# DOMTRU MASTERCLASS SERIES

# THE INJECTABLES

## Mechanisms of Action

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# Learning Objectives

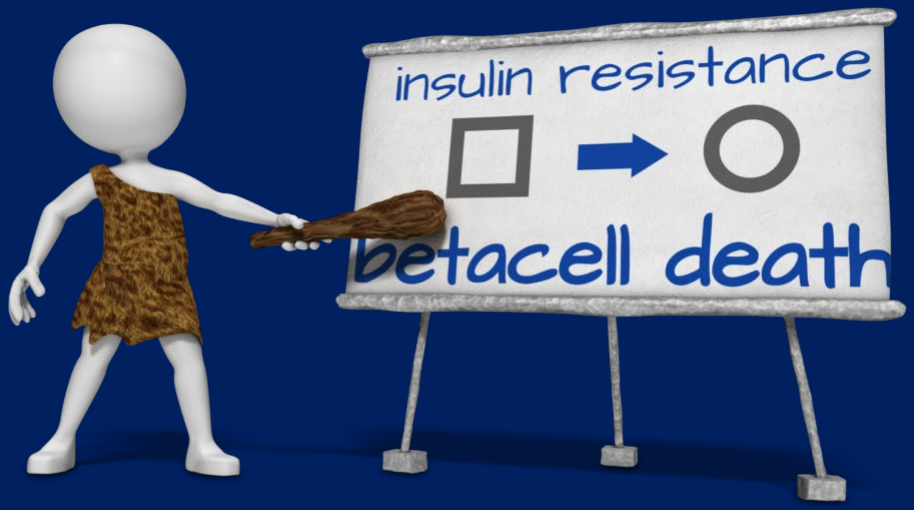
1. Understand the action of GLP1 Receptor Agonist injectables in the treatment of T2D
2. Aware of the potential side effects of GLP1- RA therapy
3. Understand the action of insulin
4. Understand the different preparations of insulin with their different profiles
5. Be Aware of the potential side effects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

# The Injectables

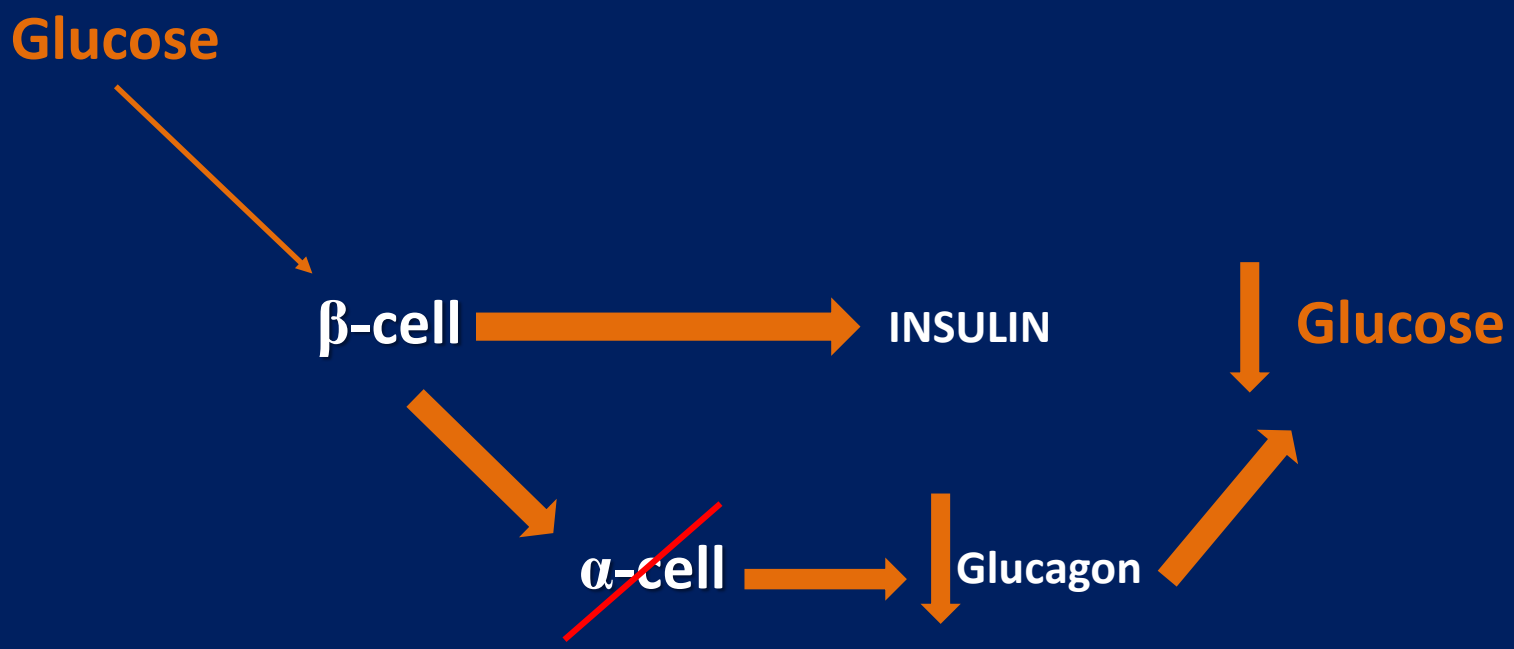
Glucagon Like Peptide 1 Receptor Analogue (GLP1-RA)

