Insulin Intensification in Patients with T2DM

Atieh Amouzegar, MD

Endocrine Research Center

Research Institute for Endocrine Sciences

Shahid Beheshti University of Medical Sciences

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Insulin Therapy

- Many adults with type 2 diabetes eventually require and benefit from insulin therapy
- See insulin administration technique, above, for guidance on how to administer insulin safely and effectively
- The progressive nature of type 2 diabetes should be regularly and objectively explained to individuals with diabetes
- Clinicians should avoid using insulin as a threat or describing it as a sign of personal failure

Barriers to Insulin

Average HbA1c of ≥ 75mmol/mol (9%) for up to 2 years before starting…

Patient:

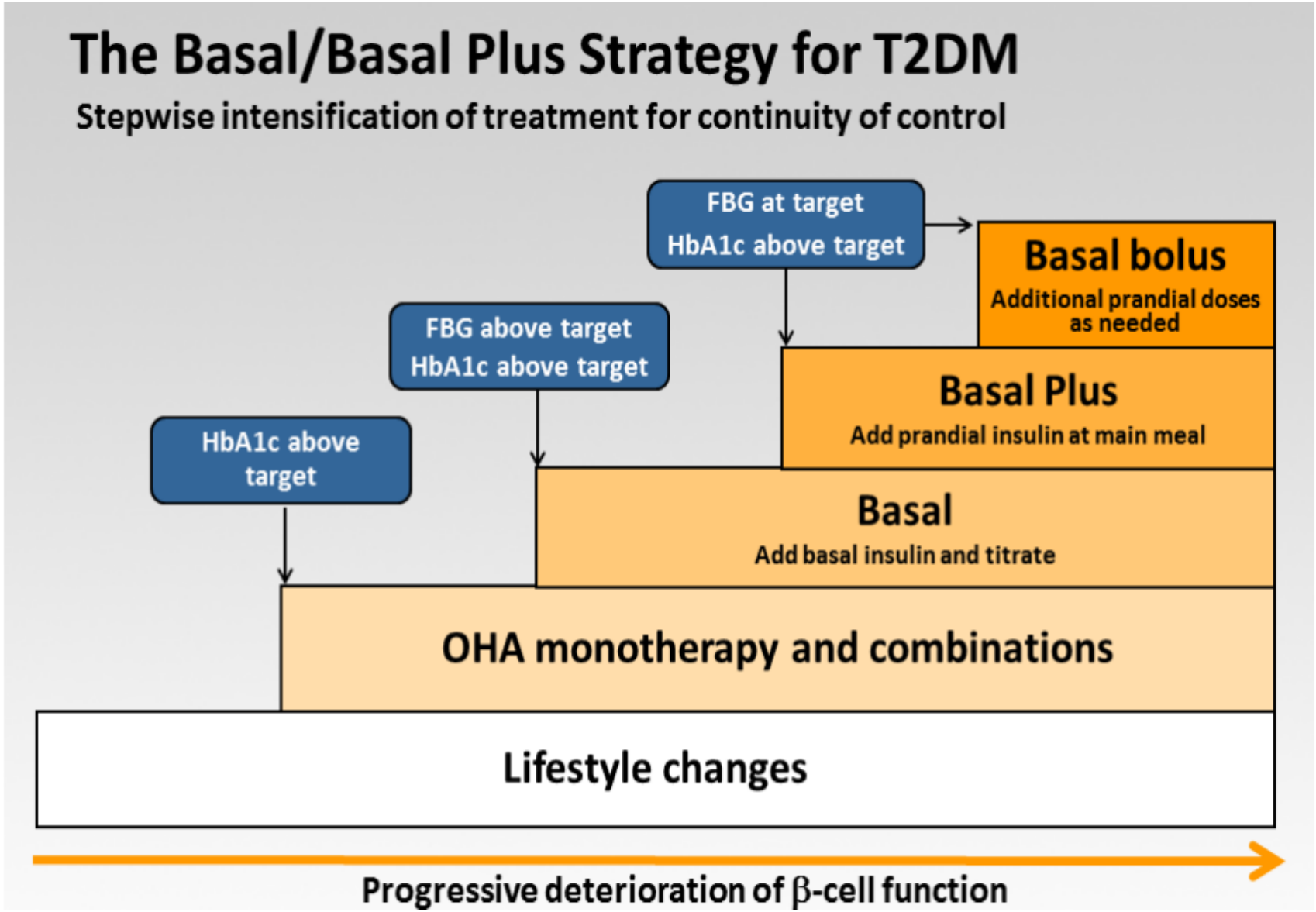
- Fear/ inconvenience of injections
- Social/ work issues
- Hypoglycaemia
- Fear of 'inevitable end stage of disease'
- Perception of failure
- Weight gain

