

# DOMTRU MASTERCLASS SERIES



# THE INJECTABLES

## Mechanisms of Action



## dr chee khoo



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# Learning Objectives

1. Understand the action of GLP1 Receptor Agonist injectables in the treatment of T2D
2. Aware of the potential side effects of GLP1- RA therapy
3. Understand the action of insulin
4. Understand the different preparations of insulin with their different profiles
5. Be Aware of the potential side effects of insulin therapy



# The Injectables



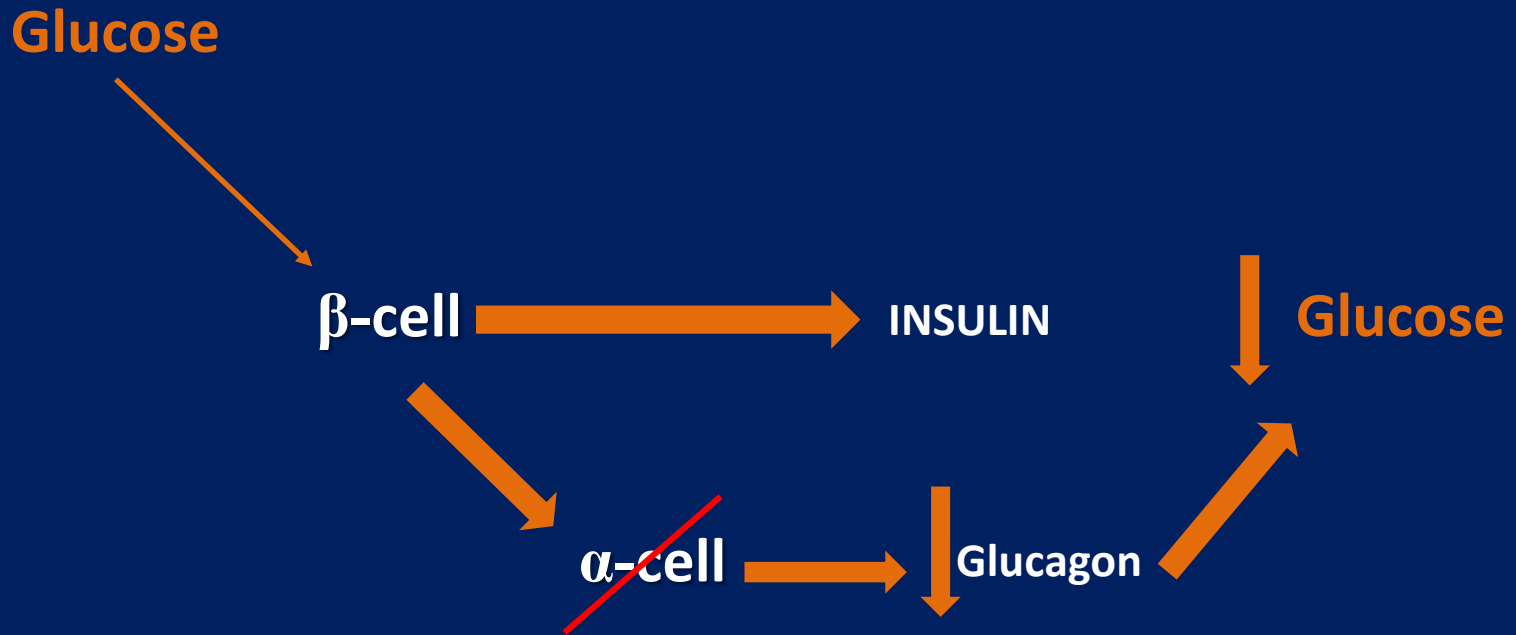
**Glucagon Like Peptide 1  
Receptor Analogue  
(GLP1-RA)**