Insulins

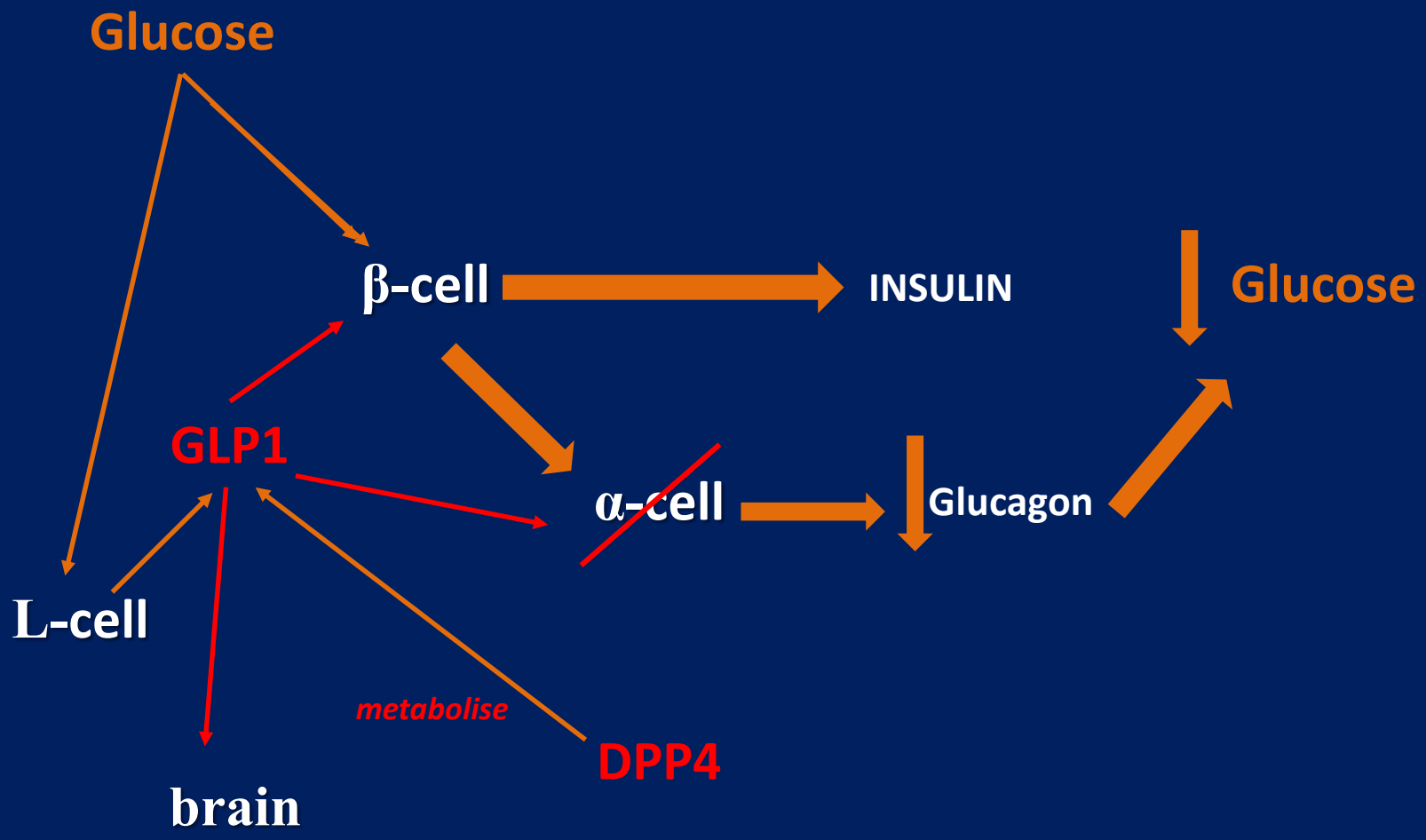
# Life used to be simple



# 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®)

Meal time glucose

- ***Long* Acting (once daily)**
  - Liraglutide (Victoza®, Saxenda®)

Fasting glucose

- **Longer Acting (weekly)**
  - Exenatide XR (Bydureon®)
  - Dulaglutide (Trulicity®)
