Dr Michelle Downie

Southern DHB

SANOFI

(Room 3)

Thursday, August 08, 2019

8:30 - 10:30 WS #2: Diabetes Basics

11:00 - 13:00 WS #9: Diabetes Basics (Repeated)

GP CME
Workshop 2
Michelle Downie
August 2019

SAANZ.GLA.19.07.0365. Date of preparation July 2019

insulin masterclass

Declarations

- I have received travel funding and speaker fees from todays sponsor
- There has been no input from the sponsors in designing my presentation today

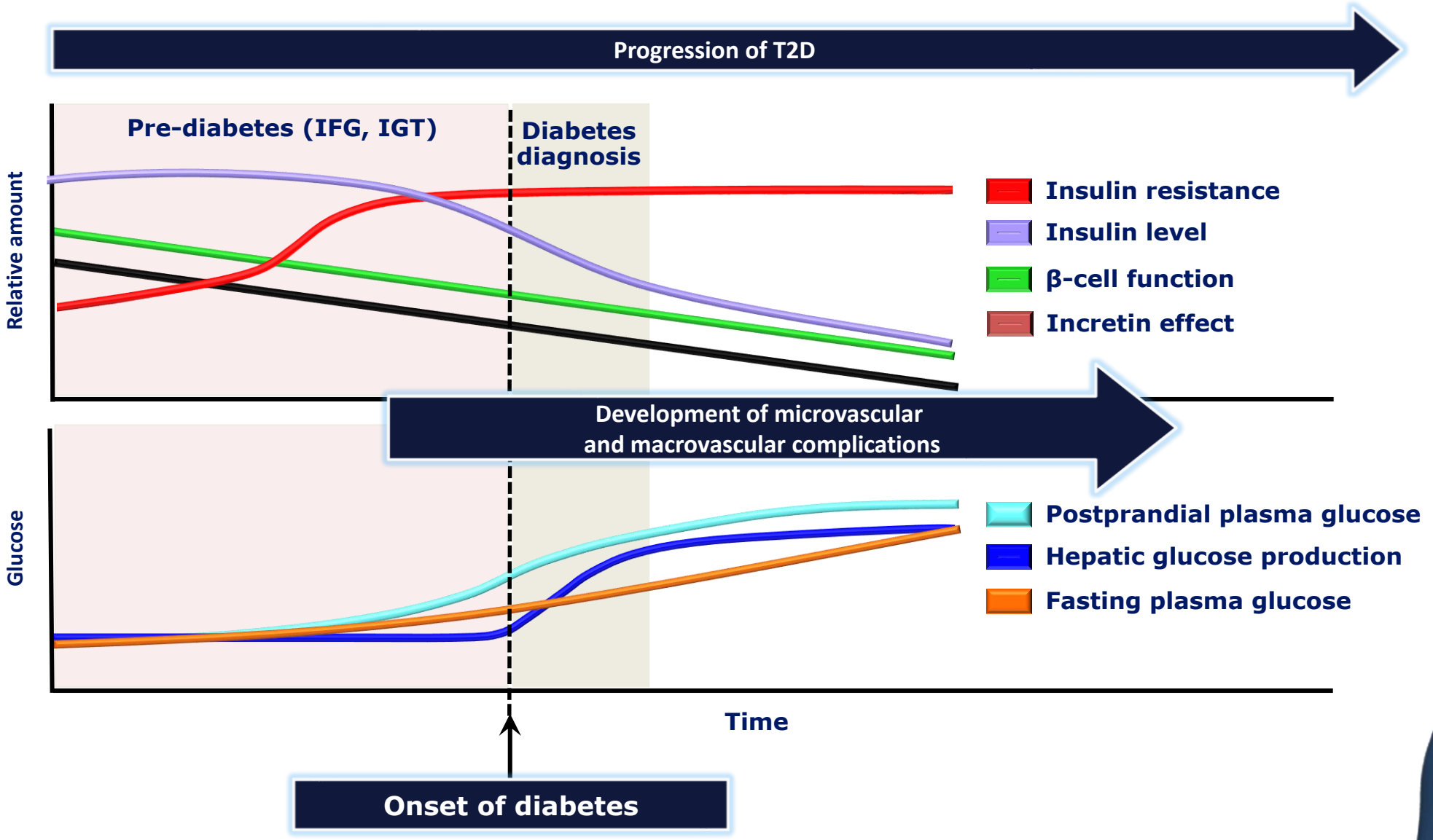
Type 2 Diabetes is a progressive condition...and changes with time.

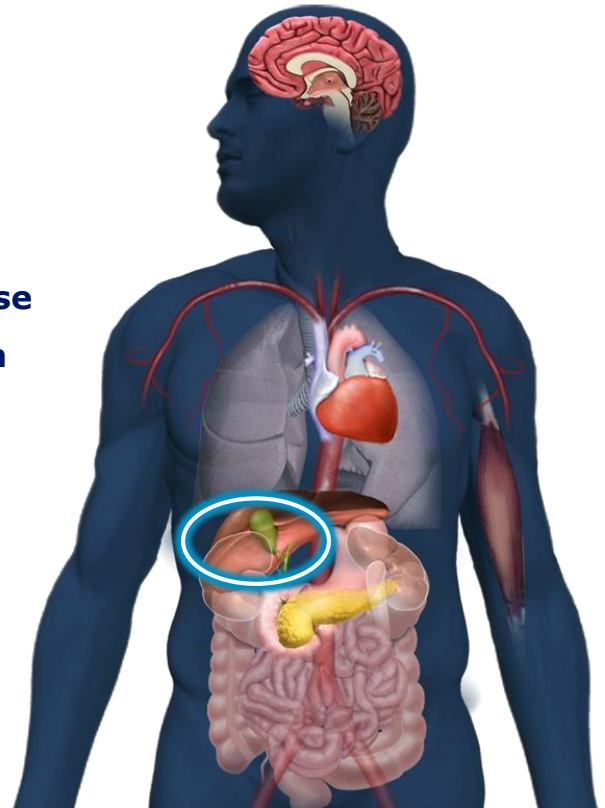
The mechanisms of T2DM are multifactorial including:

- Pancreatic islet cell dysfunction
  - Deficient insulin response due to decline in functional β-cells
  - Excessive production of glucagon by α-cells
- Excessive hepatic output of endogenous glucose
  - A consequence of diminished insulin & insulin sensitivity, and excess glucagon
- Impaired uptake of glucose in the peripheral tissues
  - A consequence of insulin resistance

With progressive worsening over time

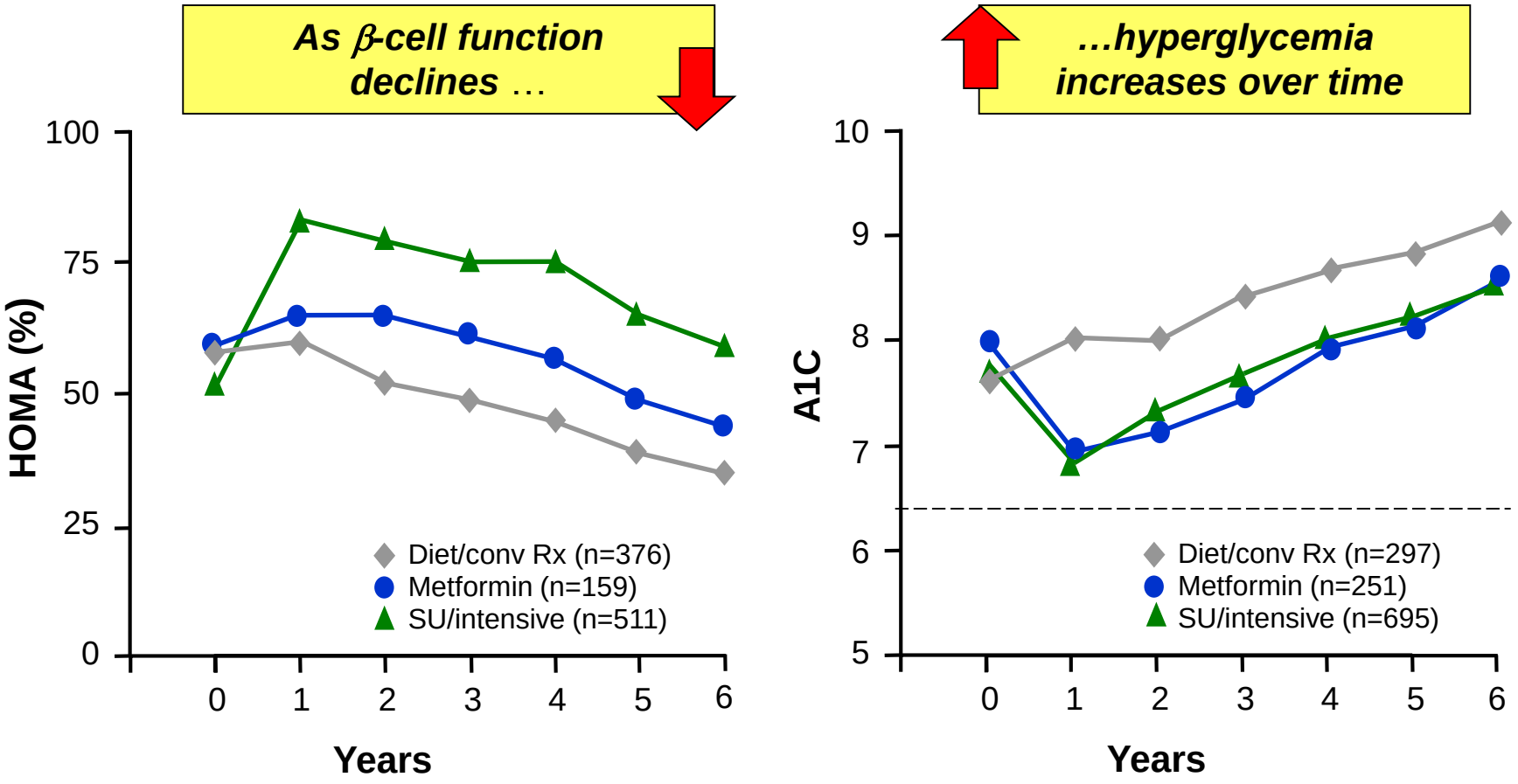
Insulin dysfunction, incretin, the liver and glucose