Doctor:

- Benefit to patient unclear
- Doing harm (hypos/ weight gain)
- Time and resources
- Expertise/ confidence

Dose adjustment- First fix fasting

- Slow dose adjustment
- Increase thr dose 2-3 U every 2-3 days


The Basal/Basal Plus Strategy for T2DM
Stepwise intensification of treatment for continuity of control
FBG at target
HbA1c above target
Basal bolus
Additional prandial doses as needed
FBG above target
HbA1c above target
Basal Plus
Add prandial insulin at main meal
HbA1c above target
Basal
Add basal insulin and titrate
OHA monotherapy and combinations
Lifestyle changes
Progressive deterioration of β-cell function

Case

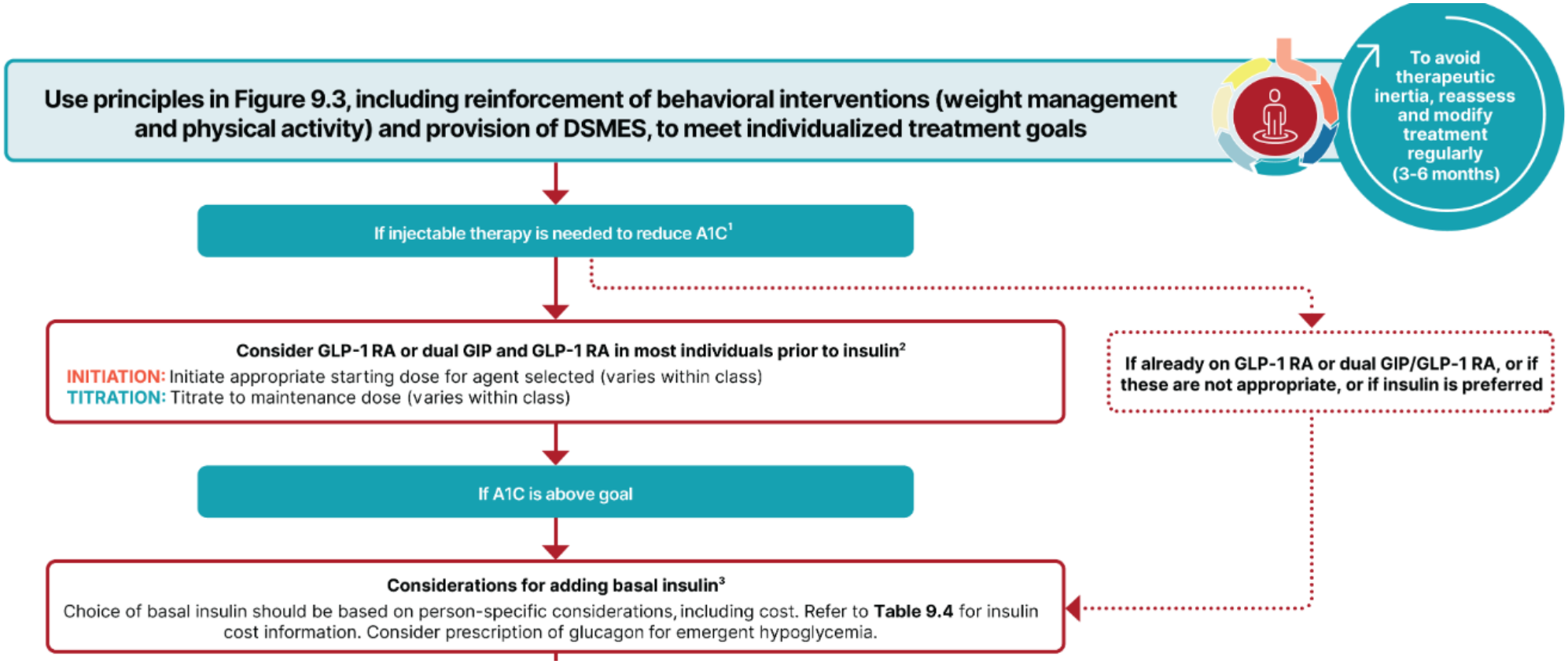
- A 57-year-old woman
- PMH:
  - Diabetes since 8 years ago
  - Non-proliferative diabetic retinopathy
  - Hypertension since 16 years ago
- Medications:
  - Insulin glargine 28 U at bedtime
  - Linagliptin 5 mg daily
  - Atorvastatin 20 mg daily
  - Amlodipine/valsartan/HCTZ 5/160/12.5 mg daily

