Incretin-based therapies: Appropriate prescribing practices

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Radcliffe Medical Education

Knowledge recap

Incretin hormones, **GIP** and **GLP-1** are produced by the GI tract in response to incoming nutrients and have important actions contributing to glucose homeostasis

GLP-1s

- Receptors are mainly in islet cells and central nervous system
- Once produced, are **rapidly metabolised by DPP-4** enzyme
- **Glucose-lowering actions** include:

Enhanced glucose-dependent insulin secretion

Inhibition of glucagon secretion and hepatic glucose production

Slowing of gastric emptying

Increased satiety

Safe prescribing of incretin-based drugs

GLP-1 RAs[2]

- Avoid in pts with
  - type 1 diabetes
  - history of alcoholism
  - acute pancreatitis
  - ESRF, eGFR < 15 ml/min/1.73m^2
  - pregnancy/breast feeding
  - sever GI disease
  - low BMI
- Avoid in pts with CKD
  - eGFR <50 (exenatide ER)
  - eGFR <30 (exenatide IR)
  - eGFR <30 (lixisenatide, *cautions if eGFR 30-50*)
- Prescribe safely in pts with
  - eGFR < 15 ml/min/1.73m^2 (semaglutide, dulaglutide, liraglutide)

DPP-4is[3]

- Avoid in pts with
  - ketoacidosis
  - hepatic impairment (vildagliptin, saxagliptin, alogliptin)
  - HF (vildagliptin, saxagliptin, alogliptin in severe HF; alogliptin in moderate HF)
- Dose reduction required as eGFR drops (except for linagliptin)
- Refer to individual prescribing information for pts
  - with ≥ moderate renal impairment
  - with ≥ moderate hepatic impairment
  - with ≥ moderate HF
  - with a history of pancreatitis
  - who are elderly

Key factors to consider when prescribing GLP-1 RAs[1]

Potential benefits
Weight loss and glucose lowering with low risk of hypoglycaemia

Dose titration
When and how to increase drug dose

Side effects
Nausea, vomiting, diarrhoea and worsening of gastro-oesophageal reflux disease (due to slowing gastric emptying and increasing satiety). If history of gall stones or elevated TG or alcohol abuse and severe abdominal symptoms, consider pancreatitis, STOP GLP-1 RAs, check amylase and closely monitor

Blood Glucose Monitoring
Regular blood glucose monitoring if combined with SU or insulin therapy

Risk of Hypoglycaemia
Low hypoglycaemia risk unless combined with SU or insulin therapy. Advise on any dose reduction of other medications if necessary

Increased satiety
GLP-1 RAs may lead to a smaller appetite. Advise pts to reduce their meal sizes to reduce the risk of side effects such as nausea and vomiting

DVLA and Driving
Notification not necessary if not dosed with another agent (e.g. SU or insulin), as this drug is not a hypo-inducing agent

Sick day Rules
In symptomatic pts (e.g. severe GI symptoms) with intercurrent illnesses (e.g. acute kidney injury) STOP if at risk of dehydration until well again.

Other
- Advise the injection technique, disposal of sharps, storage of medication
- Advise to AVOID pregnancy or STOP the therapy at least 3 months prior toplanned conception.
- Advise the next review date

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; DPP-4, dipeptidyl peptidase-4; DPP-4i, dipeptidyl peptidase 4 inhibitor; DVLA, driver and vehicle licensing agency; eGFR, estimated glomerular filtration rate; ER, extended-release; ESRF, end-stage renal failure; GI, gastrointestinal; GIP, gastric inhibitory polypeptide; GLP-1, glucagon-like peptide-1; GLP-1 RAs, glucagon-like peptide-1 receptor agonists; HF, heart failure; IR, immediate-release; IV, intravenous; pts, patients; SU, sulfonylurea; TG, triglycerides; T2DM, type 2 diabetes mellitus

References: **1.** Royal College of Nursing. Starting injectable treatment in adults with type 2 diabetes. RCN guidance for nurses. 2019 Available at www.rcn.org.uk **2.** GLP-1 receptor agonists in type 2 diabetes: An underused asset? Updated January 2021. Available at www.pcdsociety.org **3.** Diabetes – type 2: DPP-4 inhibitors. Last revised July 2021. Available at cks.nice.org.uk