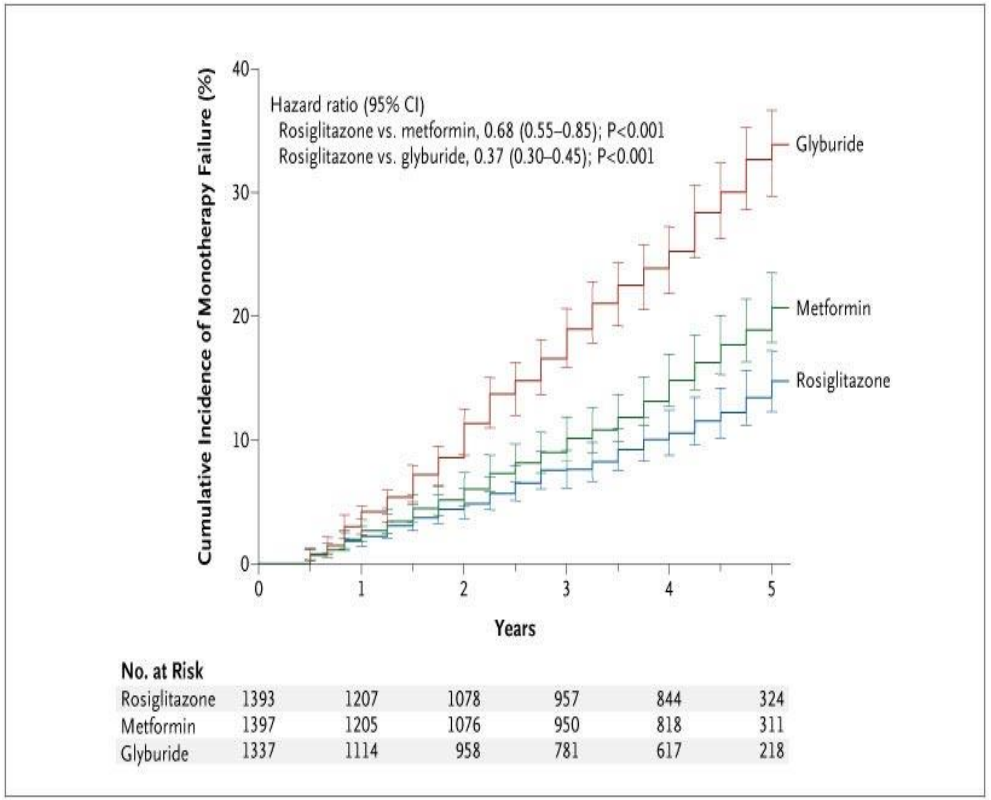
Adapted from Kendall DM et al. Am J Med 2009:122(6 Suppl):S37–S50. Schematic representation for illustrative purposes only

β-Cell Function & Glycaemic Control in T2DM



UKPDS=United Kingdom Prospective Diabetes Study; SU=sulfonylurea.
Reprinted UK Prospective Diabetes Study Group 16. *Diabetes.* 1995;44:1249–1258.

ADOPT Study: Monotherapy Failure at 5 Years



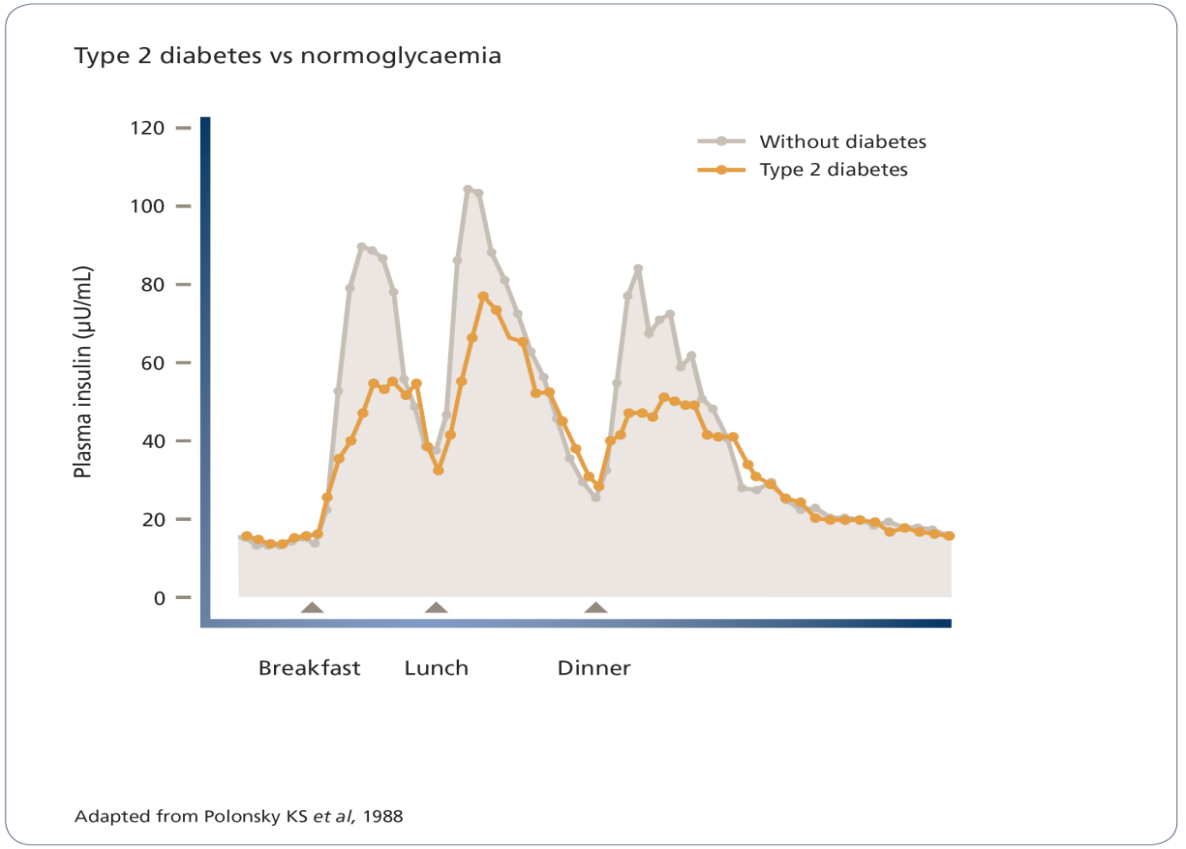
No. at Risk						
Rosiglitazone	1393	1207	1078	957	844	324
Metformin	1397	1205	1076	950	818	311
Glyburide	1337	1114	958	781	617	218