Case *(cont.)*

- Ph/Ex:
  - BMI: 24 kg/m²
  - BP: 125/75 mmHg
- Recent lab tests:
  - Cr: 1.8 mg/dL (eGFR: 44 mL/min/1.73m²)
  - Urine albumin/cr: 60 mg/g (confirmed)
  - FPG: 145-155 mg/dL, HbA1c: 8.8%
  - TC: 120 mg/dL, LDL-C: 50 mg/dL, HDL-C: 38 mg/dL, TG: 160 mg/dL

Don’t forget to modify OADs

- Add GLP-1RA to basal insulin
- Initiate premixed insulin/GLP-1RA
- Add a prandial insulin to basal insulin
- Initiate basal bolus insulin
- Initiate premixed insulin



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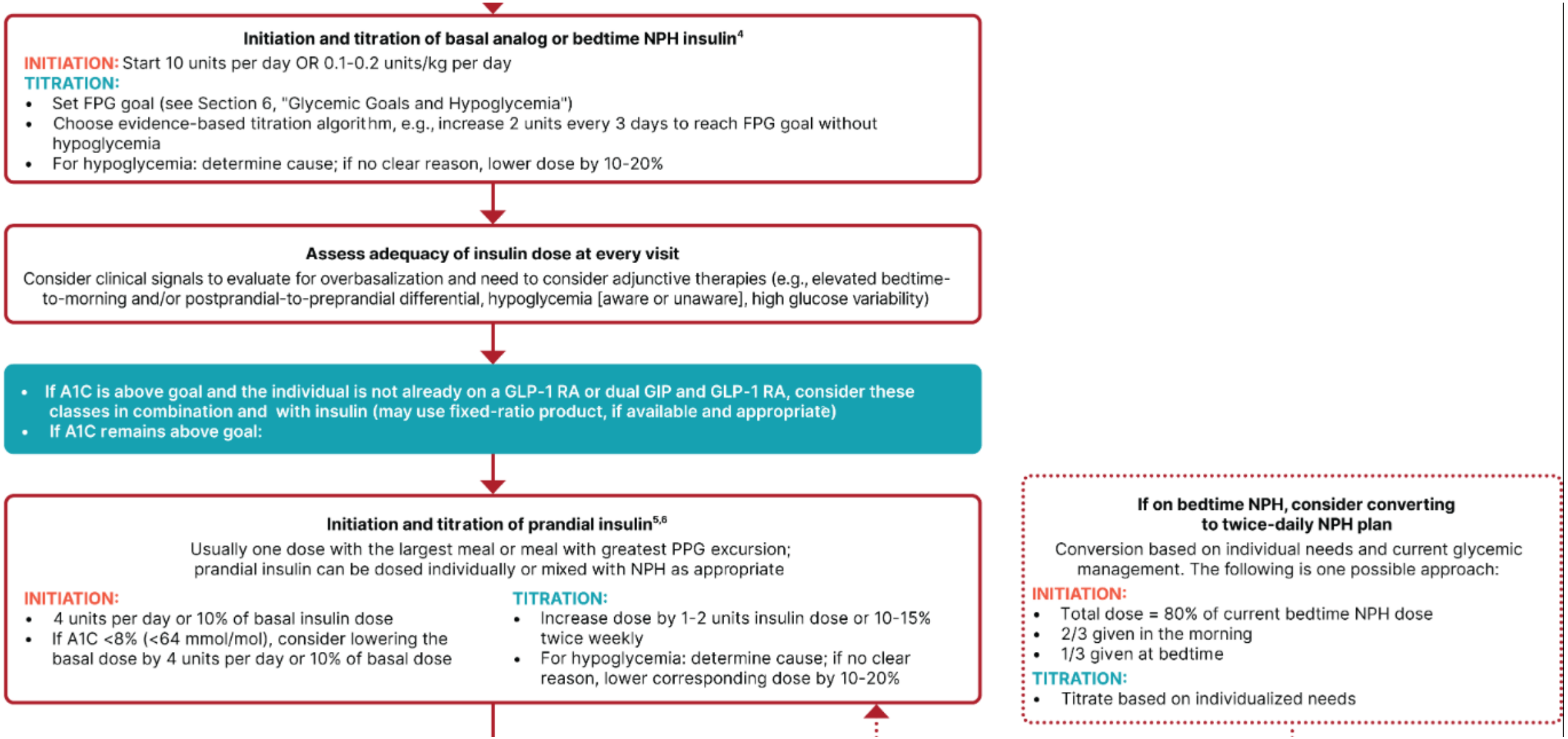
Overbasalization

