinitiated at the same dosage as the basal insulin →	IDegAsp 15 u Split **0-7-8 u****



PRACTICAL RECOMMENDATION[1-2]

- People with T2DM whom did **not achieve** adequate glycemic control and require **simplification** of complex regimen
- Following **switching** from basal bolus (3 injection), IDegAsp may be given **split dose**

*: Individual needs, IDegAsp is given with the largest meals **: Splitting the dose not necessarily 50:50, Assuming largest meals taken in evening, 2nd largest meals is lunch.

References: 1. Sarah Galtras et al. J Clin Med 2020. 2. Roopa M et al. Diabetes Obes Metab. 2020;1-15

SGLT- 2	• If SGLT-2 added to IDegASp: **decrease dose 10-20%** • & titrated weekly to reduce the risk of side effects
SUs	• Caution when combining IDegAsp with (SUs) Sulphonylureas.
P	evidence
Met **Acarb** **DPP4-inh**	
GLP-1	• Add IDegAsp to GLP-1RA, **no decrease** in insulin dose. Daily dose 10 u is recommended. • If GLP-1RA added to IDegAsp, insulin dose **may be decreased**, depending on HbA1C level

SU → OD: 1/2 dose reduction

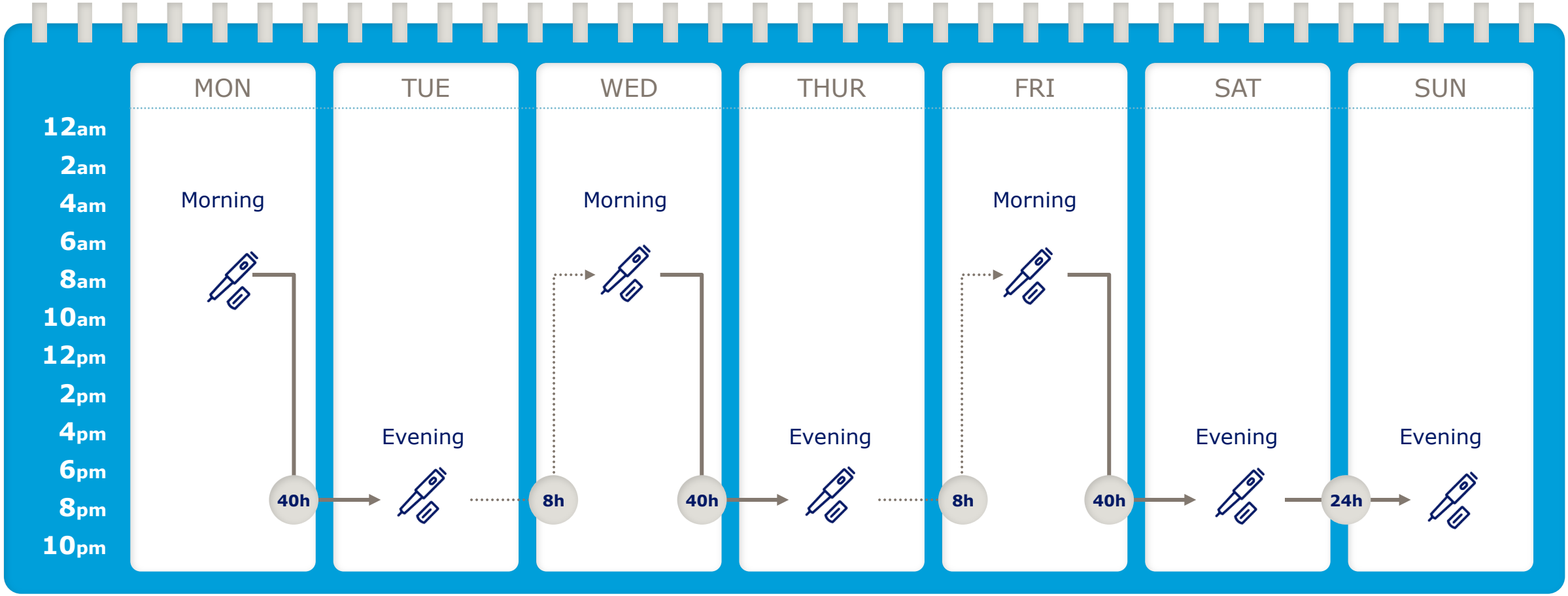
BID: Discontinued

IDEACON 2024

References: 1. Sarah Galtras et al. J Clin Med 2020. 2. Roopa M et al. Diabetes Obes Metab. 2020;1-15 3. Diabetes Care 2023;46(Suppl. 1):S5–S9 | https://doi.org/10.2337/dc23-SREV

Flexible administration of IDeg was tested in both T1D and T2D

Two phase 3a clinical trials (6 and 12 months)



IDeg, insulin degludec; T1D, type 1 diabetes; T2D, type 2 diabetes

Meneghini *et al. Diabetes Care* 2013;36:858–64; Mathieu *et al. J Clin Endocrinol Metab* 2013;98:1154–62

GLP – 1 R. Agonists

Incretin - Based Drugs

Incretin Medication


VICTOZA®
liraglutide
(rDNA origin) injection
18 mg/3 mL (6 mg/mL)
Each pen delivers doses of 0.6 mg, 1.2 mg or 1.8 mg
Subcutaneous use only
Discard pen 30 days after first use
REFRIGERATE – DO NOT FREEZE
NDC 0169-4060-13
List 406013
Single patient use only
Rx Only
Contains: 3 Victoza Pens, Product Literature
Dispense the enclosed Medication Guide to each patient
Intended for use with Novo Nordisk disposable needles
3 Pens: 30 doses of 1.8 mg
Victoza®
liraglutide (rDNA origin) injection