Kahn SE et al. N Engl J Med 2006;355:2427-2443

The NEW ENGLAND JOURNAL of MEDICINE

The problem with type 2 diabetes

The mealtime insulin secretory response is blunted…

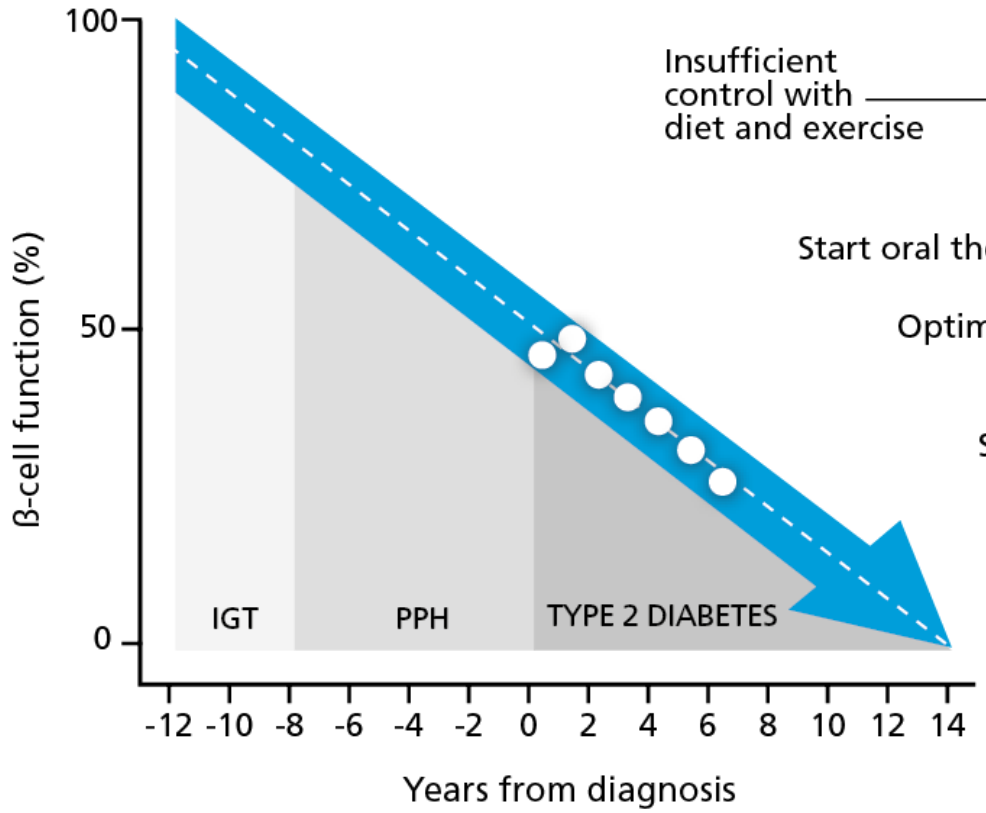


…..resulting in undesired mealtime glucose excursions

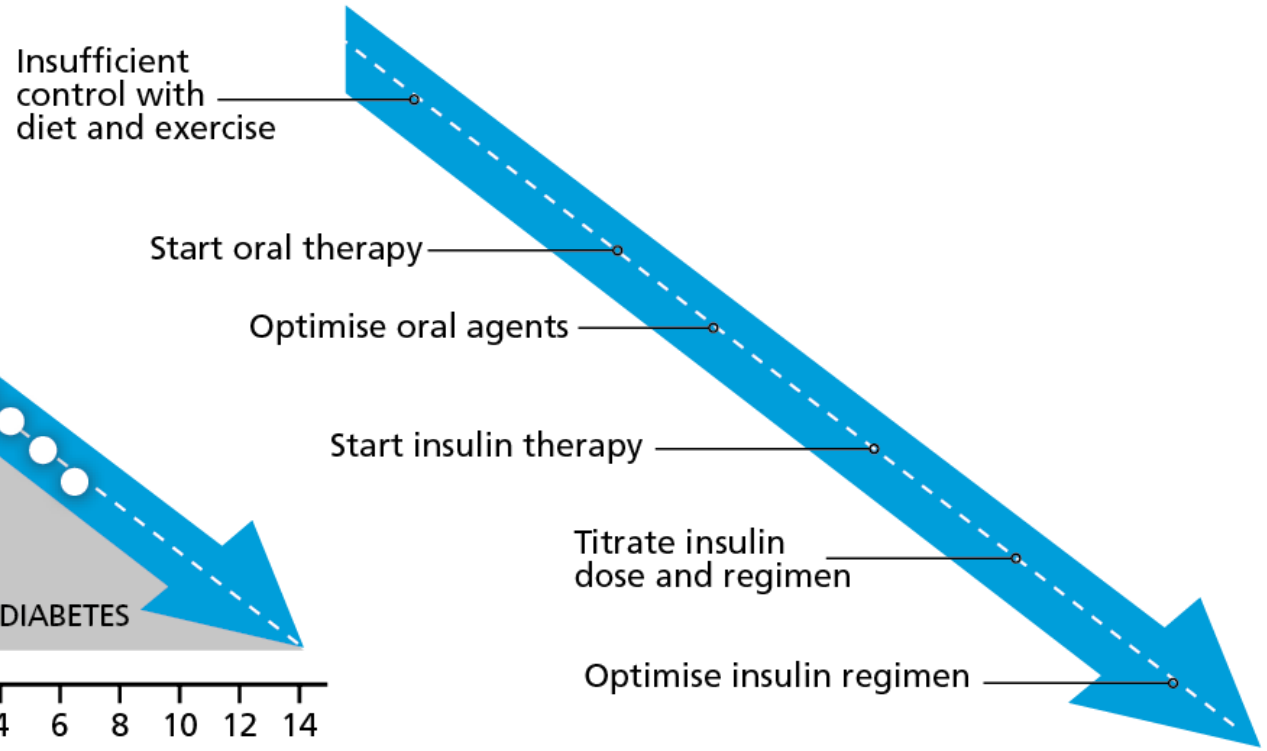
Polonsky KS *et al*. *New Engl J Med* 1988; 318:1231–1239.

As diabetes progresses, intensifying or switching insulin may be necessary

ß-cell function and insulin secretion progressively decline in type 2 diabetes

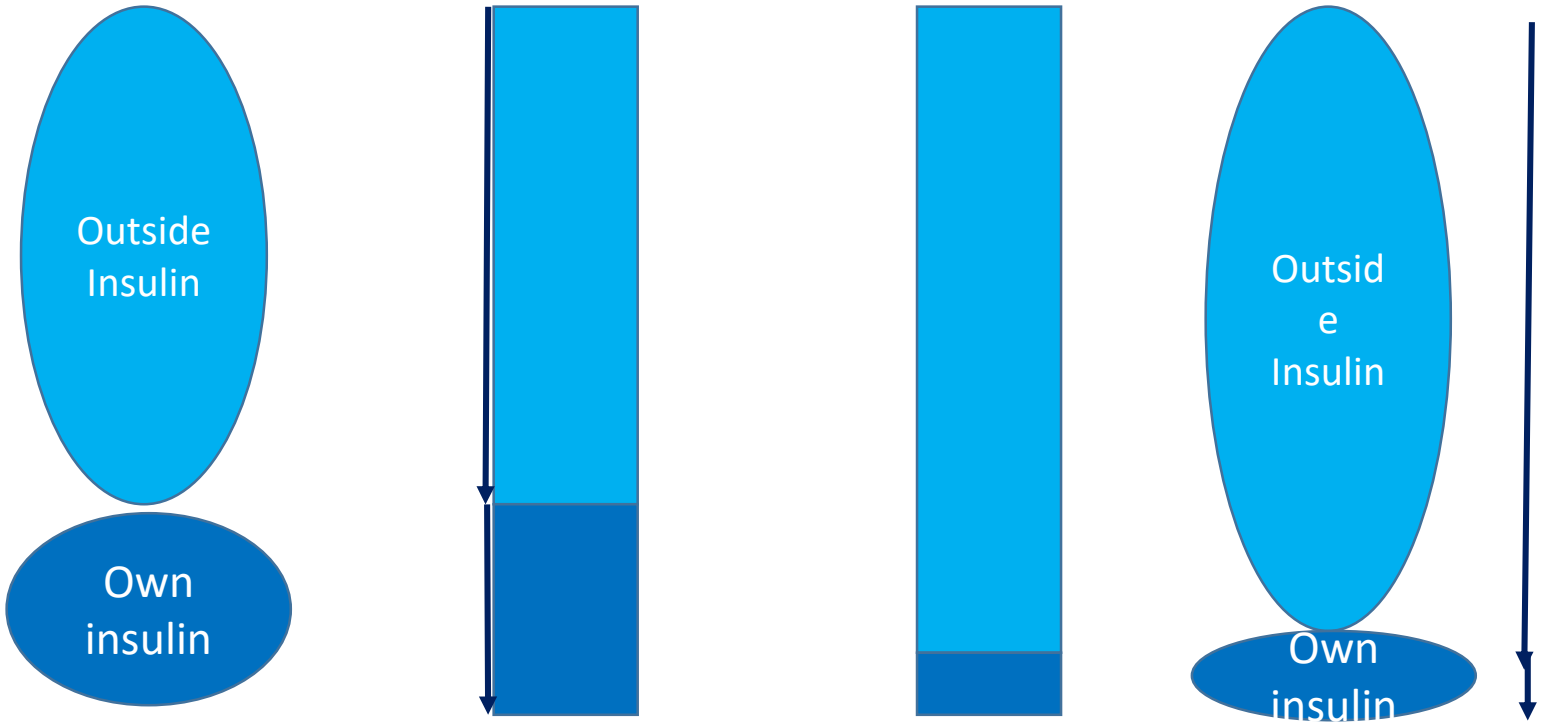


Usual progression of therapy in type 2 diabetes



IGT: impaired glucose tolerance; PPH: postprandial hyperglycaemia
Adapted from DeWitt DE & Hirsch IB. JAMA 2003; 289:2254–64.

Hypoglycaemia risk increases with time in T2D



Early T2D

Late T2D

Medications

Shane

T2D

7 Years

insulin masterclass

Medications

Metformin	1000 mg three times daily
Glargine	52 units evening
Atorvastatin	40 mg once daily
Cilazapril	5 mg once daily

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Pathology results

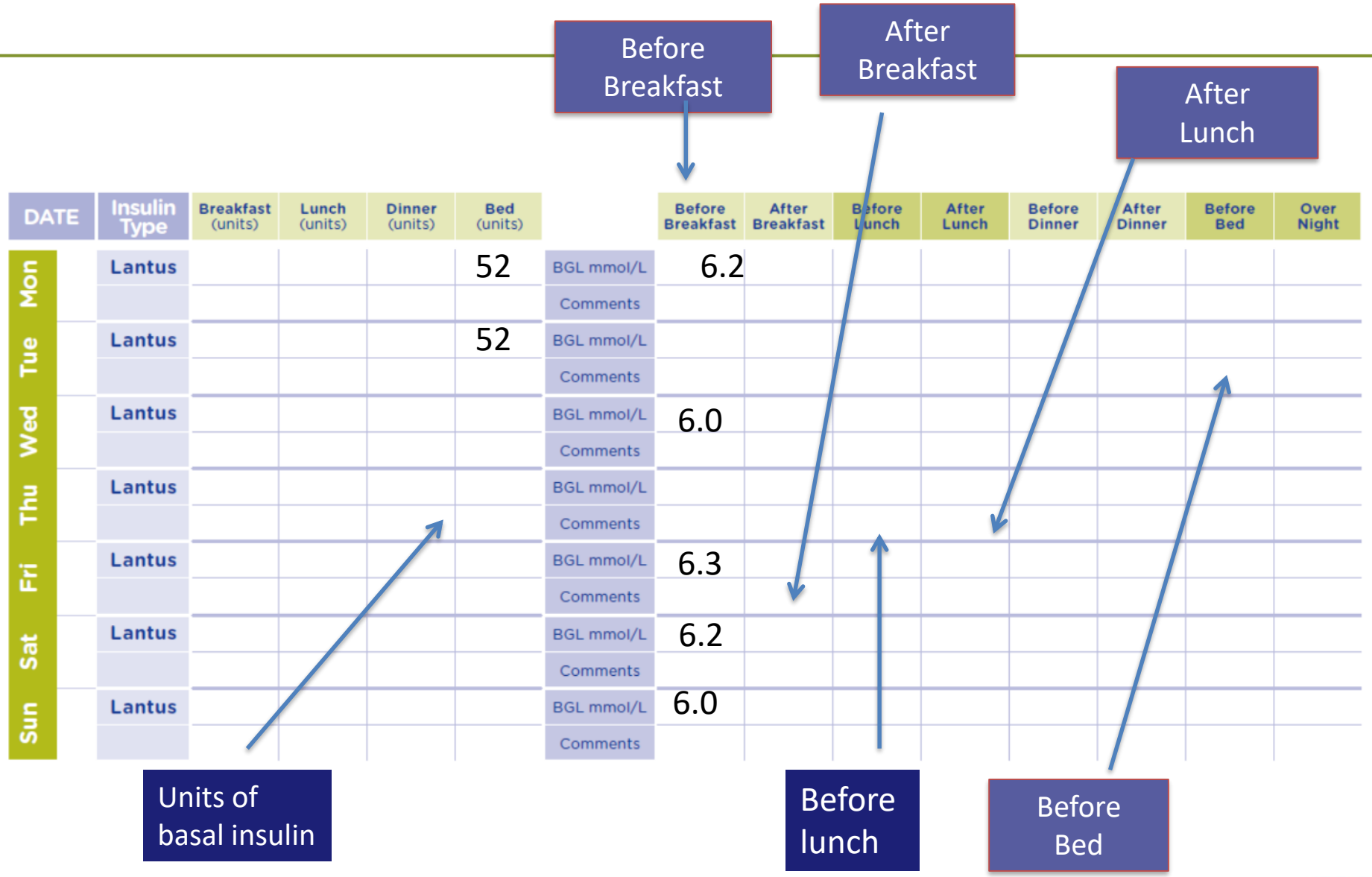
HbA_{1c}	68 mmol/mol
TC	4.3 mmol/L <5
TG	2.1 mmol/L <2
HDL	1.1 mmol/L >1
LDL	2.7 mmol/L <3.4
eGFR	>60 mL/min
ACR	5g/mmol <3.5
Microalbuminuria	50 mg/L <30