- Clinical signals that should prompt evaluation for overbasalization include
- High bedtime-to-morning
- Preprandial-to-postprandial glucose differential (e.g., bedtime-to-morning glucose differential ≥50 mg/dL
- hypoglycemia (aware or unaware)
- High glucose variability
- Evidence of overbasalization should prompt reevaluation of the glucose-lowering treatment plan to better address **postprandial hyperglycemia**



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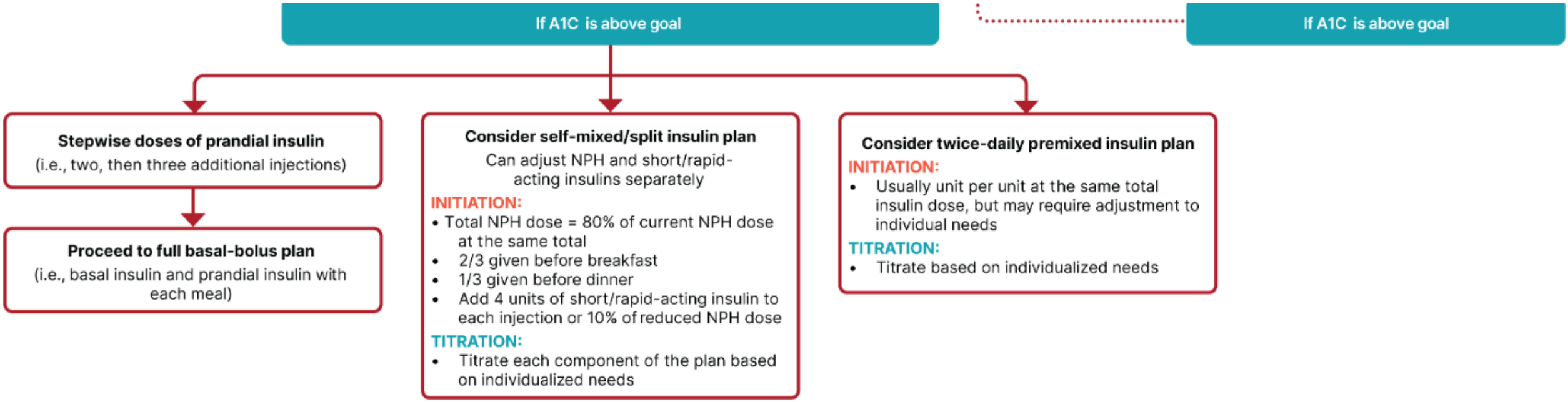