  - **Albiglutide (Tanzeum®)**
  - **Lixisenatide (Lyxumia®)**
  - **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

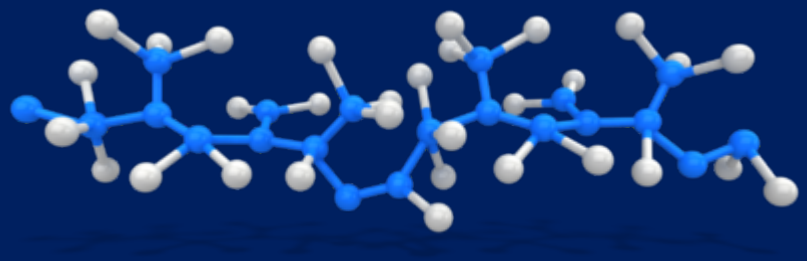
# Essentially,

- 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



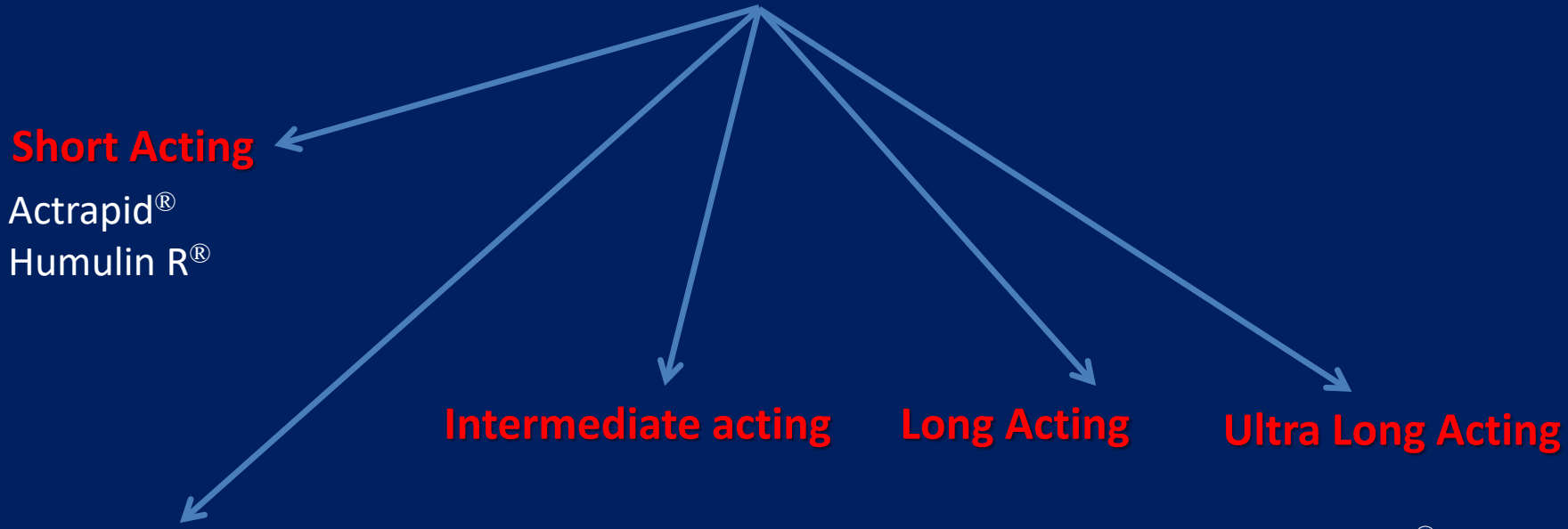
# What does insulin do?