insulin masterclass

Examination

Height:	1.75 m
Weight:	103 kg
BMI:	33.6 kg/m^2
Waist:	102 cm
BP:	135/90 mmHg
Feet :	Sensation adequate, pulses easily felt
Urinalysis:	No abnormalities noted

Log book readings



insulin masterclass

Improving glycaemic control

You congratulate Shane on his fasting glucose readings, but are concerned that his HbA1C is still too high.

What should you look for at this stage?

Finding hidden hypers

You discuss with Shane that you suspect that there are periods of hyperglycaemia causing his HbA1c to remain elevated. You discuss that he will need to monitor his BGLs at different times of the day to see when they are occurring. You suspect his large dinner may be contributing to his elevated HbA1c.

Finding hidden hypers

What BGL testing would you advise Shane to do over the next weeks?

1. 2 hours after breakfast
2. Before lunch
3. 2 hours after lunch
4. Before bed
5. Other

	Insulin Injections					Monitoring Blood Glucose								Remarks Activity, illness, diet changes, time of hypos (noting blood glucose and treatment).
	Types of Insulin	Units Given				Breakfast		Lunch		Dinner		Before Supper or Bed	Over-night	
		Breakfast	Lunch	Dinner	Before Bed	Before	After	Before	After	Before	After			
Mon						✓	✓					✓		
Tues						✓		✓	✓					
Wed										✓	✓			
Thu						✓	✓					✓		
Fri						✓		✓	✓					
Sat										✓	✓			
Sun						✓	✓					✓		

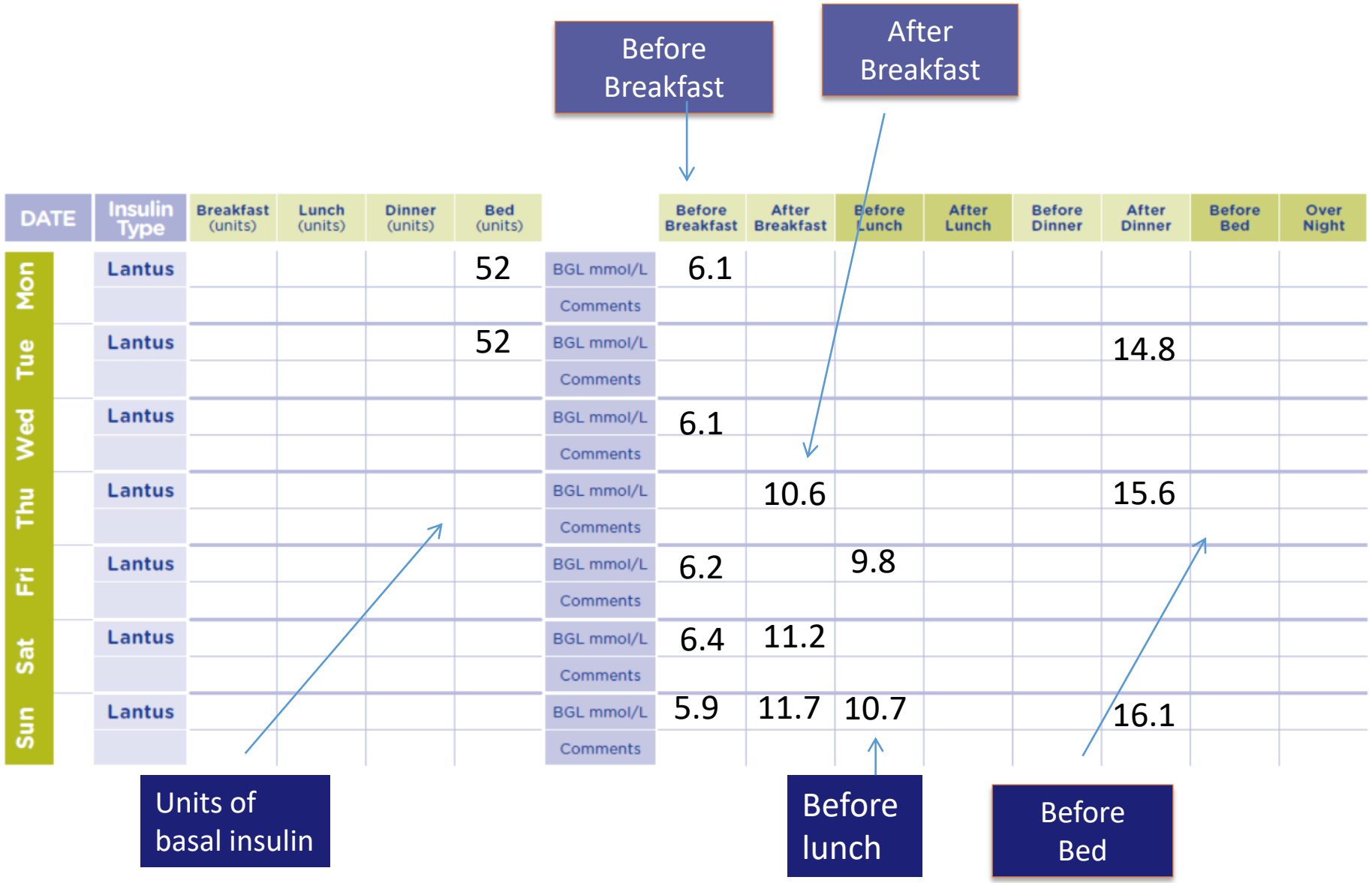
		Units					Breakfast		Lunch		Dinner		BeforeBed
	Date	Insulin	PreBrkfst	PreLunch	PreDinner	B/Bed	Before	After	Before	After	Before	After	
Fri	07-Jan						X	X					
Sat	08-jan						X			X			
Sun	09-Jan						X					X	
Mon	10-Jan						X		X				
Tue	11-Jan						X				X		
Wed	12-Jan						X						X
Thur													

Next steps

Shane is off on a big overseas trip and promises to return as soon as he comes back.

You instruct him to now also make a point of recording 2 hour post meal BGLs (in addition to his fasting one which he already does) and discuss managing insulin while overseas with the practice nurse

Log book readings



Improving glycaemic control

You inform Shane that his BGLs 2 hours after dinner are consistently high indicating hyperglycaemia after dinner.

What treatment options would you discuss with Shane?

1. Exercise after dinner (brisk walk)
2. Seek dietitian’s advice on carbohydrate intake
3. Consider altering existing insulin therapy
4. All of the above