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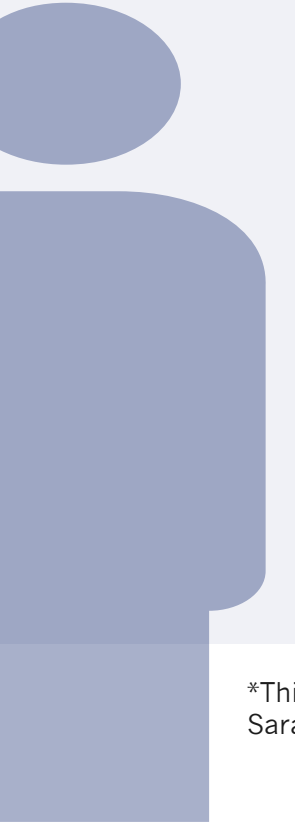
IDeg Asp

- IDegAsp may be considered for treatment intensification in people with T2D with inadequate glycemic control on basal insulin
- A unit-to-unit dose conversion of the basal insulin component
- The dose may need to be reduced for those experiencing hypoglycaemia or for those previously on insulin glargine 300 units/mL

Ideg-Asp(Ryzodeg)Recommended starting dose for initiations



Starting dose

10 Unit/OD

With largest meals

Severe Hyperglycemia
HbA1c >10% *

>10 Unit/OD

With largest meals

Followed by subsequent **INDIVIDUAL** dosage **weekly** adjustment until the desired **FPG** reached

*This posology is based on expert recommendations from Sarah G et al.

References: 1. Sarah Galtras et al. J Clin Med 2020. 2. Roopa M et al. Diabetes Obes Metab. 2020;1-15 3. Ryzodeg® Locally Patient-Friendly label in Iran version Dec-2020.

Timing of IDegAsp dose

Main Meal Concept versus Adherence Strategy

Main Meal concept - Most carbohydrate-rich meal*


50 g carbohydrates


30 g carbohydrates


100 g carbohydrates

OD


30 g carbohydrates


50 g carbohydrates


100 g carbohydrates

BID

*Main meal is the meal with the highest carbohydrate content in the meal and not the portion size of the complete meal
IDegAsp, insulin degludec/insulin aspart; OD, once daily; BID, twice daily. Mehta R, et al. *Diabetes Obes Metab*. 2020;10.1111/dom.14128.

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. • For IDegAsp **OD**, SUs may need to be discontinued or dose reduced • For IDegAsp **BID**, SUs should be discontinued
Pioglitazone	• The combination has been associated with the development of heart failure. • Pioglitazone reduces risk of stroke or myocardial infarction in people with history of stroke and evidence of insulin resistance and prediabetes.
Metformin Acarbose DPP4-inh	• No additional consideration are required.
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

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

Clinical guidance for the use of IDegAsp

Clinical use of IDegAsp	
Dosing	Licensed once or twice-daily with main meal(s) Timing of meals not important, as long as interval is at least 4 h Timing of meals can vary between days
Insulin-naïve starting dose	Should be individualised Recommended starting dose is 10 U with a main meal, based on clinical trial protocols Dose adjustment should be weekly If appropriate, additional IAsp dose(s) can be given at other meals Combination with oral agents is often optimal
Prior insulin user switching doses	From full multiple injection regimen: choose dose(s) to keep the total basal dose unchanged From premix insulin: keep total dose unchanged From basal insulin only: keep total dose unchanged, unless in very poor control when some increment may be appropriate For all switches, doses should be determined by individual requirements
Titration	Dose adjustments should be based on FPG measurements and hypoglycaemia A dose titration algorithm is provided in the IDegAsp European SmPC (12)
Practical advantages compared with premixed or multiple injection regimens	Stable consistent glucose-lowering effect because of ultra-long flat pharmacodynamics of IDeg basal component Fewer injections leading to a less-complex regimen Straightforward dose titration Less hypoglycaemia in some circumstances, especially nocturnal hypoglycaemia
Dose timing	Before any main meal, or combination of main meals (but not within 4 h), and can be varied from day to day