**Insulins**

# Life used to be simple

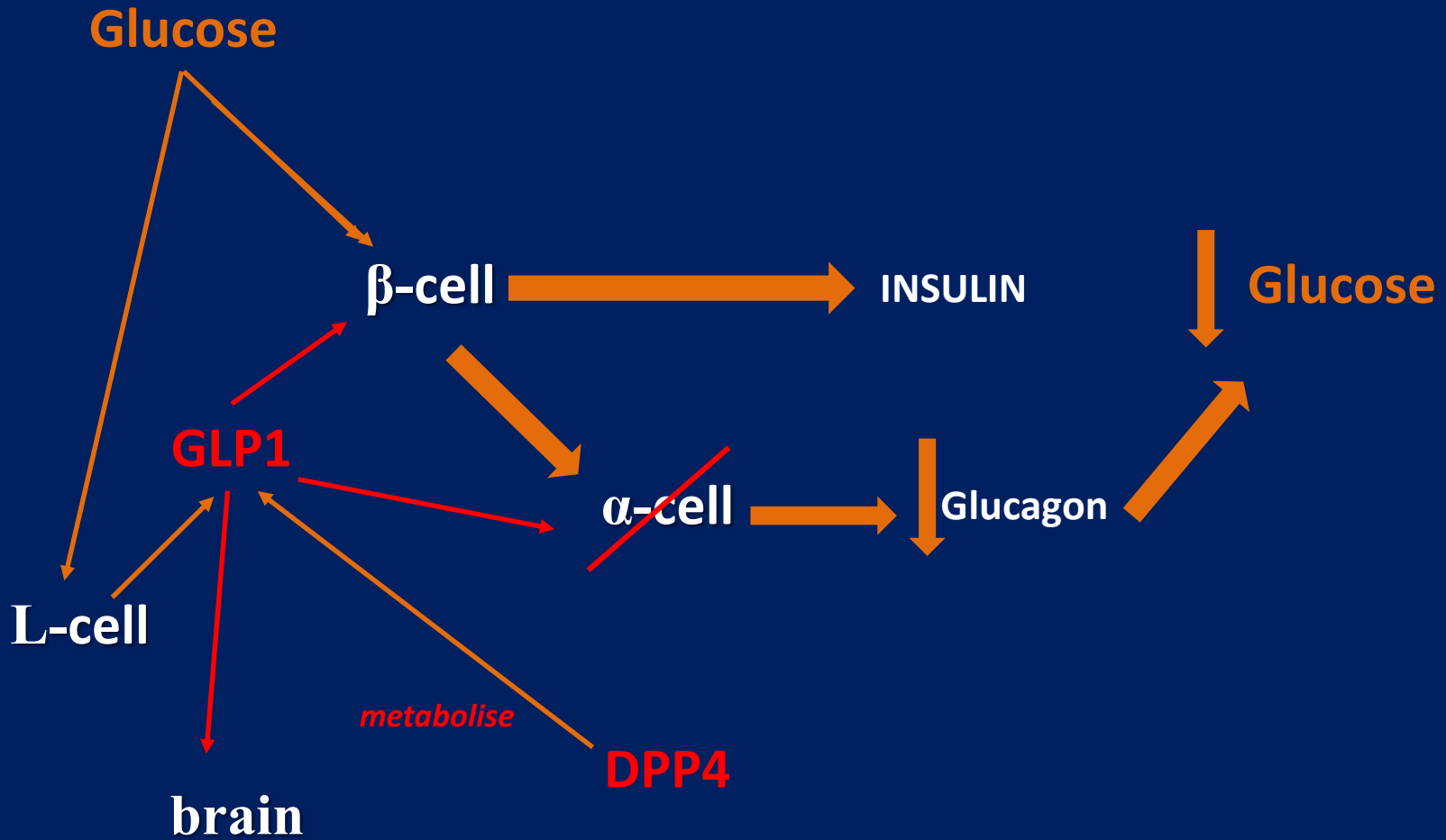


# How the world works?





# The Incretin Effect



## In T2D

- Decreased GLP1 secretion
- Reduced insulin response to GLP1
- Reduced brain response to GLP1 → reduced appetite suppression

# The Agents

- **Short Acting (twice daily)**

- Exenatide (Byetta<sup>®</sup>)