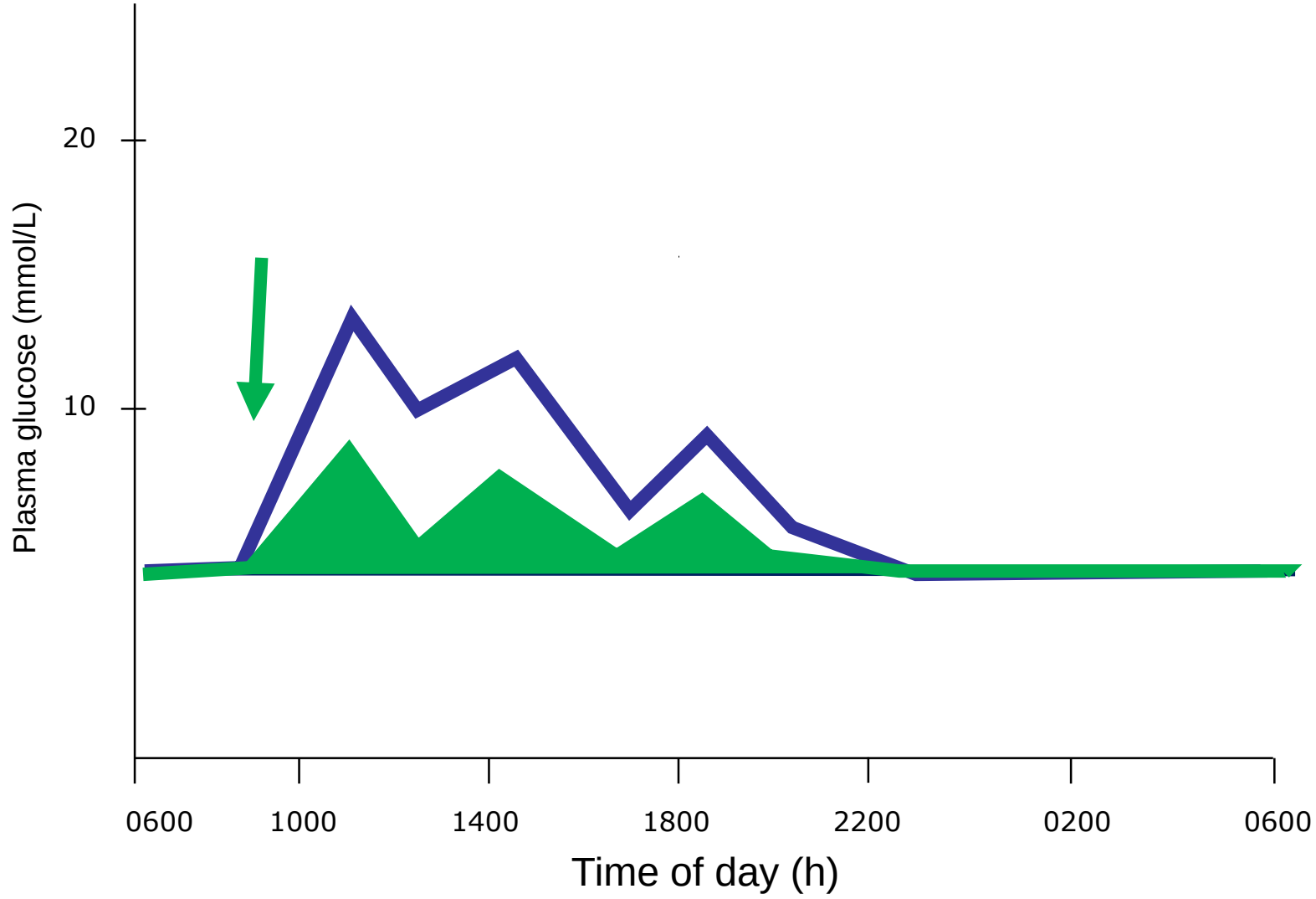
Adjusting insulin therapy

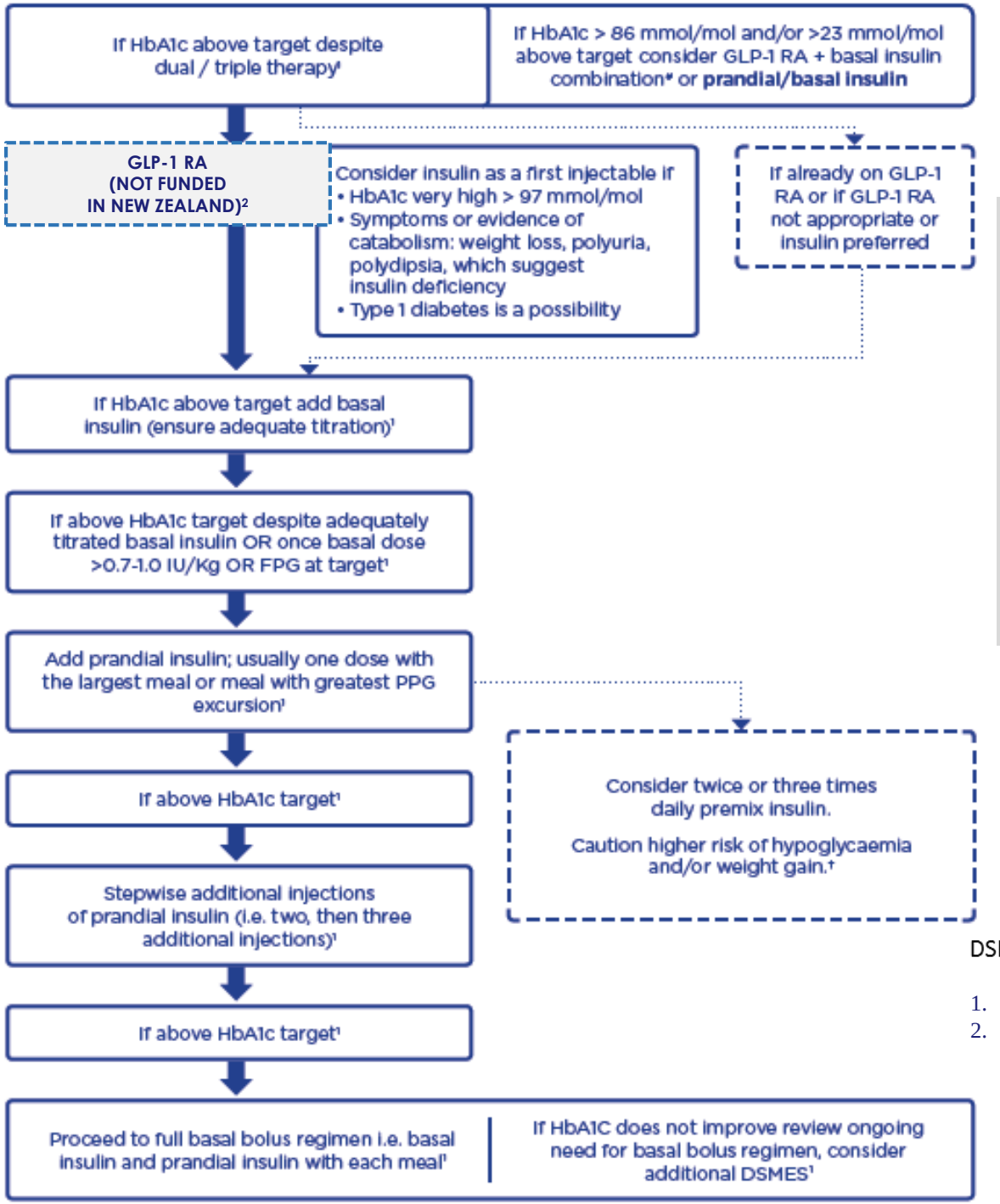
You discuss treatment options with Shane and agree that modifying the insulin schedule is the best option for him.

What alterations in Shane's insulin schedule would you recommend?

1. Increasing the basal insulin dose
2. Add a single dose of rapid-acting insulin at breakfast
3. Add a single dose of rapid-acting insulin at dinner
4. Not sure
5. Other

Tackle the meal responsible for the greatest glycaemic excursion



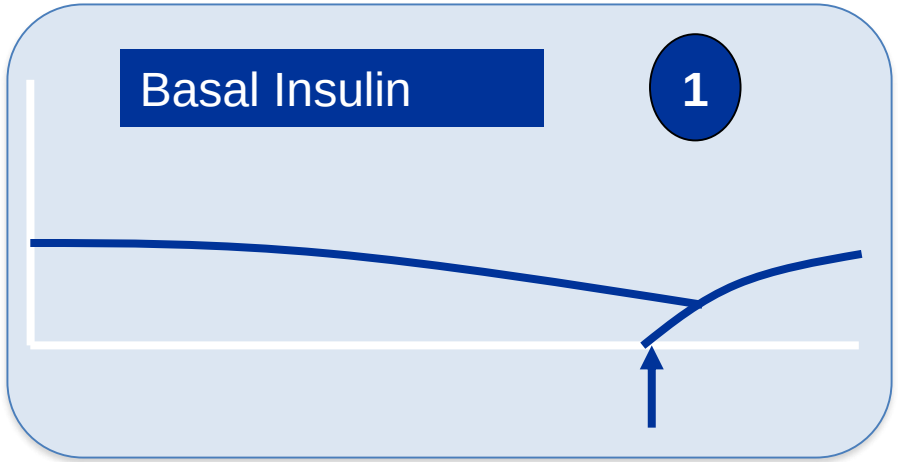


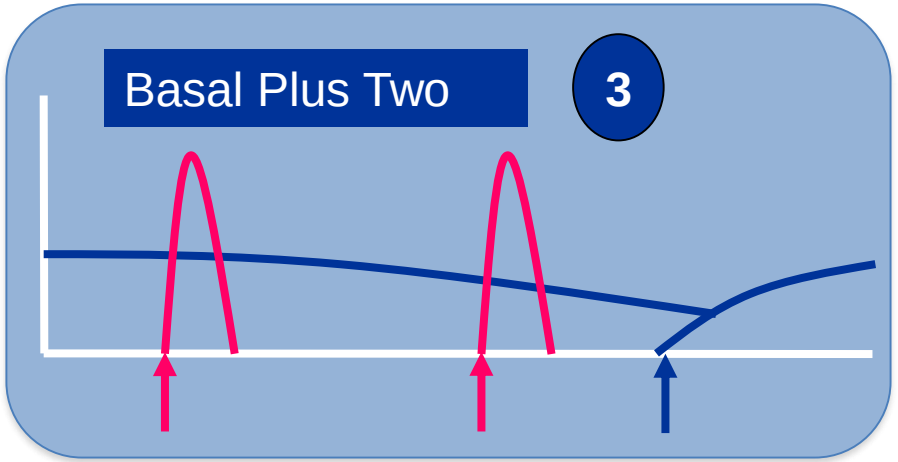
ADA/EASD Guidelines for for the management of hyperglycaemia in Type 2 Diabetes : Injectable therapies[1]

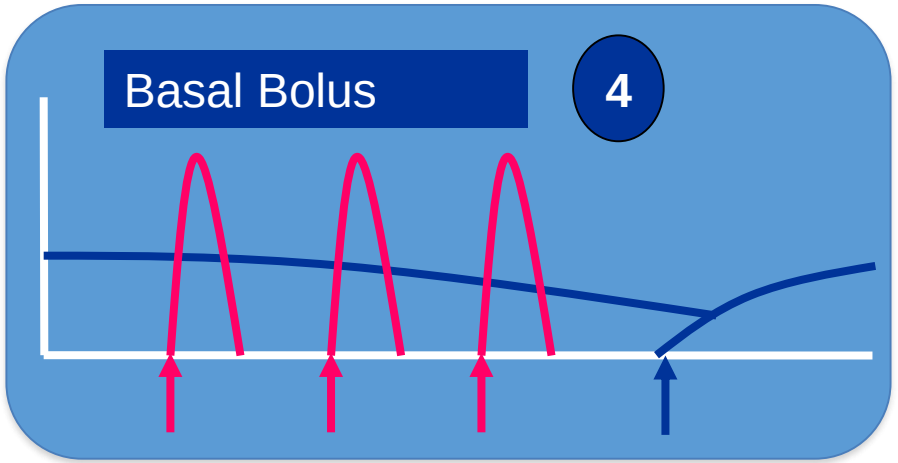
DSMES:Diabetes Self Management Education and Support