Saxenda®
(liraglutide) injection
Saxenda®
liraglutide injection 3mg

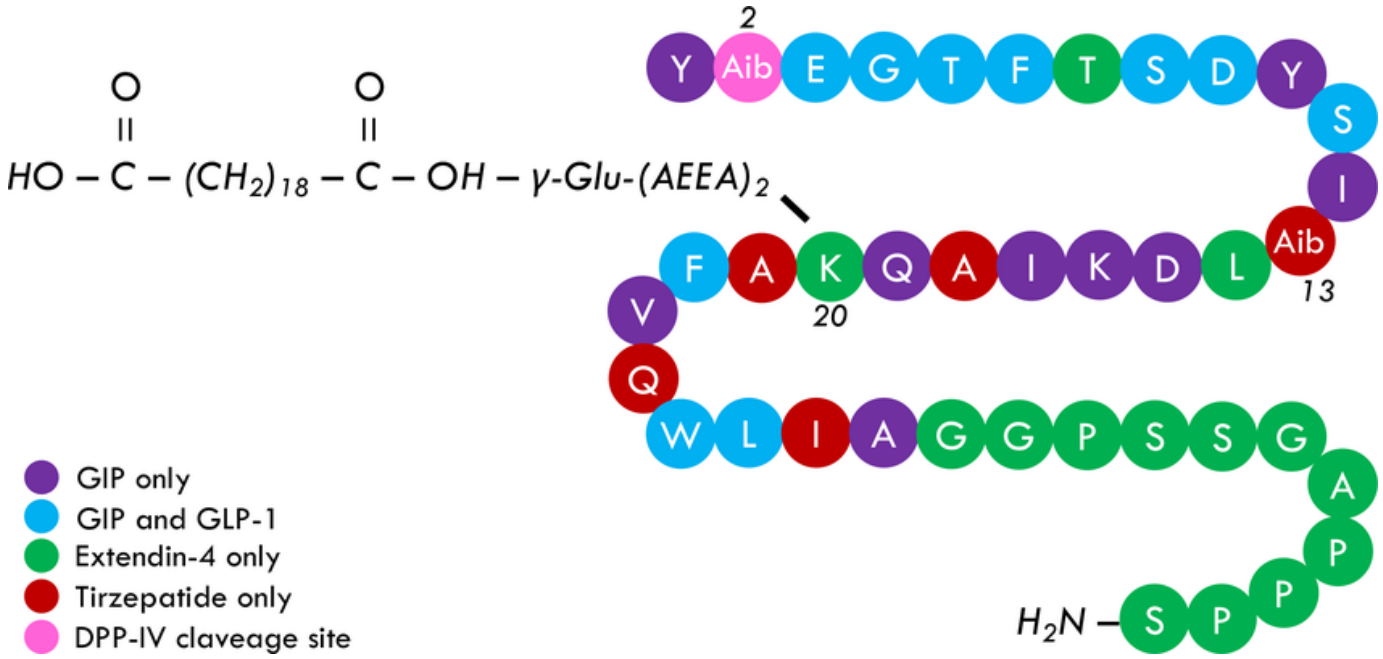
آمپول ملیتاید

Dual GIP/GLP 1 Receptor Agonists

Dual Agonist

