Oral therapies in T2 diabetes

Dr Gary Kilov

T2D Guidelines - What's New?
What comes after metformin?

Seaport Diabetes

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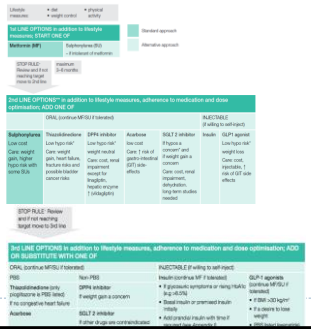
Part 1

- *T2D Guidelines*

RACGP guidelines 2014/15



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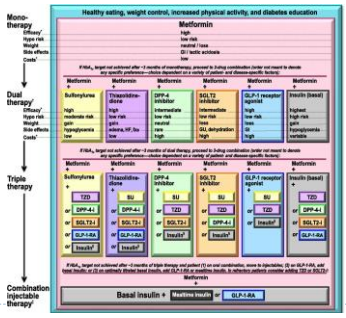
ADA-EASD: Anti-Hyperglycaemic therapy 2015



Inzucchi S E et al. Dia Care 2015;38:140-149

American Diabetes Association.

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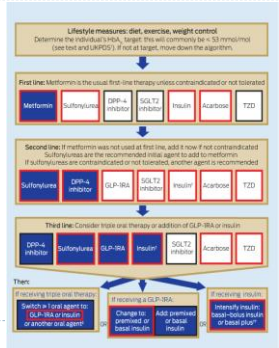
ADS guidelines 2015



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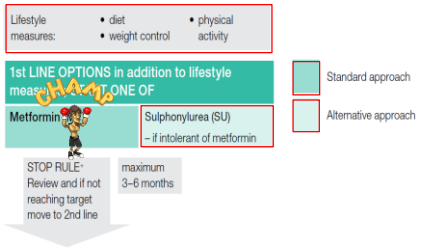
Part 2

- *What comes after metformin?*

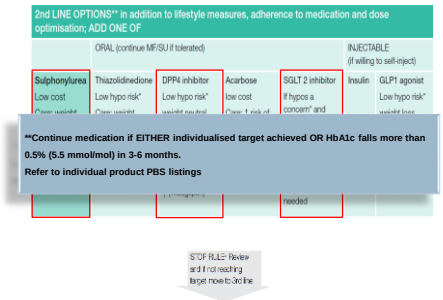
Current RACGP guidelines: Lifestyle measures and 1st line options



*STOP RULE: If BG targets not being attained after max. of 6 months, despite adequate titration doses, STOP and check health literacy, review adherence and exclude occult infection, concurrent meds and consider alternate diagnosis

General practice management of type 2 diabetes – 2014–15. Melbourne: The Royal Australian College of General Practitioners and Diabetes Australia, 2014.

Current RACGP guidelines: Lifestyle measures and 2nd line options

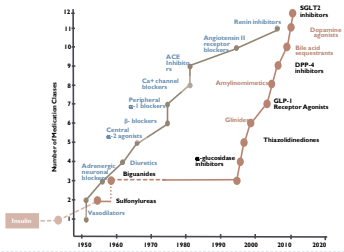


General practice management of type 2 diabetes – 2014–15. Melbourne: The Royal Australian College of General Practitioners and Diabetes Australia, 2014.

2nd line agents

- *Why is selecting a second line agent so challenging?*

Hypertension and Diabetes: Drug Classes over Past Half-Century



Determinants of selection of 2nd line agents

- *Patient Characteristics*
- *HbA$_1$C target*
- *Characteristics of the pharmaco-therapeutic agent*

Determinants of selection of 2nd line agents

- *Patient Characteristics*

Considerations in selecting an anti-diabetic medication:

- A = **A**ge
- B = **B**ody weight
- C = **C**omplications (micro and macro-vascular)
- D = **D**uration of diabetes
- E = Life **E**xpectancy
- E = **E**xpense- can the patient afford it?