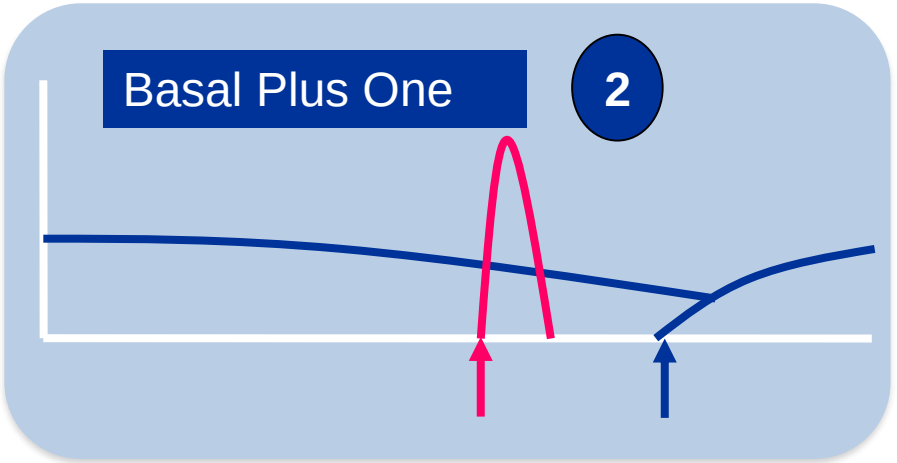
1. Melanie J. Davies et al. Diabetes Care 2018; 41: 2669-2701
2. Pharmacuetical Schedule. PHARMAC April 2019

Basal Plus Strategy: Stepwise Intensification









Rapid acting analogues

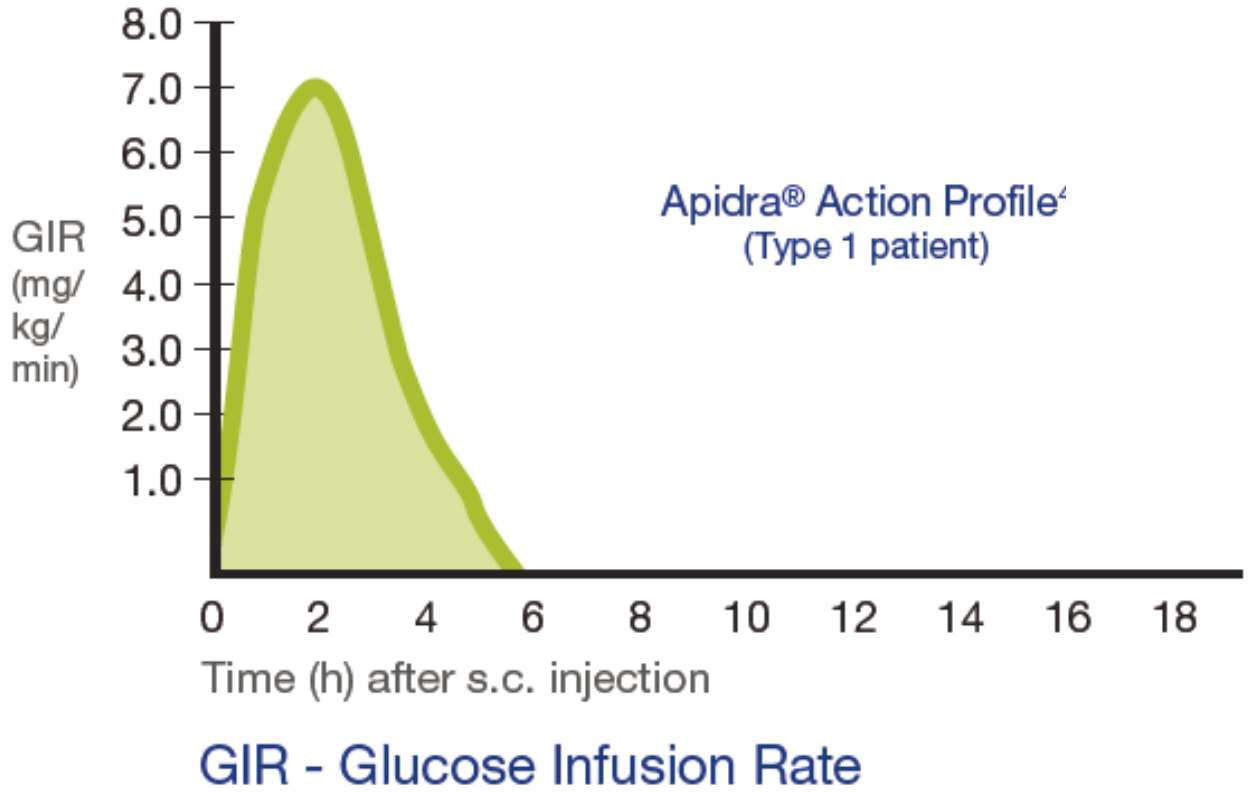
Glulisine	=	Apidra
Lispro	=	Humalog
Aspart	=	Novorapid

Prandial insulin

Insulin preparations	Onset of action	Peak of action (h)	Duration of action (h)
Regular human insulin	30–60 min	2–4	6–8
Lispro/aspart/glulisine	5–15 min	1–2	3–4

Ulrich H, et al. Vascular Health and Risk Management.2007:3(3)245-254

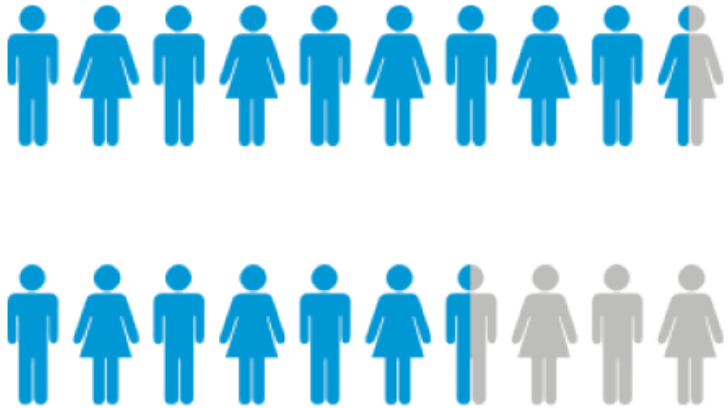
Apidra®(insulin glulisine)



Adapted from Becker et al 2008.
Mean GIR in subjects with Type 1 diabetes after SC injection of 0.15 u/kg

Patients are more likely to reach HbA_{1c} target when treating both PPG and FPG

How many patients achieving both PPG and FPG control met HbA_{1c} target <53 mmol/mol vs those achieving FPG control alone?



94%

PPG and FPG control
(≤7.8 mmol/L and ≤5.6 mmol/L, respectively)

vs

64%

FPG control only
(≤5.6 mmol/L)

94% of patients will achieve HbA_{1c} <53 mmol/mol when you achieve PPG in addition to FPG control.

64% of patients will achieve HbA_{1c} <53 mmol/mol when you achieve FPG control alone.

Woerle HJ et al. Diabetes Res Clin Pract 2007; 77: 280-5.

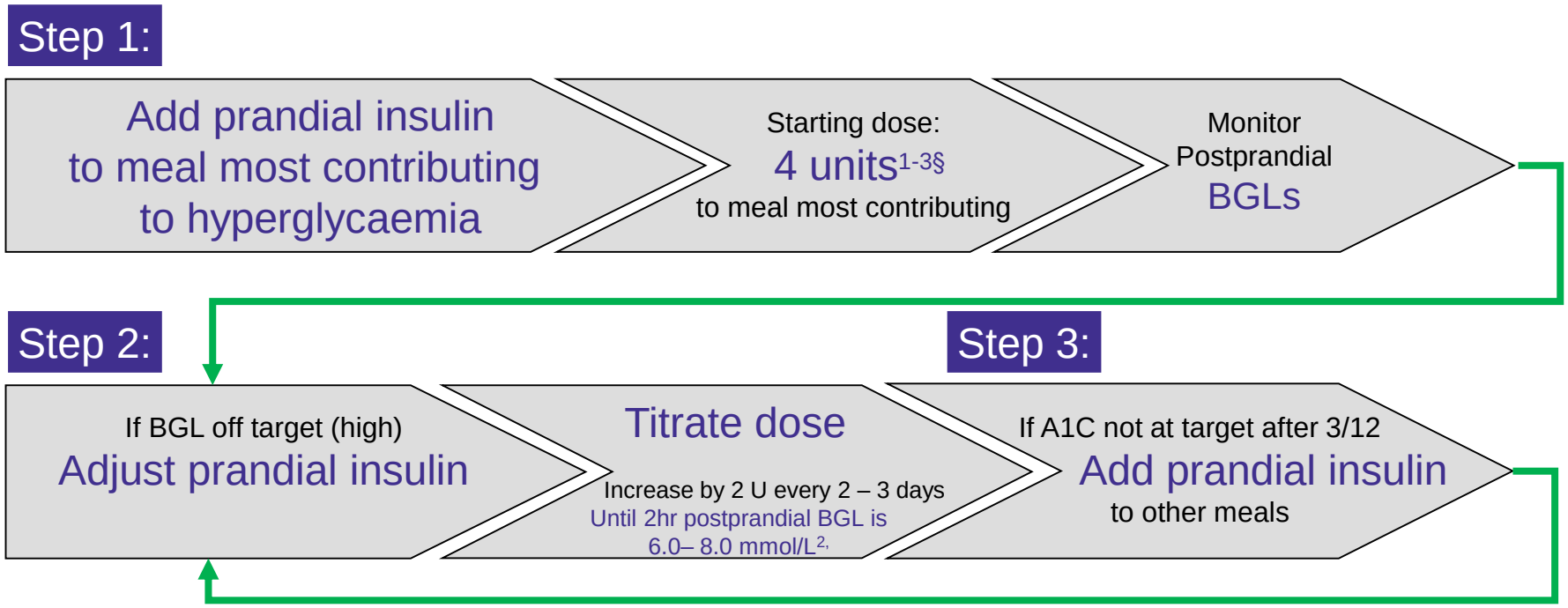
Starting prandial insulin

You both agree that adding a single dose of prandial insulin prior to the meal contributing most to hyperglycaemia would be appropriate as he finds it difficult to change his evening eating habits and exercise schedule.