FPG, fasting plasma glucose; IAsp, insulin aspart; IDegAsp, insulin degludec/insulin aspart; SmPC, Summary of Product Characteristics, U, unit.

Kumar A, et al. Int J Clin Pract 2016;70(8):657-667.

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

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

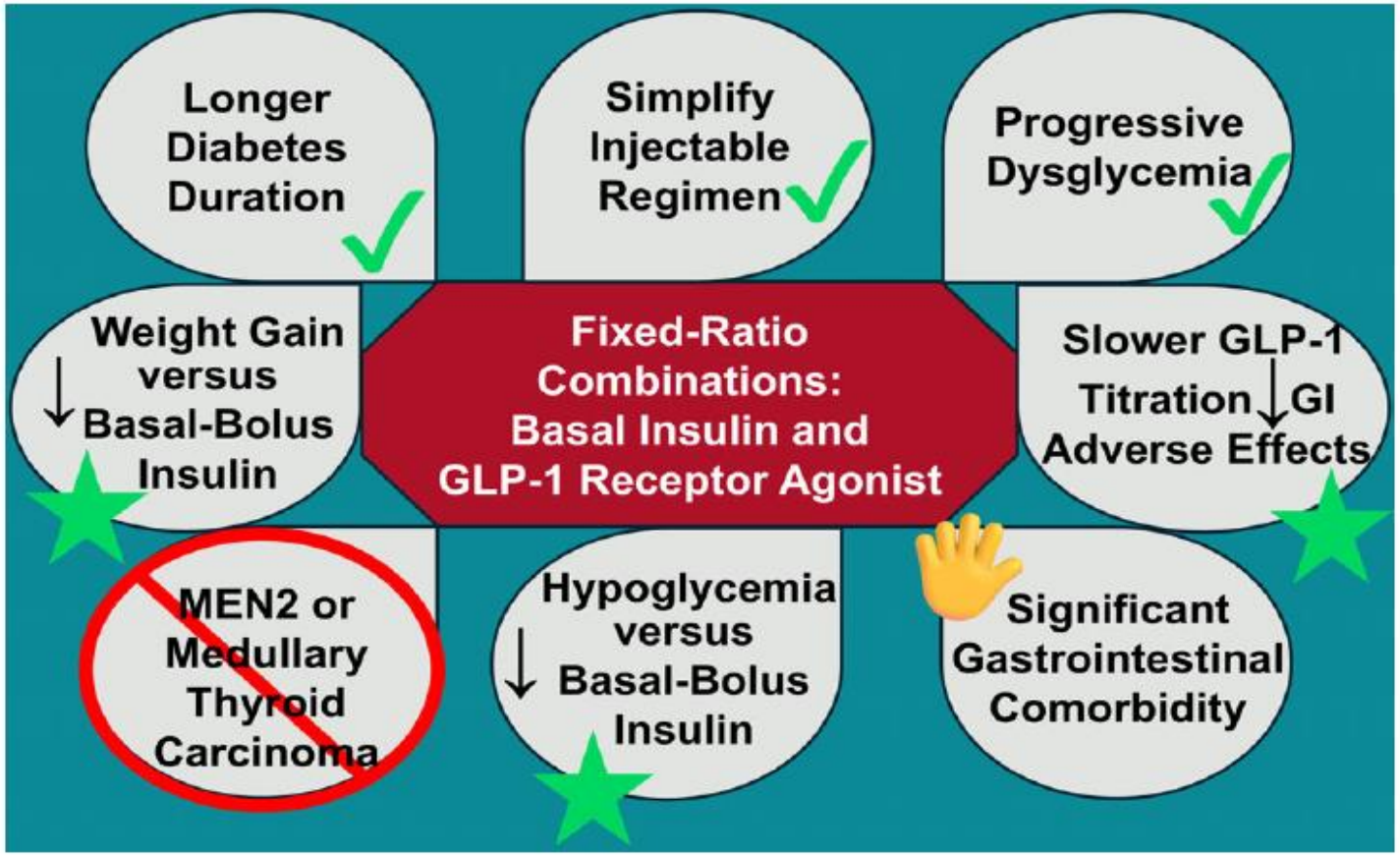


FIGURE 1 Patient characteristics and choosing fixed-ratio combinations. ✓, characteristic identifying people more likely to benefit from use. ✋, characteristic requiring caution and detailed review before use. ☆, potential benefits of use. GI, gastrointestinal; GLP-1, glucagon-like peptide-1 receptor agonist; MEN2, multiple endocrine neoplasia type 2.

Cowart K, Carris NW. Diabetes Obes Metab 2025;27(Suppl. 7):3-13.

Impact of initiating fixed-ratio combinations on glycemia, hypoglycaemia, and body weight

Drug	Population			Glycated haemoglobin reduction	Hypoglycaemia (events/patient year)	Weight change
iDegLira	OAD only	→	iDegLira	−1.9% to −2.0%	~1.8 to 2.6	−0.5 to −1.5 kg
	Basal insulin	→	iDegLira	−1.1% to −1.9%	~1.0 to 2.6	−0.5 to −2.0 kg
	GLP-1 RA	→	iDegLira	−1.0% to −1.3%	~0.5 to 1.8	+1 to +2 kg
iGlarLixi	OAD only	→	iGlarLixi	−1.5% to −2.9%	~1.4 to 2.4	−0.3 to −1.3 kg
	Basal insulin	→	iGlarLixi	−1.1% to −1.3%	~1.4 to 3.0	−0.5 to −1.0 kg
	GLP-1 RA	→	iGlarLixi	−1.0% to −1.2%	~0.7 to 2.0	+1.0 to +2.5 kg