Meal time glucose

- **Long Acting (once daily)**

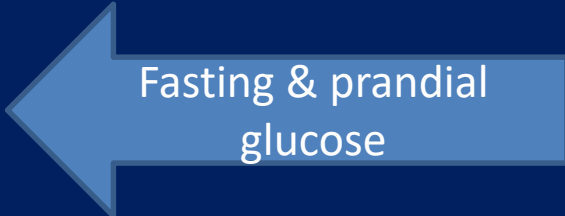
- Liraglutide (Victoza<sup>®</sup>, Saxenda<sup>®</sup>)



Fasting glucose

- **Longer Acting (weekly)**

- Exenatide XR (Bydureon<sup>®</sup>)
- Dulaglutide (Trulicity<sup>®</sup>)
- **Albiglutide (Tanzeum<sup>®</sup>)**
- **Lixisenatide (Lyxumia<sup>®</sup>)**
- **Semiglutide (injectable or oral)**



Fasting & prandial  
glucose

# Cardiovascular safety/benefits

- Cardiovascular safe – byetta, bydureon
- Cardiovascular benefit - liraglutide



# What to watch out for



- Potential hypoglycaemia if used with insulin/SU
- Side effects
  - Nausea, vomiting
- Renal caution
  - not for severe renal impairment (eGFR <30)
- Pancreatitis – uncertain significance
- Thyroid C cancer in mice – no human signals
- Pregnancy – GLP-RA not allowed
- Deterioration in retinopathy

# Essentially,

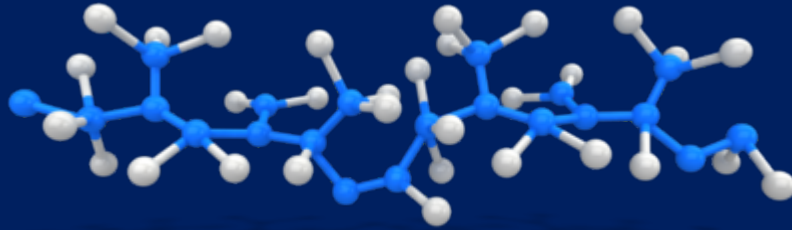
- **GLP1 RA lower glucose levels without hypos**
- **GLP1 RA reduce appetite**
- **GLP1 RA can assist in weight loss**
- **Some GLP1 RA may have cardiovascular benefits**
- **GLP1 RA differ in their efficacy, duration of action and their effect on fasting and prandial glucose**
- **But GLP1 RA cannot replace insulin especially, if there are no beta cells left to stimulate! (T1D and advanced T2D)**

# When to use GLP1 RA

1. After metformin +/- sulphonylurea
2. Before insulin
3. Add on to insulin to reduce insulin dose, reduce hypoglycaemia, weight loss or reduce weight gain



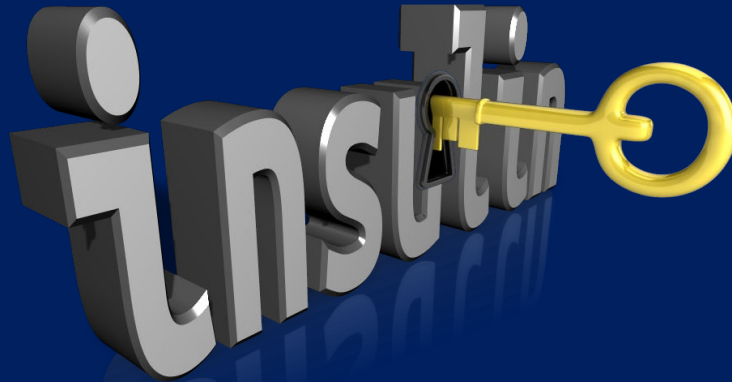
# Insulins





# What does insulin do?

1. Glucose – put glucose away in muscles, fat and liver
2. Reduce glucose release from liver and kidneys
3. Protein – put amino-acids away into muscles
4. Fat – put fatty acids away in fat



