Use Principles in Figure 9.1 including reinforcement of behavioral interventions (weight management and physical activity) and provision of DSMES to meet individualized treatment goals.

To Avoid Therapeutic Inertia - Reassess and modify treatment regularly (3-6 months)

If injectable therapy is needed to reduce A1C[1]

Consider GLP-1 RA in most individuals prior to insulin[2]

INITIATION: Initiate appropriate starting dose for agent selected (varies within class)

TITRATION: Titration to maintenance dose (varies within class)

If already on GLP-1 RA or if GLP-1 RA not appropriate OR insulin preferred

If above A1C target

Add basal insulin[3]

Choice of basal insulin should be based on person-specific considerations, including cost. Refer to **Table 9.3** for insulin cost information.

Add basal analog or bedtime NPH insulin

INITIATION: Start 10 IU a day **OR** 0.1-0.2 IU/kg a day

TITRATION:

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

Assess adequacy of basal insulin dose

Consider clinical signals to evaluate for overbasalization and need to consider adjunctive therapies (e.g., basal dose >0.5 IU/kg, elevated bedtime-morning and/or post-preprandial differential, hypoglycemia [aware or unaware], high variability)

If above A1C target

Add prandial insulin[5]

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

INITIATION:

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

TITRATION:

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

Consider GLP-1 RA if not already in regimen

For addition of GLP-1 RA, consider lowering insulin dose dependent on current glycemic assessment and patient factors

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

Conversion based on individual needs, glycemic control. The following is one possible approach:

INITIATION:

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

TITRATION: Titrate based on individualized needs

If above A1C target

Stepwise additional injections of prandial insulin

(i.e., two then three additional injections)

Proceed to full basal-bolus regimen

(i.e. basal insulin and prandial insulin with each)

Consider self-mixed/split insulin regimen

Can adjust NPH and short/rapid-acting insulins separately

INITIATION:

- Total NPH dose = 80% of current NPH dose
- 2/3 given before breakfast
- 1/3 given before dinner
- Add 4 IU of short/rapid-acting insulin to each injection or 10% of reduced NPH dose

TITRATION:

- Titrate each component of the regimen based on individualized needs

Consider twice daily premix insulin regimen

INITIATION:

- Usually unit per unit at the same total insulin dose, but may require adjustment to individual needs

TITRATION:

- Titrate based on individualized needs

1. Consider insulin as the first injectable if evidence of ongoing catabolism, symptoms of hyperglycemia are present, when A1C levels (>10% [86mmol/mol]) or blood glucose levels (≥300mg/dL [16.7mmol/L]) are very high, or a diagnosis of type 1 diabetes is a possibility.
2. When selecting GLP-1 RA, consider: individual preference, A1C lowering, weight-lowering effect, or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit. Oral or injectable GLP-1 RA are appropriate.
3. For those on GLP-1 RA and basal insulin combination, consider using a fixed-ratio combination product (iDegLira or iGlarLixi).
4. Consider switching from evening NPH to a basal analog if there is hypoglycemia and/or the individual frequently forgets to administer NPH in the evening and would be better with an AM dose of long-acting basal insulin
5. If adding prandial insulin to NPH, consider initiation of a self-mixed or premixed insulin regimen to decrease the number of injections required.

ADA Standards of Care 2021 Figure 9.2 – Intensifying to injectable therapies. DSMES, diabetes self-management education and support; FPG, fasting plasma glucose; FRC, fixed-ratio combination; GLP-1RA, glucagon-like peptide 1 receptor agonist; max, maximum; PPG, postprandial glucose. Adapted from Davies et al. (33).