Abbreviations: GLP-1 RA, glucagon-like peptide-1 receptor agonist; iDegLira, insulin degludec/liraglutide fixed-ratio combination; iGlarLixi, insulin glargine/lixisenatide fixed-ratio combination; OAD, oral antihyperglycemic drugs.

Cowart K, Carris NW. Diabetes Obes Metab 2025;27(Suppl. 7):3-13.

Fixed-ratio combination initiation and titration

Medication change			Starting dose	Weekly dose adjustment	Maximum dose
OAD only	→	iDegLira	10 units	Above FPG Goal Range +2 units Within FPG Goal Range No Change Below FPG Goal Range −2 units	50 units
Basal insulin	→	iDegLira	16 units		
GLP-1 RA	→	iDegLira	16 units		
OAD only	→	iGlarLixi	15 units	Above FPG Goal Range +2 to +4 units Within FPG Goal Range No Change Below FPG Goal Range −2 to −4 units	60 units
Basal insulin dose ≥30 units	→	iGlarLixi	30 units		
Basal insulin dose <30 units	→	iGlarLixi	15 units		
GLP-1 RA	→	iGlarLixi	15 units		

Abbreviations: FPG, fasting plasma glucose; GLP-1 RA, glucagon-like 1 peptide receptor agonist; iDegLira, insulin degludec/liraglutide fixed-ratio combination; iGlarLixi, insulin glargine/lixisenatide fixed-ratio combination; OAD, oral antihyperglycemic drug.

[a]All fixed-ratio combinations are dosed daily and dosed based on the insulin component.

Cowart K, Carris NW. Diabetes Obes Metab 2025;27(Suppl. 7):3-13.

Thanks for your attention!

Photo by Majid Valizadeh, MD