# Without insulin

1. Glucose increases
2. Fat increases, triglycerids increases
3. Muscle wasting



# Insulins

```
graph TD; Insulins --> ShortActing[Short Acting]; Insulins --> RapidActing[Rapid acting]; Insulins --> IntermediateActing[Intermediate acting]; Insulins --> LongActing[Long Acting]; Insulins --> UltraLongActing[Ultra Long Acting];
```

## Short Acting

Actrapid<sup>®</sup>  
Humulin R<sup>®</sup>

## Rapid acting

Lispro (Humalog<sup>®</sup>)  
Aspart (NovoRapid<sup>®</sup>)  
Glulisine (Apidra<sup>®</sup>)

## Intermediate acting

NPH  
Determir  
• Levemir<sup>®</sup>

## Long Acting

Glargine  
• Lantus<sup>®</sup>

## Ultra Long Acting

Toujeo<sup>®</sup>  
Degludec

*Toujeo<sup>®</sup> = insulin glargine 300 units/mL  
Lantus<sup>®</sup> = insulin glargine 100 units/mL*

# Insulins

30 mins – 6 hrs

## Short Acting

Actrapid<sup>®</sup>  
Humulin R<sup>®</sup>

## Rapid acting

Lispro (Humalog<sup>®</sup>)  
Aspart (NovoRapid<sup>®</sup>)  
Glulisine (Apidra<sup>®</sup>)

15 mins – 4.5 hrs

## Faster acting IAsp

10 mins – 4 hrs

## Intermediate acting

NPH

Determir

• Levemir<sup>®</sup>

1-2 hrs – 12-16 hrs

## Long Acting

Glargine U100

• Lantus<sup>®</sup>

1-2 hrs – 14-24 hrs

## Ultra Long Acting

Toujeo<sup>®</sup>

Degludec

1-2 hrs – 26 hrs

*Toujeo<sup>®</sup> = insulin glargine 300 units/mL*

*Lantus<sup>®</sup> = insulin glargine 100 units/mL*

# The Mixed Insulins



## Intermediate + **Short Acting**

Mixtard 30/70<sup>®</sup>

HumulinMix 30/70<sup>®</sup>

Mixtard 50<sup>®</sup>

**Start: 30 mins**

**Peak: 2-5 hour**

**Last 12-16 hours**

## Intermediate + **Rapid Acting**

Novomix 30/70<sup>®</sup>

Humalog 25/75 (mix)<sup>®</sup>

**Ryzodeg 70/30<sup>®</sup>**

**Start: 5-15 mins**

**Peak: 1 hour**

**Last 12-16 hours**

**Last 26 hours**

# Insulins

```
graph TD; A[Insulins] --> B[Mealttime insulins]; A --> C[Long/Longer Acting (basal)]; A --> D[Mixed]; B --- B1[Humalog®]; B --- B2[NovoRapid®]; B --- B3[Apidra®]; B --- B4[Fiasp®]; B --- B5[Older: Actrapid Humulin R]; C --- C1[Lantus®]; C --- C2[Toujeo®]; C --- C3[Levemir®]; C --- C4[Tresiba®]; C --- C5[Others NPH Humulin]; D --- D1[Humalog 25/75®]; D --- D2[Novomix 30/70®]; D --- D3[Ryzodeg 70/30®]; D --- D4[Older Mixtard Humulin 30/70];
```

## Mealttime insulins

Humalog<sup>®</sup>  
NovoRapid<sup>®</sup>  
Apidra<sup>®</sup>  
Fiasp<sup>®</sup>

Older:  
Actrapid  
Humulin R

## Long/Longer Acting (basal)

Lantus<sup>®</sup>  
Toujeo<sup>®</sup>  
Levemir<sup>®</sup>  
Tresiba<sup>®</sup>

Others  
NPH  
Humulin

## Mixed

Humalog 25/75<sup>®</sup>  
Novomix 30/70<sup>®</sup>  
Ryzodeg 70/30<sup>®</sup>

Older  
Mixtard  
Humulin 30/70

# Insulin Regimens

1. Long acting only (Basal)
2. Long acting + mealtime (Basal plus or Bolus-bolus)
3. Mix – once, twice, three times
4. Basal plus GLP1-RA



# Case 1 – Mrs G

Antibodies neg  
for T1D

42 yo lady of Indian extract, BMI 23

GDM on insulin 13 years ago (30yo!)