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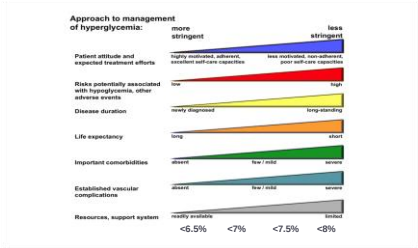
Pathophysiologic Approach to Therapy in Patients With Newly Diagnosed Type 2 Diabetes
RALPH A. DEFRONZO, MD; DIABETES CARE, VOLUME 36, SUPPLEMENT 2, AUGUST 2013

Determinants of selection of 2nd line agents

- *HbA_1C target*

Selecting an A1C target



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Inzucchi S E et al. Dia Care 2015;38:140-149

Set an A_1c target

Populations	HbA_{1c}	
	%	SI units
General	≤7%	≤53 mmol/L
Diabetes of short duration and no clinical CVD		
• Requiring lifestyle modification ± metformin	≤6.0%	≤42 mmol/L
• Requiring any antidiabetic agents other than metformin or insulin	≤6.5%	≤48 mmol/L
• Requiring insulin	≤7.0%	≤53 mmol/L
Pregnancy or planning pregnancy	≤6%	≤42 mmol/L
Diabetes of longer duration or clinical CVD (any therapy)	≤7.0%	≤53 mmol/L
Recurrent severe hypoglycaemia or hypoglycaemia unawareness (any therapy)	≤8.0%	≤64 mmol/L
Major co morbidities likely to limit life expectancy (any therapy)	Symptomatic therapy of hypoglycaemia	

Adapted from: Cheung NW, et al. MJA 2009; 191: 339–344; Jones GRD, et al. MJA 2011; 195: 45–46.

Determinants of selection of 2nd line agents

- *Characteristics of the pharmaco-therapeutic agent*

Selecting a second line agent

- Step 1: Metformin
- Step 2: Efficacy required - A1c drop required
- Step 3: Safety- potentially dangerous adverse effects
- Step 4: Tolerability – potentially unpleasant adverse effects
- Step 5: Affordability – PBS reimbursed or private script
- Step 6: review response

Choosing a 2nd line agents: The new 'class wars'

A CASE STUDY

Case Study

Patient History

- A = Age: 56yrs Taxi driver
- B = Body weight : 98kg (167cm) BMI 35.1
- C = Complications: (microvascular and macrovascular) Nil
- D = Duration of diabetes: 3yrs
- E = Life Expectancy : long
- E = Expense: Can't afford non subsidised meds

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Case Study

Patient History

- BP: 146/84 p. 74
- weight : 98kg (167cm) BMI 35.1
- Meds:
  - Metformin XR 2g nocte
  - Atorvastatin 40/Amlodipine 5 (Caduet) 1 mane
  - Perindopril 10mg 1 mane

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Case Study

Patient History

- A1C:7.6% (60mmol/mol)
- Chol (Lipids): TC: 3.4;LDL 1.8;Trigs 1.2 ; HDL 1.0
- U&Es within normal limits, eGFR 87
- LFTs Mild transaminitis

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What is this gentleman's A1C target? What is the preferred 2nd line agent?

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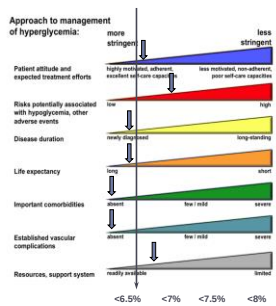
Considerations in selecting an A1C target



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Properties of 2nd line agents

Property	SU	TZD	DPP4i	Acarbose	SGLT2i	Insulin	Glp1a
Efficacy required - A1c drop required	+++	+++	++	+	++	++++	+++
Safety- potentially dangerous adverse effects:							
• renal impairment,	++	+++	+++	++	++	+++	++
• CV disease	++	+	+++	+++	+++	+++	+++
• Low risk of drug to drug interactions	++	++	+++	++	++	+++	+++
• Low risk of hypoglycaemia	++	+++	+++	+++	+++	+	+++
Tolerability – Absence of potentially unpleasant adverse effects	++	+	+++	++	++	++	++
Affordability – PBS reimbursed or private script	+++	++	++	+++	++	+++	++

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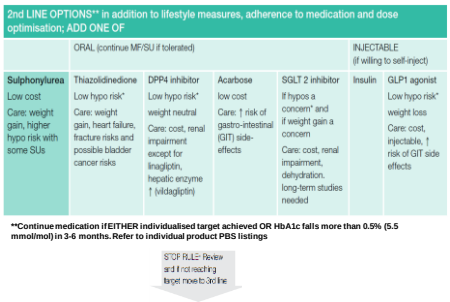
• Low risk of hypoglycaemia	++	+++	+++	+++	+++	+	+++
Tolerability – Absence of potentially unpleasant adverse effects	++	+	+++	++	++	++	++
Affordability – PBS reimbursed or private script	+++	++	++	+++	++	+++	++

2nd line options- What's your preference?



