Diabetes Update: Keeping patients safe

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Declaration of Interests

- I have received funding from the following companies for providing education sessions, attending advisory and editorial boards and received travel grants to attend conferences:
  - Boehringer Ingelheim and Lilly Diabetes Alliance
  - Sanofi
  - Astellas Pharma
  - MSD
  - Lilly Diabetes
  - Janssen Pharmaceuticals
  - Astra Zeneca

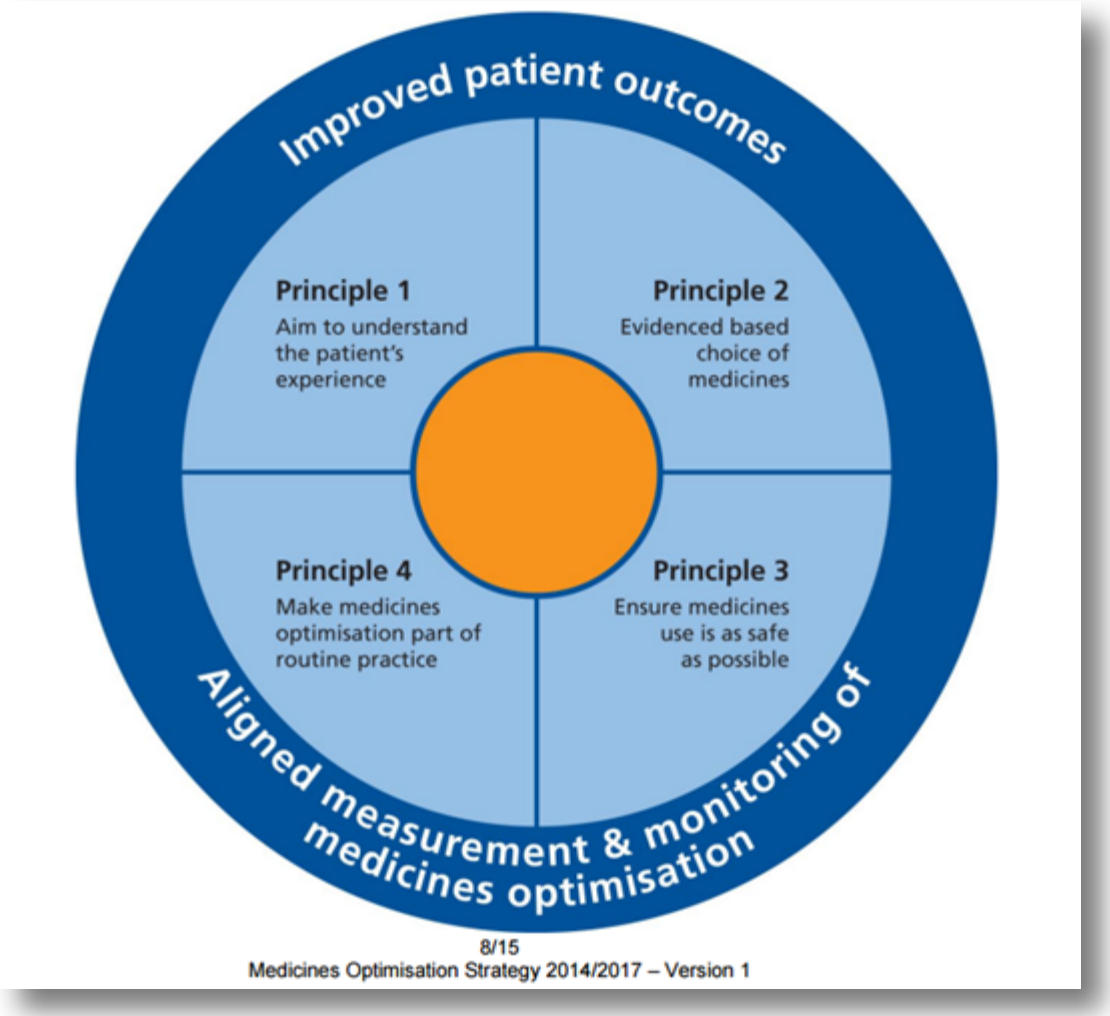
- I am involved in projects locally that receive funding support from the following companies:
  - Sanofi
  - Lilly Diabetes
  - AstraZeneca
  - Novo Nordisk

Introduction

This evening we will cover:

- Medicines optimisation
- Making insulin safer
- Transfer of care
- New medication for type 2 diabetes

Medicines Optimisation...