Tirzepatide: From Molecular Design to Guideline Recommendation

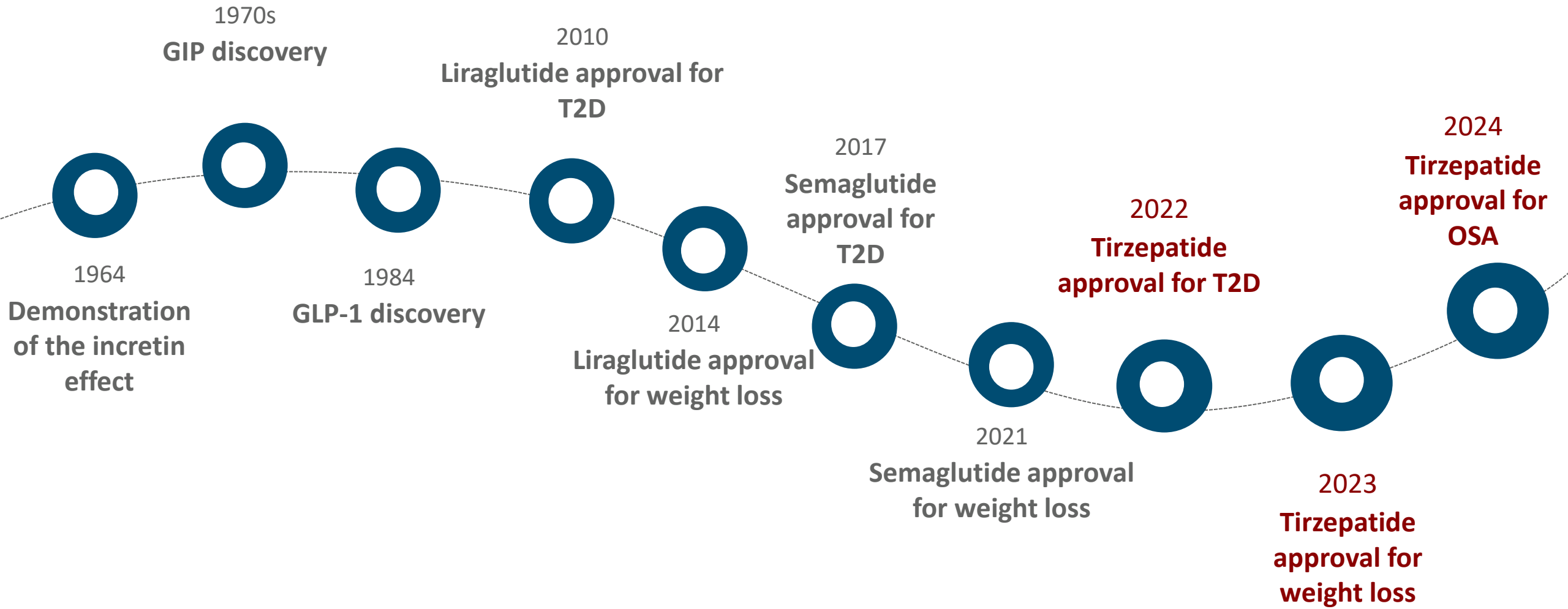
Tirzepatide: incorporating GLP-1 activity into the GIP sequence