How would you calculate the initial dose of prandial or bolus insulin?

1. One-third the basal dose
2. 4 units
3. 0.1 u/kg
4. Not sure

Start prandial insulin at 4 Units[1-3]



These dosing guidelines are based on recommendations from a number of authors. They are provided for guidance only. All insulin dosing and titration / adjustments require professional judgment and should be individualised to patient circumstances .

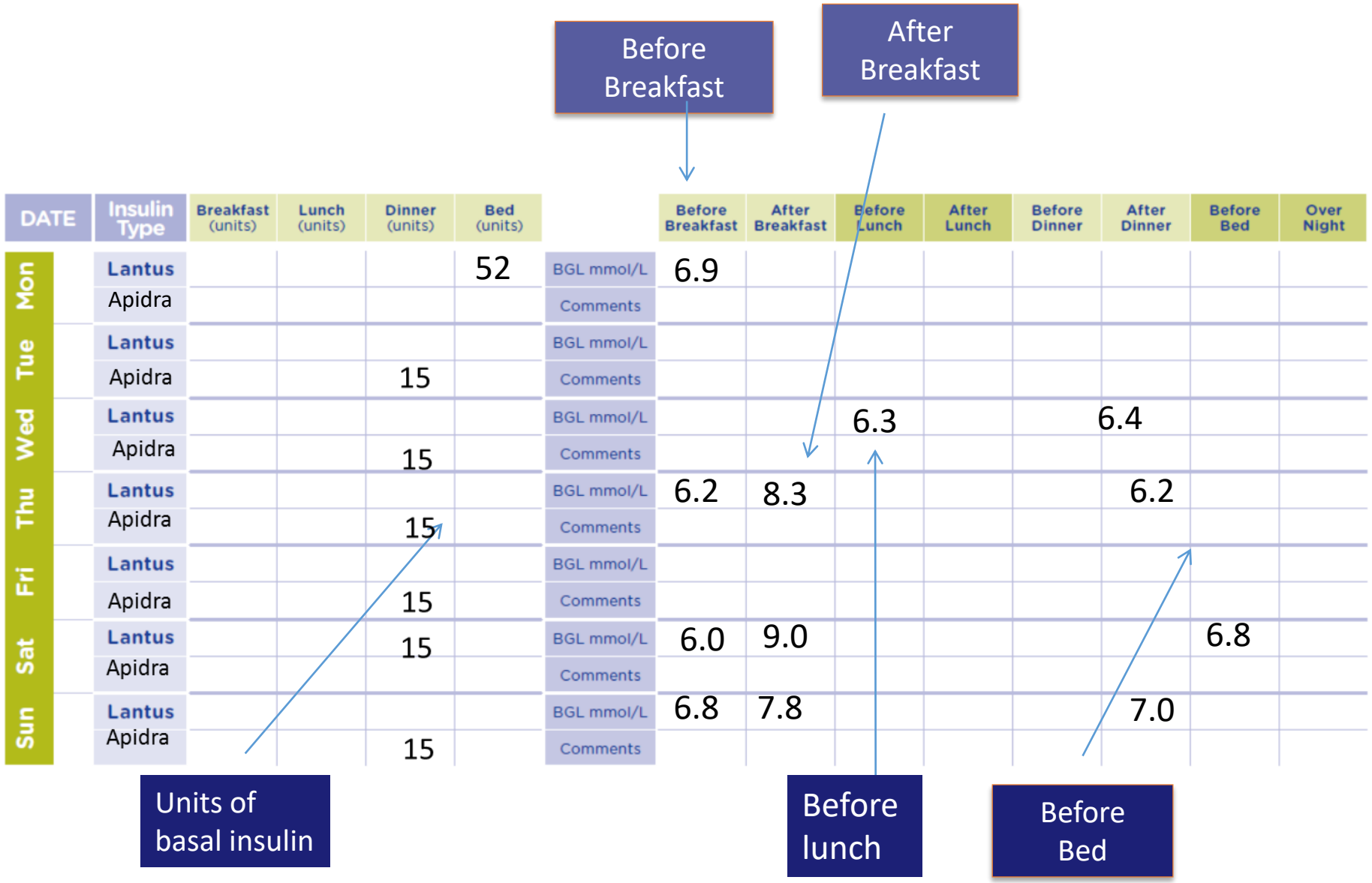
Once prandial insulin is added, insulin secretagogues should be discontinued

1. Nathan D et al. Diabetes Care 2009; 32: 193−203.
2. Diabetes Australia/RACGP Diabetes Management in General Practice.2016/2018
3. Inzucchi SE , et al . Diabetes Care,2015;38:140-149

Shane: Review of Blood glucose levels

- 4 weeks after adding in prandial insulin
- Prandial insulin (15 units) at dinner
- Blood glucose profile improved

Log book readings



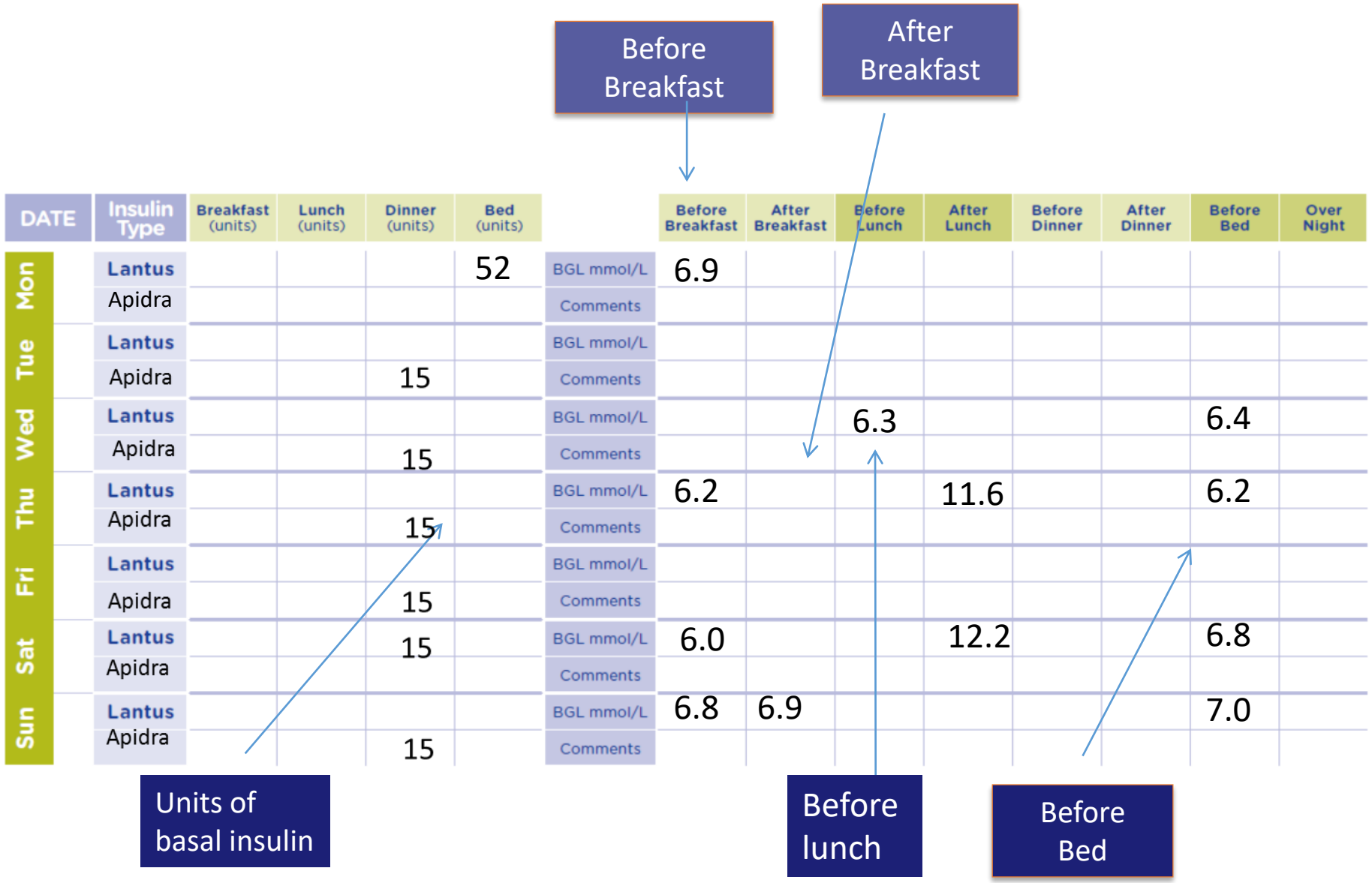
Reviewing BGLs: 4 weeks later

- You congratulate Shane on achieving great readings
- His BGLs are all within range
- You suggest Shane keep his basal dose at 52 units
- You ask Shane to maintain his bolus dose at 15 units
- Shane is asked to return in another 3 months
    - Practice nurse will remain in contact with him in the interim
    - Reminder letter and pathology request will be sent prior to the next visit