Diabetes did not disappear post partum, multiple oral agents and HbA1c still high (8-8.9 % over last 1-2 years)

*minimal rice no nan bread  
mornings still high 6-7 or more  
sometimes post dinner 11  
not much drop overnight  
maximal orals  
minimal carbs  
?insulin*



## Case 2 - George

- 79 year old, mild to moderate dementia (alcohol related), ex-wife visits 1-2 times a week
- On DPP4 inhibitor (Kombiglyze) but still high glucose all over the place 10- 20 mmol/L
- Fasting glucose 13-20, HbA1c 9.0%
- Lantus added - 10 units and titrating.....
- HbA1c now 6.9%
- Compliance becoming a problem
- Currently on 18 units at night
- ?long acting weekly GLP1-RA

## Case 3 - Abdul

37, Bangladeshi chicken farmer, diabetes for 13 years, first diagnosed with random BSL 27mmol/L

Quadruple oral agents to no avail

Most fasting 10+, most post dinner 16-18 mmol/L

Commenced on lantus 5 years ago but not seen endocrinologist for 4 years

Random SMBG readings, repeat scripts but never monitored

Last blood test 18 months ago HbA1c 10-14%

Urine MA – 165.8

Options?

Antibodies neg  
for T1D

## *What to watch for*



Hypoglycaemia

Weight gain

Lipodystrophy

Injection techniques

Poor diet

Allergies to insulin

Pregnancy

## *Check list after starting:*

- Injection sites, lipodystrophy
- Pen care, Storage, Needles, Strips, Lancets, Travelling
- Sharps disposal
- Glucose monitoring - structured and supervised
- NDSS – forms, forms, forms
- 5 to drive, Sick day management
- Hypoglycaemia recognition & management
- Drivers licencing authority (DLA) issues
- Diet and exercise discussion
- Contact person



# *Insulin in pregnancy*

Insulin	Brand	Pregnancy Category
Regular	Actrapid	B3
Aspart	Novorapid	A
Lispro	Humalog	A
Glulisine	Apidra	B3
NPH	Humulin N, Protaphane	A
Determir	Levemir	A
Glargine	Lantus	B3
Degludec	Tresiba	C



# Learning Objectives

1. Understand the action of GLP1 Receptor Agonist injectables in the treatment of T2D ✓
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4. Understand the different preparations of insulin with their different profiles ✓
5. Be Aware of the potential side effects of insulin therapy ✓