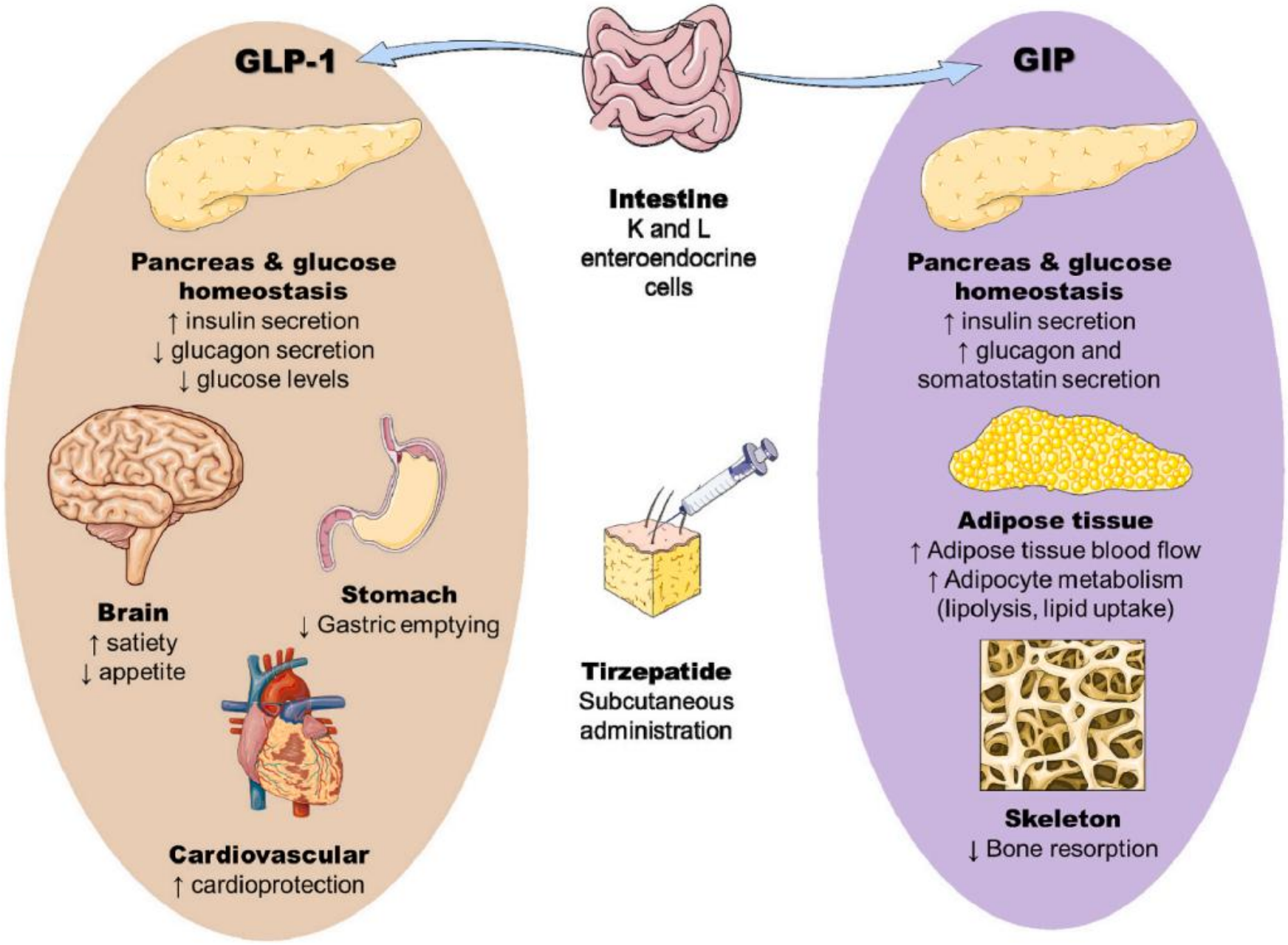
Tirzepatide acts as an imbalanced **dual agonist:** it has equal affinity for the GIP receptor compared to native GIP, but approximately five times weaker affinity for the GLP-1 receptor than native GLP-1.