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



**Short Acting**

Actrapid®
Humulin R®

**Rapid acting**

Lispro (Humalog®)
Aspart (NovoRapid®)
Glulisine (Apidra®)

**Intermediate acting**

NPH
**Determir**
- Levemir®

**Long Acting**

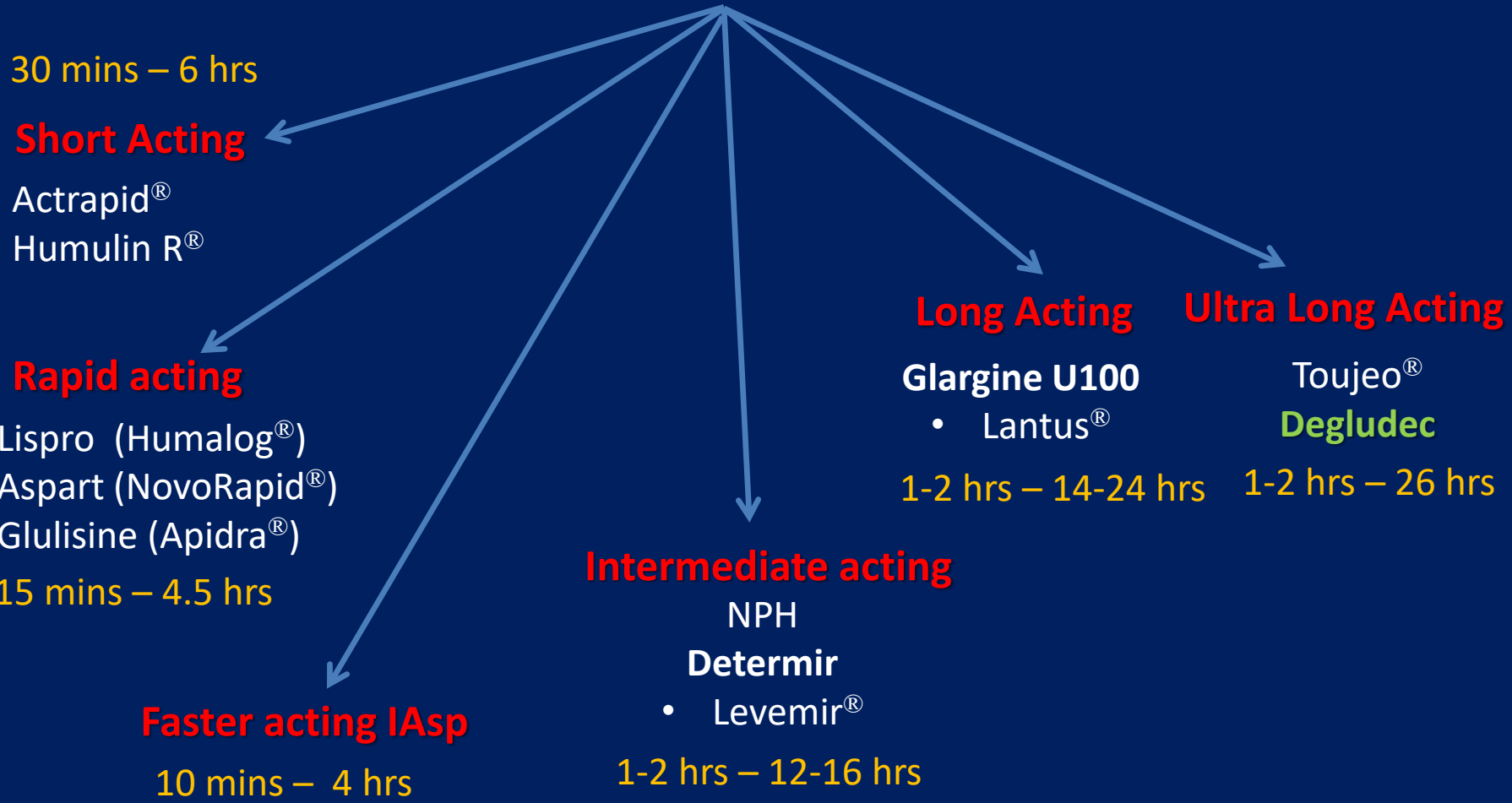
**Glargine**
- Lantus®

**Ultra Long Acting**

Toujeo®