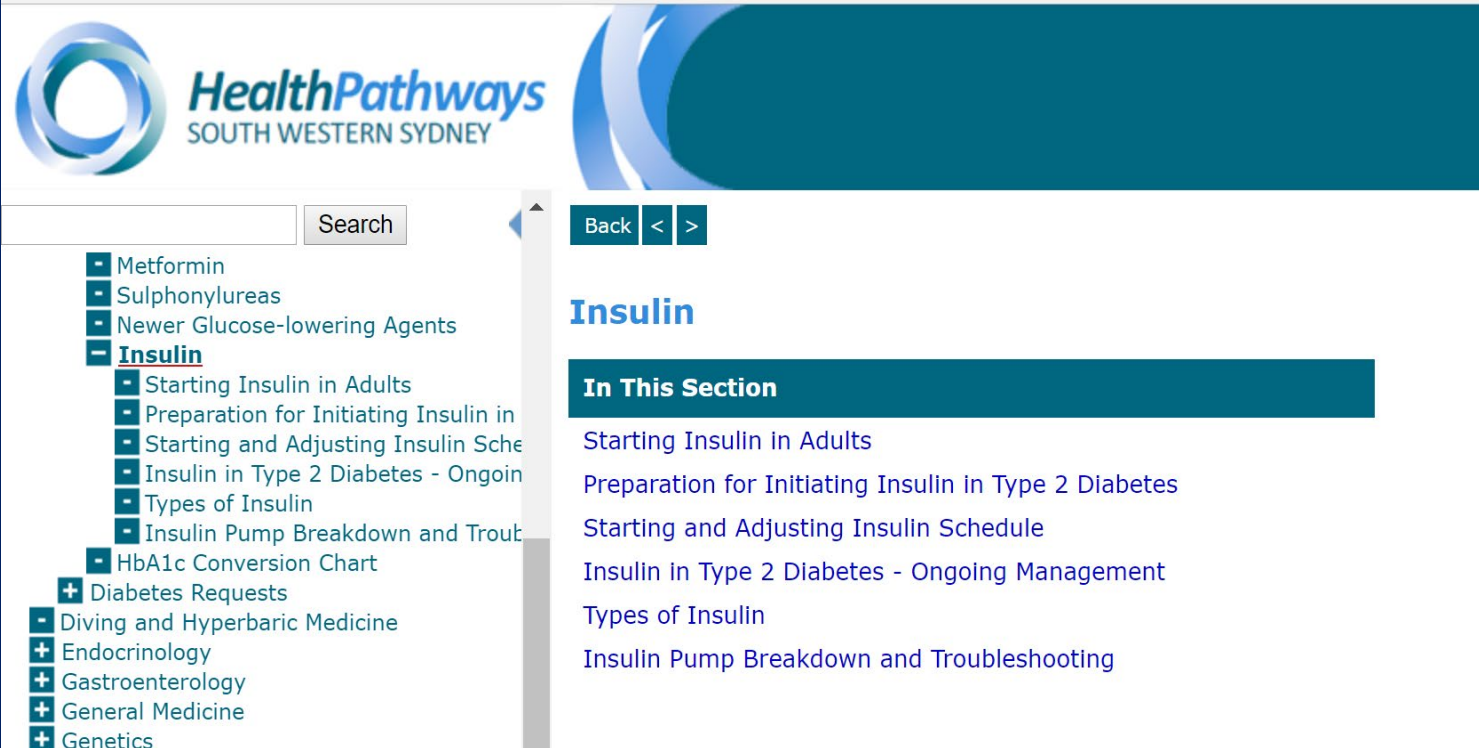


# More learning?



# Healthpathways

<https://sws.healthpathways.org.au/index.htm>



The screenshot displays the HealthPathways South Western Sydney website interface. At the top left is the logo, which consists of a blue circular graphic and the text "HealthPathways SOUTH WESTERN SYDNEY". Below the logo is a search bar with the word "Search" inside. To the right of the search bar is a navigation bar with "Back", "<", and ">" buttons. A left-hand navigation menu lists various medical topics, with "Insulin" highlighted in red. The main content area on the right is titled "Insulin" and features a dark teal header "In This Section" followed by a list of sub-topics: "Starting Insulin in Adults", "Preparation for Initiating Insulin in Type 2 Diabetes", "Starting and Adjusting Insulin Schedule", "Insulin in Type 2 Diabetes - Ongoing Management", "Types of Insulin", and "Insulin Pump Breakdown and Troubleshooting".

**HealthPathways**  
SOUTH WESTERN SYDNEY

Search

Back < >

- Metformin
- Sulphonylureas
- Newer Glucose-lowering Agents
- **Insulin**
  - Starting Insulin in Adults
  - Preparation for Initiating Insulin in
  - Starting and Adjusting Insulin Sche
  - Insulin in Type 2 Diabetes - Ongoin
  - Types of Insulin
  - Insulin Pump Breakdown and Troub
- + HbA1c Conversion Chart
- + Diabetes Requests
- Diving and Hyperbaric Medicine
- + Endocrinology
- + Gastroenterology
- + General Medicine
- + Genetics