This imbalance is considered important for maximizing its efficacy.

Timeline of milestones in the Development of Incretin-Based Therapies



Major Physiological Roles of GLP-1 and GIP



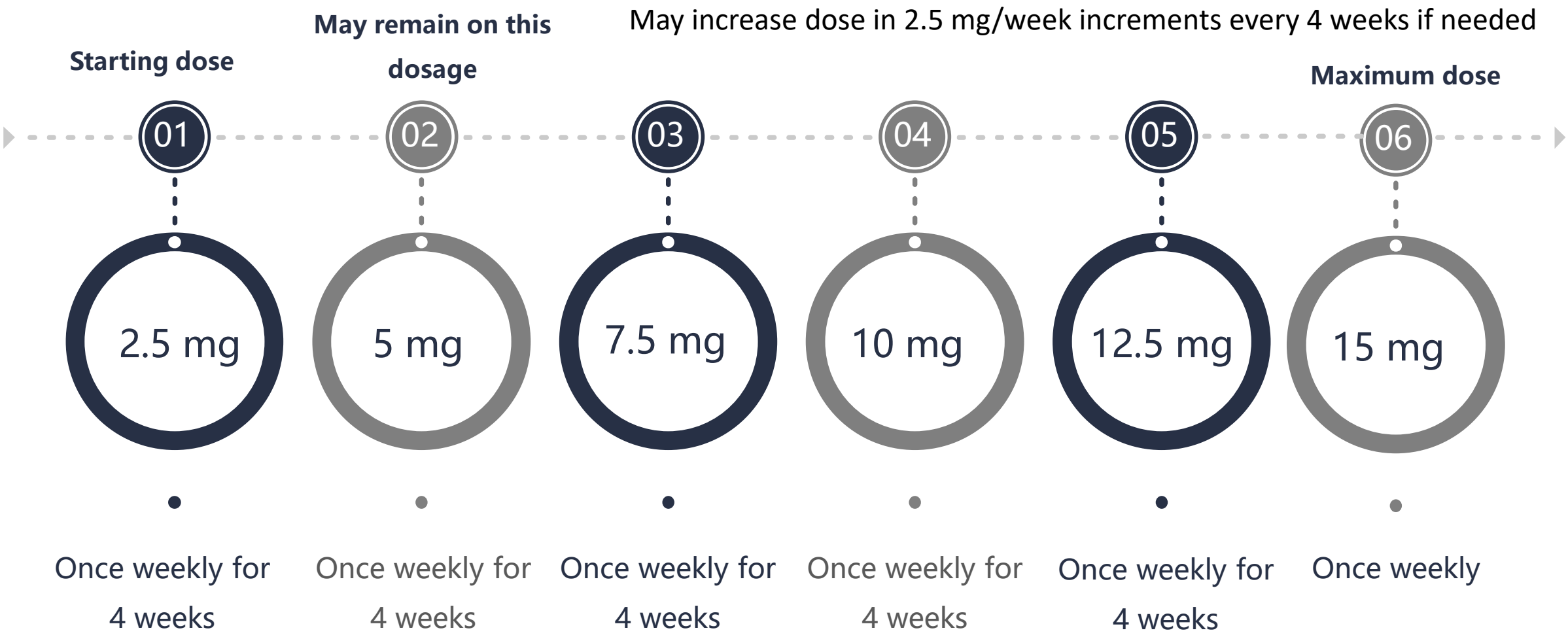
Use: Labeled Indications

Diabetes mellitus, type 2, treatment: Adjunct to diet + physical activity
In adults with type 2 diabetes mellitus