**Degludec**

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

# Insulins




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

# The Mixed Insulins

**Intermediate + Short Acting**

Mixtard 30/70®
HumulinMix 30/70®
Mixtard 50®

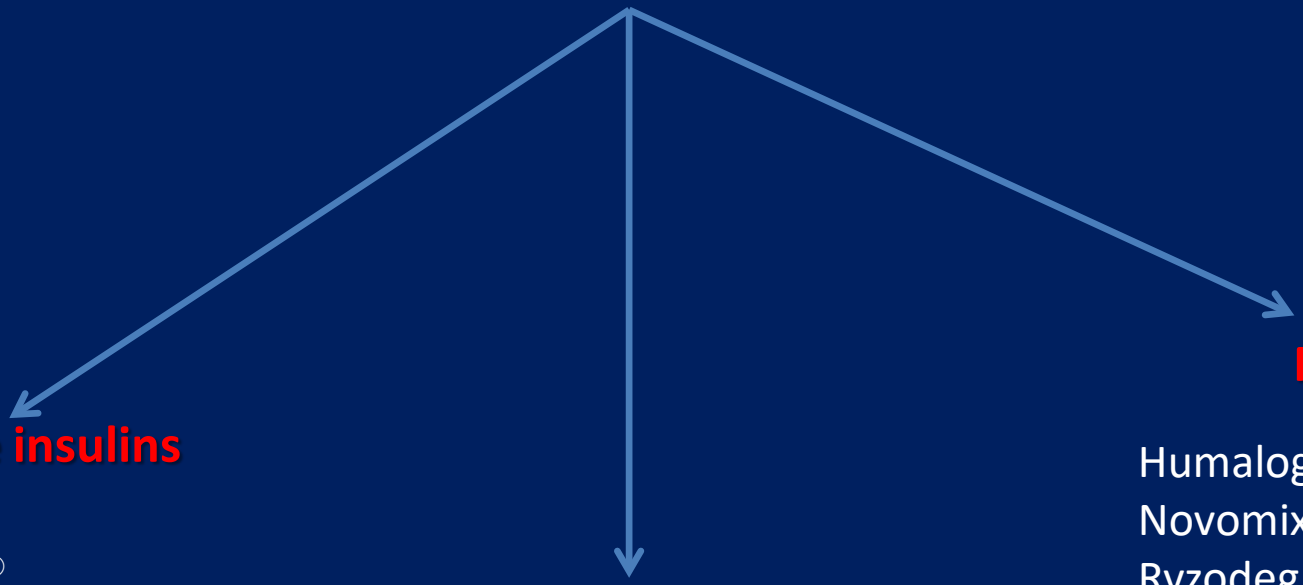
**Start: 30 mins**
**Peak: 2-5 hour**
**Last 12-16 hours**