## Insulin

### In This Section

- Starting Insulin in Adults
- Preparation for Initiating Insulin in Type 2 Diabetes
- Starting and Adjusting Insulin Schedule
- Insulin in Type 2 Diabetes - Ongoing Management
- Types of Insulin
- Insulin Pump Breakdown and Troubleshooting



# Healthpathways

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The screenshot displays the HealthPathways website interface. At the top left is the logo for HealthPathways South Western Sydney. A search bar is located below the logo. A navigation menu on the left lists various medical topics, with 'Newer Glucose-lowering Agents' highlighted. The main content area features a section titled 'Newer Glucose-lowering Agents' with a 'Back' button and navigation arrows. The text in this section discusses algorithms for lowering glucose in Type 2 diabetes, references the Pharmaceutical Benefits Scheme (PBS), and provides information on eGFR and creatinine clearance. Below the text are several expandable sections for different drug classes: DPP-4 inhibitors, GLP-1 analogue, SGLT2 inhibitor, Thiazolidinediones (glitazones), and Alpha-glucosidase inhibitors.

**HealthPathways**  
SOUTH WESTERN SYDNEY

Search

- Glycaemic Control - Type 2 Diabetes
- Metformin
- Sulphonylureas
- **Newer Glucose-lowering Agents**
- Insulin
  - Starting Insulin in Adults
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- + Endocrinology
- + Gastroenterology
- + General Medicine
- + Genetics
- + Haematology
- + Infectious Diseases
- + Nephrology
- + Neurology
- + Obesity

Back < >

## Newer Glucose-lowering Agents

See [Algorithm for lowering glucose in Type 2 diabetes](#).

Refer to the [Pharmaceutical Benefits Scheme \(PBS\)](#) for latest guidelines regarding licensed insulin lowering drugs.

eGFR may be unreliable in very large or small patients, in children, and in acute kidney failure. estimated creatinine clearance. Check eGFR or calculate creatinine clearance using the Cockcroft calculator.

- + **DPP-4 inhibitors**
- + **GLP-1 analogue**
- + **SGLT2 inhibitor**
- + **Thiazolidinediones (glitazones)**
- + **Alpha-glucosidase inhibitors**

# AUS-CDEP



Cambridge Diabetes  
Education Programme  
Australia

Online competency-based tool for Diabetes

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
CONTACT US

## LEARNING TOPICS...

### Diabetes

Please select from the topics on the right, you will be taken to the competencies section and into the quiz questions.

Topics are shown as follows:

-  Completed topics
-  Incomplete topics

Select a topic to focus your learning on

-  What is Diabetes
-  Hypoglycaemia
-  Oral Therapies
-  Injectable Therapies
-  Managing Adults with Diabetes in Hospital
-  Pregnancy - Pre-conception Care

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### Mark these DATES

Practice Nurse Diabetes Workshop Series Workshop 2 - Open for Registration Now

Diabetes Tech & Talk Symposium 18-19th May 2018

## CT and US Guided Injections – what goes where for what conditions

Interventional procedures have evolved and improved over time since epidural injection was first introduced for low back pain and sciatica in 1901. One of the major contributors in the improvement of these interventions is the advancement of imaging guidance technologies. The utilisation of image guidance has dramatically improved the accuracy and safety of these interventions. It is sometimes confusing to know what injections go where for what conditions?...

## Opioids or codeine not recommended? What do we do with patients with severe back and leg pains?

May 1, 2018 Dr Chee L Khoo

Chronic, persistent low back, lower extremity pain, and radicular pain may be secondary to disc



### Articles by Categories

Select Category

### You might have miss these...

CT and US Guided Injections – what goes where for what conditions **April 29, 2018**

# More updates?

- May Annual Diabetes Symposium
- November GP Injectable Masterclass
- Case conference



**Thank you**



# Questions?



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**GPVoice.com.au**

# NDSS navigating...

## National Diabetes Supply Scheme

1. Australian citizens
2. Diabetes only
3. **Registration** → 200 strips
4. **6 month approval** → 200 strips
5. If on insulin - **change of medications** → no further forms!
6. Needles
7. Lancets
8. “Buttons” for T1D



**Healthpathways!**