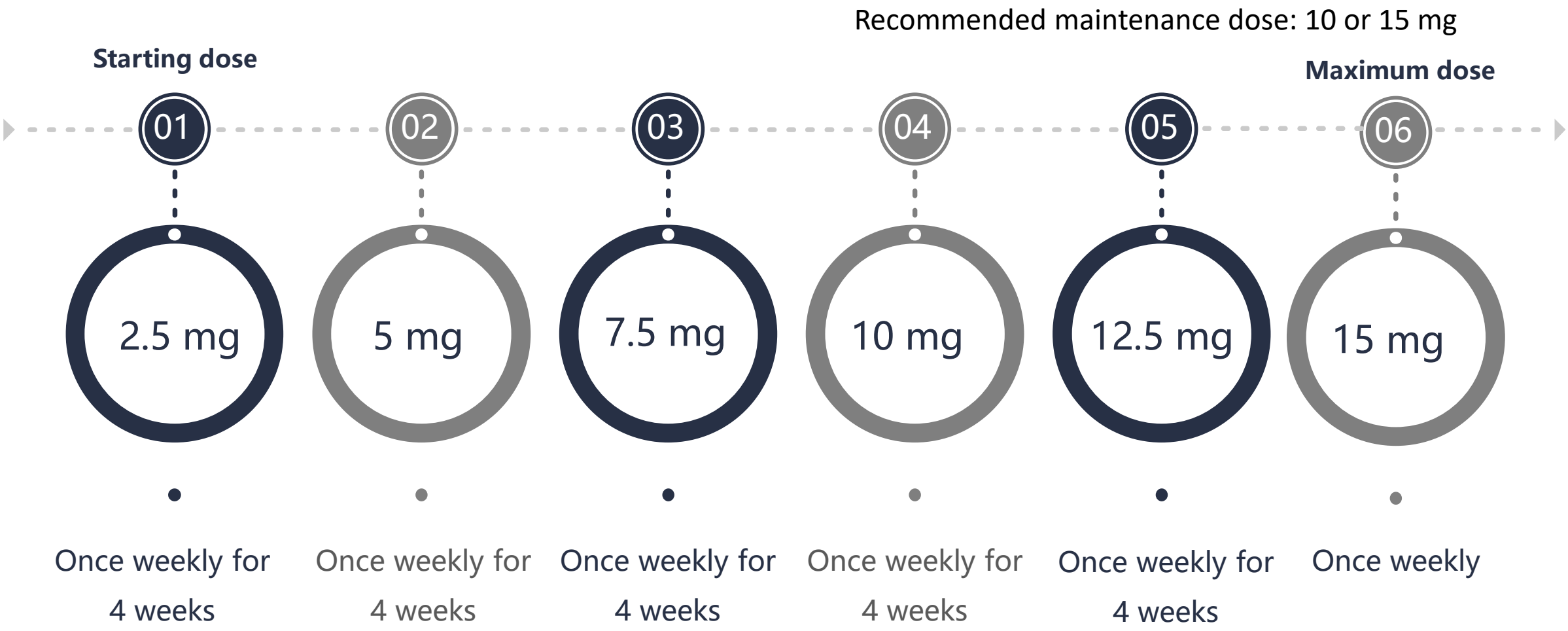
Weight management, chronic: Adjunct to diet + physical activity
Reduce weight and maintain weight reduction long-term in adults with obesity, or in adults with overweight in the presence of ≥1 weight-related comorbid condition

Obstructive sleep apnea, moderate to severe: Moderate to severe obstructive sleep apnea
In adults with obesity.