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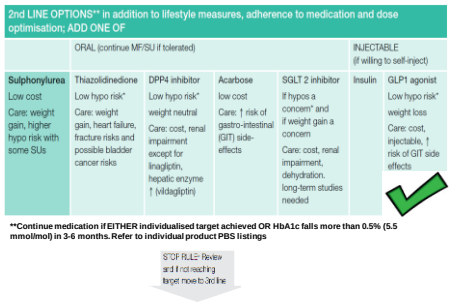
2nd line options- My preference



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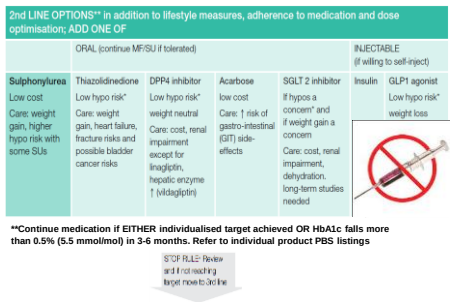
2nd line options- Patient's veto



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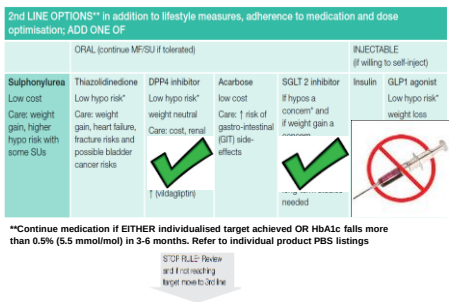
2nd line options- Negotiated settlement



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Properties of DPP4is and SGLT2is

Property	DPP4i	SGLT2i
Efficacious	+	++
Durable control	++	++
Well-tolerated • Low risk of hypoglycaemia • Weight neutral or weight loss	+++ +++ +	++ +++ ++
Can be used at all stages of disease	+++	++
Affordability	++	++
Convenient dosing	+++	+++
Simple and painless delivery system	+++	+++
Halts the progression of diabetes	-	-
Safe Including patients with renal impairment, CV disease Low risk of drug to drug interactions	++	++

Case Study

Clinical Efficacy

- **Dapagliflozin (Forxiga) 10mg once daily commenced in addition to Met XR**
- **Lifestyle modification re-enforced**
  - **Referred to:**
    - **dietitian**
    - **exercise physiologist on EPC**

Biochem

Date	12/08/14	30/11/14	Units	Range	δ
HbA1C	7.6 (60)	6.9 (52)	% (mmol/Mol)	<6.5 (47.5)	-0.7(8)
Total Cholesterol	3.4	3.5	mmol/L	(below 4.0)	+0.1
Triglycerides	1.2	1.1	mmol/L	(below 2.0)	-0.1
HDL Cholesterol	1.0	1.1	mmol/L	(above 0.9)	-0.19
LDL Cholesterol	1.8	1.9	mmol/L	(below 2.0)	+0.1
Total/HDL ratio	3.4	3.2			

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Biometrics

Biometrics	08/01/14	05/07/14	δ
Weight	98kg	95.6kg	-2.4kg
Height	167cm	167cm	
BMI	35.1	34.3	-0.8
Waist circumference	105cm	103cm	-2cm
BP	146/84	141/80	-5/4
PR	83	81	

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Case Study

Adverse Events

- **~3/12 Post initiation, patient discontinued Forxiga due to pollakiuria.**
- **Estimated 3 extra voidings per day, 2 at night.**
- **Very difficult to manage as a taxi driver!**

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Case study

Additional Information

- **Investigations revealed moderate BPH.**
- **Patient declined pharmacotherapy for LUTS (Not another pill Doc!)**
- **Awaiting Urological opinion ?TURP**
- **Would consider resuming dapagliflozin post resolution of prostatism.**
- **SGLT2i replaced by DPP4i**

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Thank you.

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