**Intermediate + Rapid Acting**

Novomix 30/70®
Humalog 25/75 (mix) ®
Ryzodeg 70/30®

**Start: 5-15 mins**
**Peak: 1 hour**
**Last 12-16 hours**
**Last 26 hours**

# Insulins



## Mealtime insulins

Humalog®
NovoRapid®
Apidra®
Fiasp®

Older:
Actrapid
Humulin R

## Long/Longer Acting (basal)

Lantus®
Toujeo®
Levemir®
Tresiba®

Others
NPH
Humulin

## Mixed

Humalog 25/75®
Novomix 30/70®
Ryzodeg 70/30®

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 |

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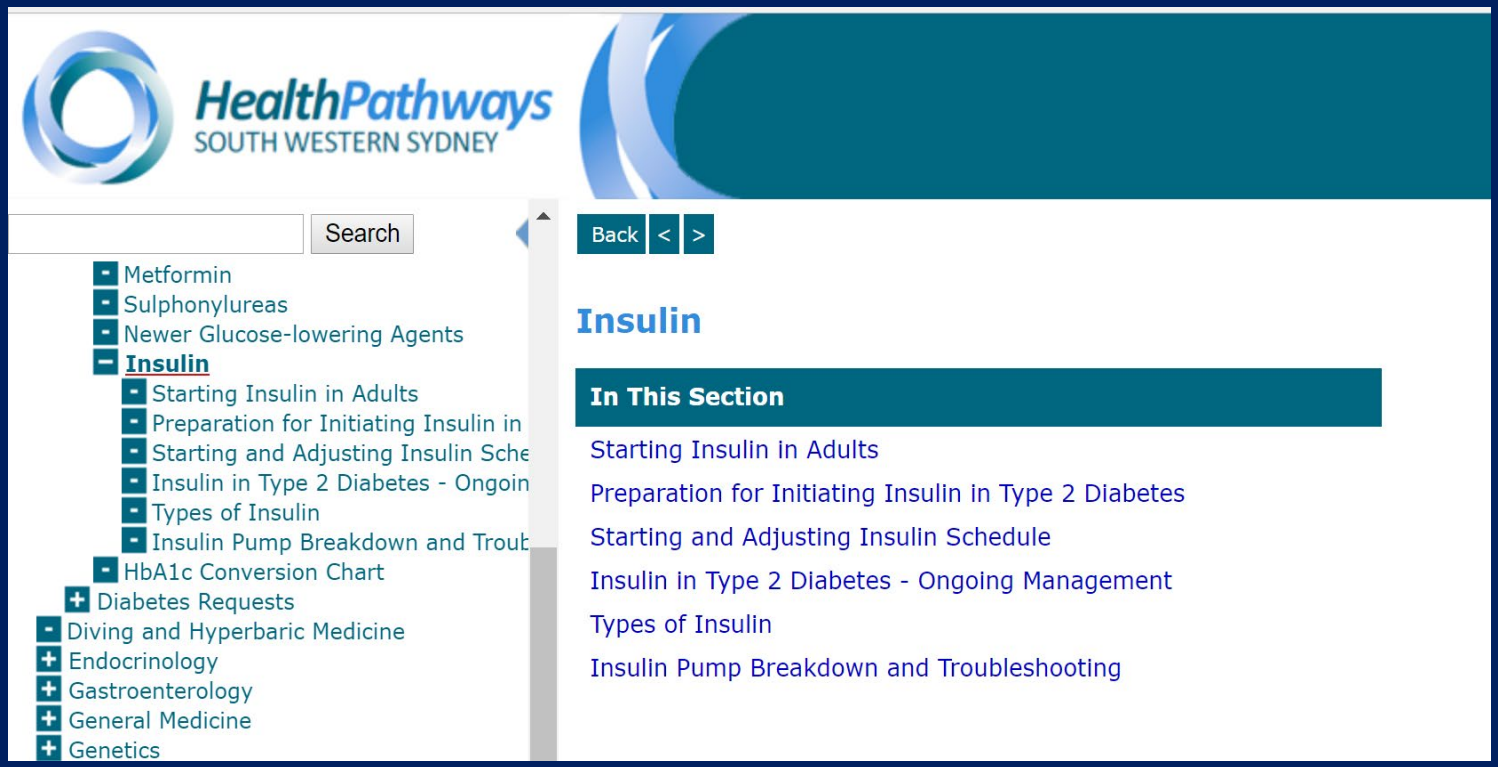
# More learning?