Tirzepatide Dosing in Weight Management and T2DM



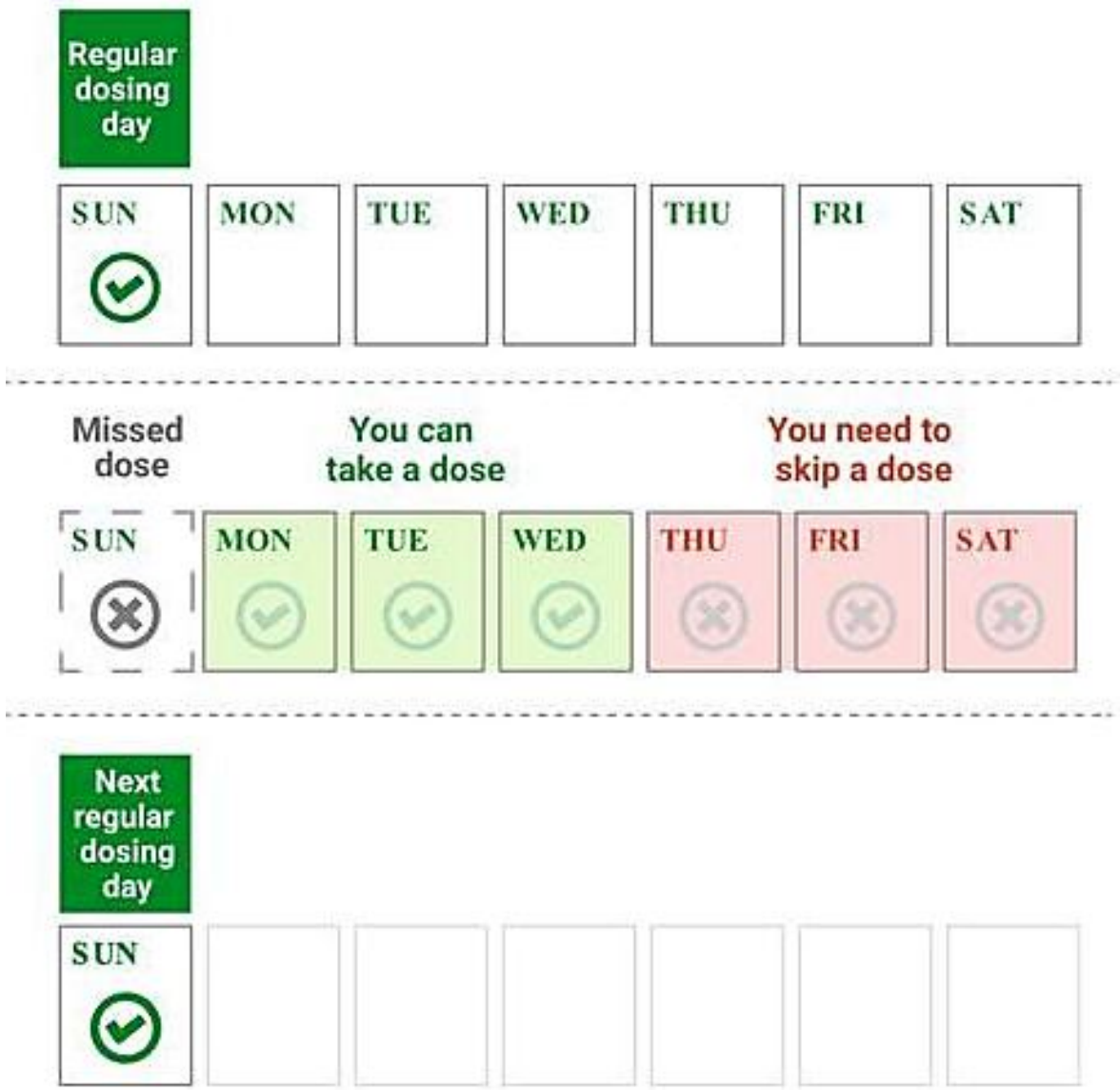
Tirzepatide Dosing in Obstructive sleep apnea, moderate to severe



Missed dose

Administer as soon as possible **within 4 days**, then the usual schedule should be resumed.