Shane: summary

- Shane self-titrated insulin dose from 10 units to 52 units
- 12 months after starting basal insulin Shane's fasting BGLs were on target
- Hidden hyperglycaemia suspected with HbA1c elevated at 12 months despite good fasting glucose readings
- Post dinner hyperglycaemia identified with more regular BGL testing
- Addition of prandial insulin considered appropriate treatment
- 15 units at dinner improved glycaemic control
- Regular review with practice nurse
- Shane to return for review in 3 months

Log book readings – 3 months later



DATE	Insulin Type	Breakfast (units)	Lunch (units)	Dinner (units)	Bed (units)		Before Breakfast	After Breakfast	Before Lunch	After Lunch	Before Dinner	After Dinner	Before Bed	Over Night
Mon	Lantus				52	BGL mmol/L	6.9							
	Apidra					Comments								
Tue	Lantus					BGL mmol/L								
	Apidra			15		Comments								
Wed	Lantus					BGL mmol/L			6.3				6.4	
	Apidra			15		Comments								
Thu	Lantus					BGL mmol/L	6.2			11.6			6.2	
	Apidra			15		Comments								
Fri	Lantus					BGL mmol/L								
	Apidra			15		Comments								
Sat	Lantus			15		BGL mmol/L	6.0			12.2			6.8	
	Apidra					Comments								
Sun	Lantus					BGL mmol/L	6.8	6.9					7.0	
	Apidra			15		Comments								

Adding in a second prandial dose

- You congratulate Shane on achieving great readings
- HbA1c has come down to 61 mmol/mol
- You have now identified he might require insulin with lunch also

- How much would you start with at lunch time?

Adding in a second prandial dose

Options:

- 4 units at lunch
- Half of the other prandial dose if that is bigger (e.g. if 15 units at dinner, start with 8 units at lunch)
- Other?

- Whatever you choose you will need to review this and support Shane to ensure he is managing and his doses are optimised

Sliding scales

- Can be simple or complicated
- Simple – 2-3 choices of dose
- Complicated - Can be done calculating ISF

Sliding scales

- Simple example:

- If BSL < 12 mmol/l – usual dose
- If BSL > 12mmol/l – add 20%

- If BSL < 12 mmol/l – 15 units
- If BSL > 12 mmol/l – 18 units

Sliding scales

- More complicated
- Insulin Sensitivity Factor (ISF)
- 100 divided by Total Daily dose insulin
- E.g. 100 divided by 50 = 2
  - 1 unit of insulin expected to reduce glucose by 2 mmol/l
  - If BGL 20 mmol/l, need approximately 5 units to reduce to 10 mmol/l
  - If standard meal time dose is 10 units, take that plus an additional 1 unit for every 2 mmol/l above target BGL

“Think like a pancreas”

- What is my blood sugar?
- What am I about to eat?
- How active will I be before my next meal?

Practice points summary

- Don’t delay insulin initiation
- Practice team approach to patient management
- Fix the fasting first
- Keep it simple for you and patient initially– 10 units basal insulin to start, 4 units prandial insulin
- Ensure patient has expectation that doses will increase and what the dose may end up at
- Titrate and optimise each therapy before starting another
- Review prandial regime regularly and alter as need be
- Monitor HbA1c every 3 months and intensify as required to achieve target with minimal hypoglycaemia

Symptoms of hypoglycaemia (HYPO)[1-3]

Caused by the body's initial reaction (trying to increase BGL)	**From the brain**
Irritability	Inability to concentrate
Anxiety	Weakness, dizziness
Hunger/feeling sick	Headache
Paleness	Confusion
Shakiness	Blurred or double vision
Heart pounding	Odd behaviour
Sweating	Slurred speech
Numbness – fingers, lips, toes	Lack of coordination/unsteady
	Lapses in consciousness/coma
	Convulsions

1. Staying well with type 2 diabetes. Diabetes New Zealand, May 2015.
2. Barnett et al. Int J clin Pract 2010; 64(8):1121-1129
3. Henderson J. et al. Diabetic Medicine. 2003; 20;1016-21

HYPO ACTION PLAN | ACT NOW!

You might feel sweaty, shaky, very hungry, fast heart beat, confused.

3 STEP TREATMENT

STEP 1

Do blood sugar test FIRST. If below 4mmol:

Take:

- 2 tablespoons jam or honey or sugar
- 1 can of sweet drink
- 10 LARGE jelly beans
- 8 Dextrose tablets
- 8 Mentos lollies

x 7-10

or

x 2

Tablespoons

or

or

STEP 2

WAIT 15 minutes – retest

If less than 4 mmol repeat step 1

STEP 3

Blood sugar above 4

NOW have a snack or meal to prevent further hypos

or

or

or

or

DO NOT GIVE FOOD OR DRINK IF DROWSY, UNABLE TO SWALLOW.
LIE THEM ON THEIR SIDE (RECOVERY POSITION).

DIAL 111

GUIDELINES AUTHORISED FROM CCDHB DIABETES SERVICE *2018*

Wairarapa DHB
Wairarapa District Health Board
Te Poari Hauora a-rohe o Wairarapa

HUTT VALLEY DHB

Capital & Coast District Health Board
Ūpoko ki te Uru Hauora

Abridged Prescribing information

Apidra® (insulin glulisine) **Indication**: Subcutaneous administration for type 1 and type 2 diabetes mellitus patients who require insulin for control ofhyperglycaemia. **Contraindications**: Hypersensitivity to insulin glulisine or any excipient. **Precautions**: Hypoglycaemia; hepatic, renal and visual impairment;lipodystrophy and other injection site or immediate-type allergic reactions; patient instruction on intercurrent conditions, blood glucose monitoring, injectiontechnique, checking insulin label if using reusable injection devices; not studied in children <4 years, pregnancy category B3, lactation; may be mixed withNPH human insulin, mixtures should not be administered intravenously**. Interactions**: Oral antidiabetic agents; cardiovascular, analgaesic, anti-inflammatory,neurological, antipsychotic agents (see full Data Sheet); antibiotics; corticosteroids, other hormonal therapies (see full Data Sheet); diuretics; protease inhibitors; sympathomimetic agents; lithium; alcohol; sympatholytics including beta-blockers; others, see full Data Sheet. **Adverse effects**: Hypoglycaemia; injectionsite reactions; others, see full Data Sheet. **Dosage and Administration**: Subcutaneous; abdominal, thigh or deltoid administration; blood glucose monitoring is recommended. Apidra® is equipotent to human insulin but with more rapid onset and shorter duration of action; should be injected within 15 minutes before or immediately after a meal. Initial dose should be determined individually, depending on desired blood glucose levels. Apidra® should normally be used in regimens that include a longer-acting or basal insulin. Apidra® can be mixed with NPH human insulin for subcutaneous administration. For secondary dose adjustments, renal, hepatic impairment: see full Data Sheet. **Presentations**: Apidra® (insulin glulisine injection) 100 U per mL (U 100) is available in packs of 10mL vials, 3mL cartridges and 3mL cartridges in SoloSTAR® pre-filled pens. **Classification**: Prescription Medicine **Sponsor**: Sanofi, Level 8, 56 Cawley Street, Ellerslie, Auckland, New Zealand. Free phone 0800 283 684. **Apidra® is a funded medicine**

Before prescribing Apidra® (insulin glulisine) please review full data sheet at https://www.medsafe.govt.nz

Abridged Prescribing information

Lantus® (insulin glargine). **Indication:** Once-daily subcutaneous administration for type 1 and type 2 diabetes mellitus patients who require insulin forcontrol of hyperglycaemia. **Contraindications:** Hypersensitivity to insulin glargine or any excipient. **Precautions:** Hypoglycaemia, possibly with delayedrecovery or altered warning symptoms; hepatic, renal and visual impairment; lipodystrophy and other injection site or immediate-type allergic reactions;antibody production; not studied in children <6 years, pregnancy category B3, lactation; not intended for i.v. use; not recommended for treatment ofdiabetic ketoacidosis; LANTUS® MUST NOT BE DILUTED OR MIXED WITH ANY OTHER INSULIN OR SOLUTION. Patient instruction on intercurrent conditions, blood glucose monitoring, injection technique recommended. **Interactions:** Oral antidiabetic agents; cardiovascular, analgesic, anti-inflammatory, neurological, antipsychotic agents, antibiotics, corticosteroids, other hormonal therapies, diuretics, protease inhibitors, sympathomimetic agents, lithium, alcohol,sympatholytics including ß-blockers, others. **Adverse effects:** Hypoglycaemia; injection site reactions; visual disturbances; others. **Dosage and Administration:**Subcutaneous, once daily; abdominal, thigh or deltoid administration; blood glucose monitoring is recommended. Lantus® is equipotent to human insulin. Initial dose should be determined individually, depending on desired blood glucose levels and doses and timing of any antidiabetic medication, including Lantus®. For changeover from once-daily NPH initial dose usually not changed; for changeover from twice-daily NPH to once-daily Lantus®, initial dose usually reduced by approximately 20% compared to total daily NPH dose; for initiation of type 2 patients, initial dose is usually approximately 10IU. For secondary dose adjustments, renal, hepatic impairment see full Data Sheet. **Medicine Classification:** Prescription Medicine.**Presentations:** Lantus® (insulin glargine injection) 100 U per mL is available in packs of 5x3mL cartridges, 5x3mL cartridges in SoloStar pre-filled pens and 10mL vials. Sponsor: Sanofi–Aventis New Zealand Limited trading as Sanofi, Level 8, 56 Cawley Street, Ellerslie, Auckland. Freephone 0800 283 684. **Lantus® is a Funded Medicine**

Before prescribing Lantus® (insulin glargine) please review full data sheet at https://www.medsafe.govt.nz