# Healthpathways

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



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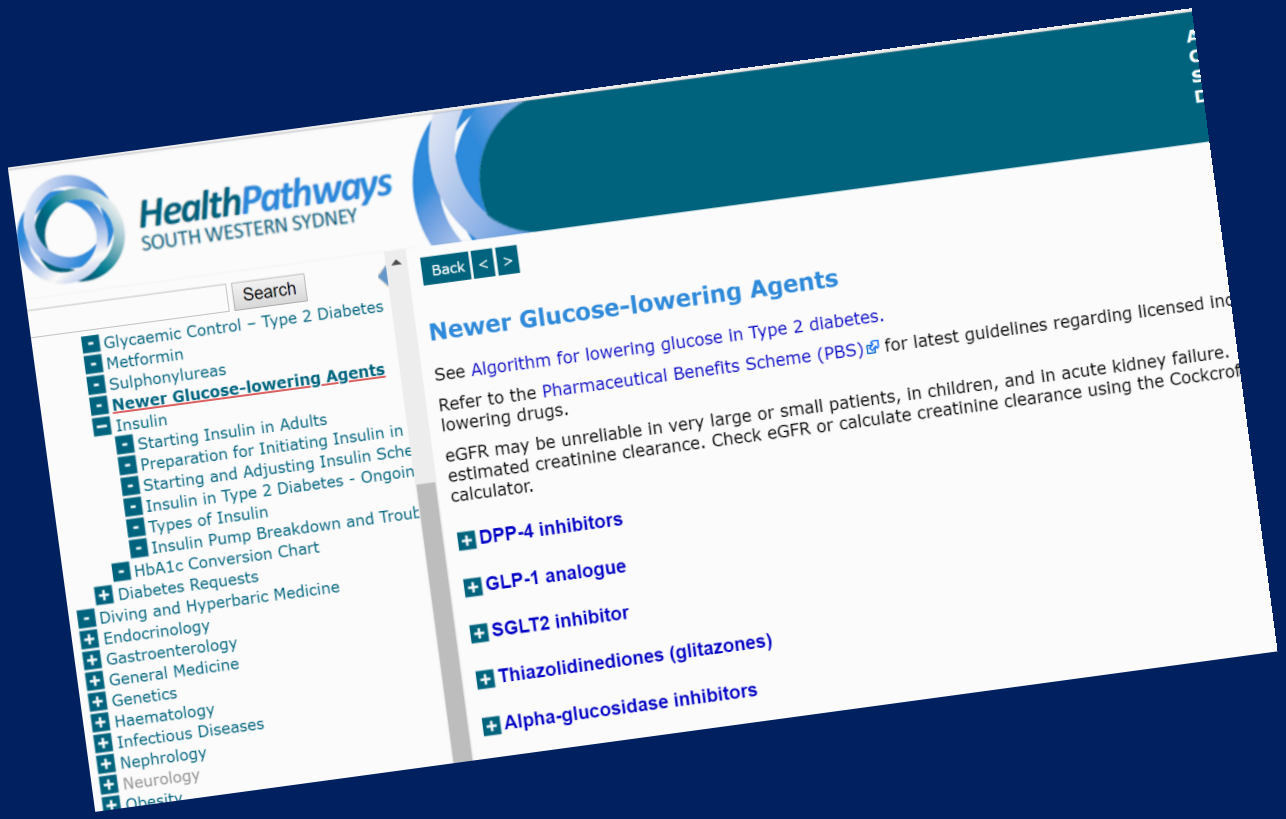

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Oral Therapies
Injectable Therapies
Managing Adults with Diabetes in Hospital
Pregnancy - Pre-conception Care

# gpvoice.com.au

# 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!