If **more than 4 days** have elapsed, the missed dose should be **skipped** and administration should be resumed at the next scheduled weekly dose.



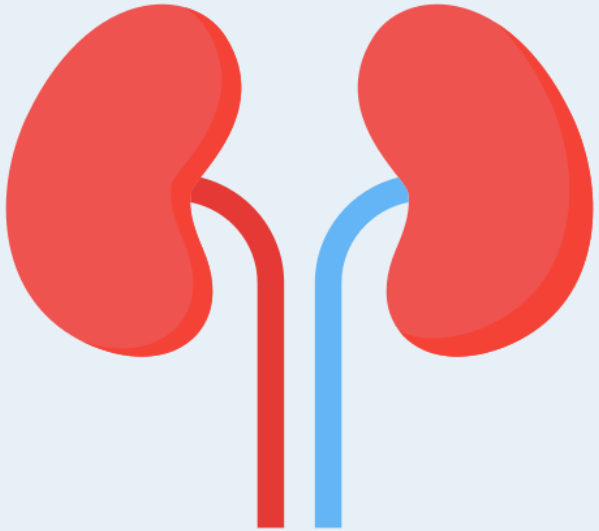
Tirzepatide Dose Adjustment

Hepatic Impairment

No dosage adjustment is necessary.

Orchid Pharmed
Sky's the Limit

Tirzepatide Dose Adjustment



Kidney Impairment

No dosage adjustment is necessary.

Orchid Pharmed
Sky's the Limit

Tirzepatide Contraindications

- Serious hypersensitivity
- History of or family history of Medullary Thyroid Cancer (MTC)
- Patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN2)

Orchid Pharmed
Sky's the Limit

Tirzepatide
Monitoring Parameters

- Plasma glucose
- GI adverse reactions
- Heart rate
- Body weight
- Renal function
- Signs/symptoms of pancreatitis
- Signs/symptoms of gallbladder disease
- Worsening of diabetic retinopathy
- HbA1c

Tirzepatide Precautions

- Diabetes mellitus: Do not use in patients with **type 1 diabetes mellitus,** or for the treatment of **diabetic ketoacidosis**; not a substitute for insulin.

- **Surgical and endoscopic procedures:** Use of GLP-1 RAs may increase the risk of adverse events during anesthesia. Individualize the decision to hold the GLP-1 RA based on patient-specific factors.

Tirzepatide and Thyroid Cancer

Risk of thyroid C-cell tumors

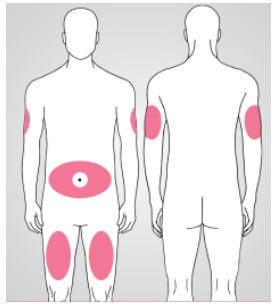
In both male and female rats, tirzepatide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether tirzepatide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined.

Tirzepatide is contraindicated in patients with a personal or family history of MTC or in patients with multiple endocrine neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of tirzepatide and inform them of symptoms of thyroid tumors (eg, a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with tirzepatide.

Administration

Once Weekly

With or Without Meal



Subcutaneous Injection

Injection: If changing the day of administration is necessary, allow at least 72 hours between two doses.

Easier administration with autoinjector, just once weekly.

Storage of Autoinjector:

- Store in a refrigerator (2-8°C).
- Do not freeze.
- Protect from light.
- Do not use this medicine if you notice that the solution is not clear and colourless or almost colourless, or if the Physioject is damaged or has been frozen.
- Do not use after the expiry date.

Gastrointestinal Adverse Event Management

The Most Common Adverse Reactions