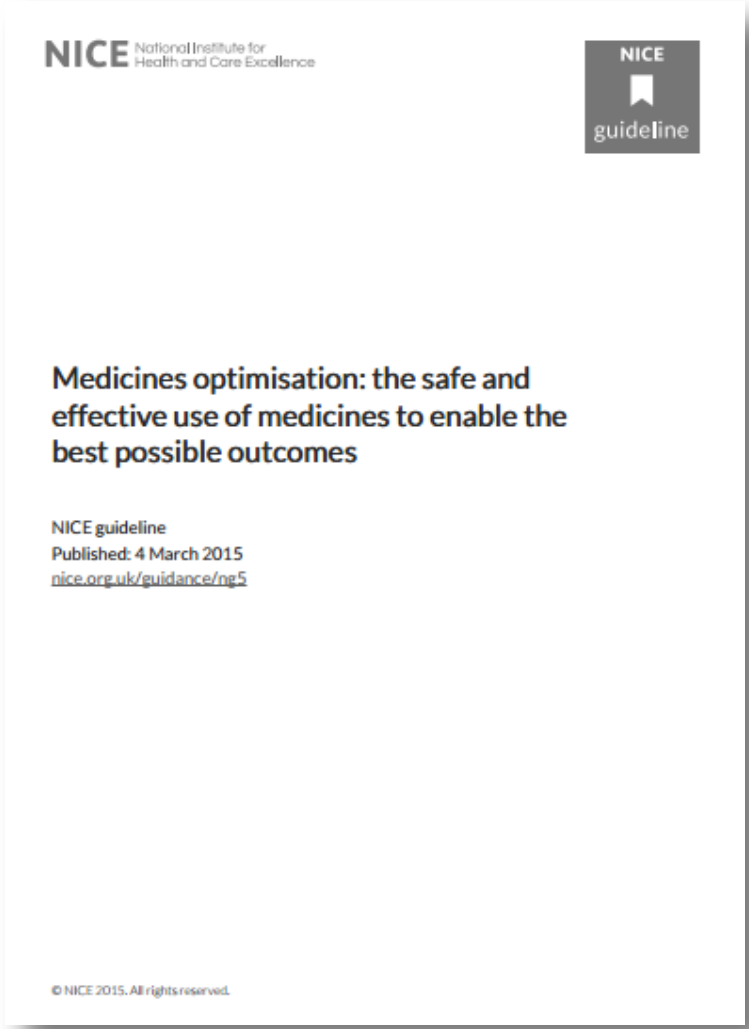
Royal Pharmaceutical Society. Helping patients make the most of medicines. May 2013

...not medicines management

- This focuses on the **patient** instead of the **drug**
- It still delivers significant cost savings but not through restriction of 'expensive' drugs
- Has a significant safety aspect

NICE Guidance: Medicines Optimisation NG5

- Key recommendations:
  - Medicines reconciliation
  - Safer transfer of care
  - Identification and reporting of medicines safety incidents
  - Medication review
  - Patient decision aids and self-management plans



NICE. NG5 -Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes. March 2015. Available at

NICE Quality Standard: QS120

- QS120 covers the safe and effective use of medicines for all people who take medicines, including people who are receiving suboptimal benefit from medicines

- QS120 is expected to contribute to improvements in the following outcomes:
  - harm attributable to errors in medication
  - patient satisfaction with outcomes from the use of medicines
  - quality of life for people with long-term conditions
  - preventable mortality
  - preventable morbidity and life expectancy for people with long-term conditions

NICE. Quality Standard 120 –Medicines optimisation. March 2016.

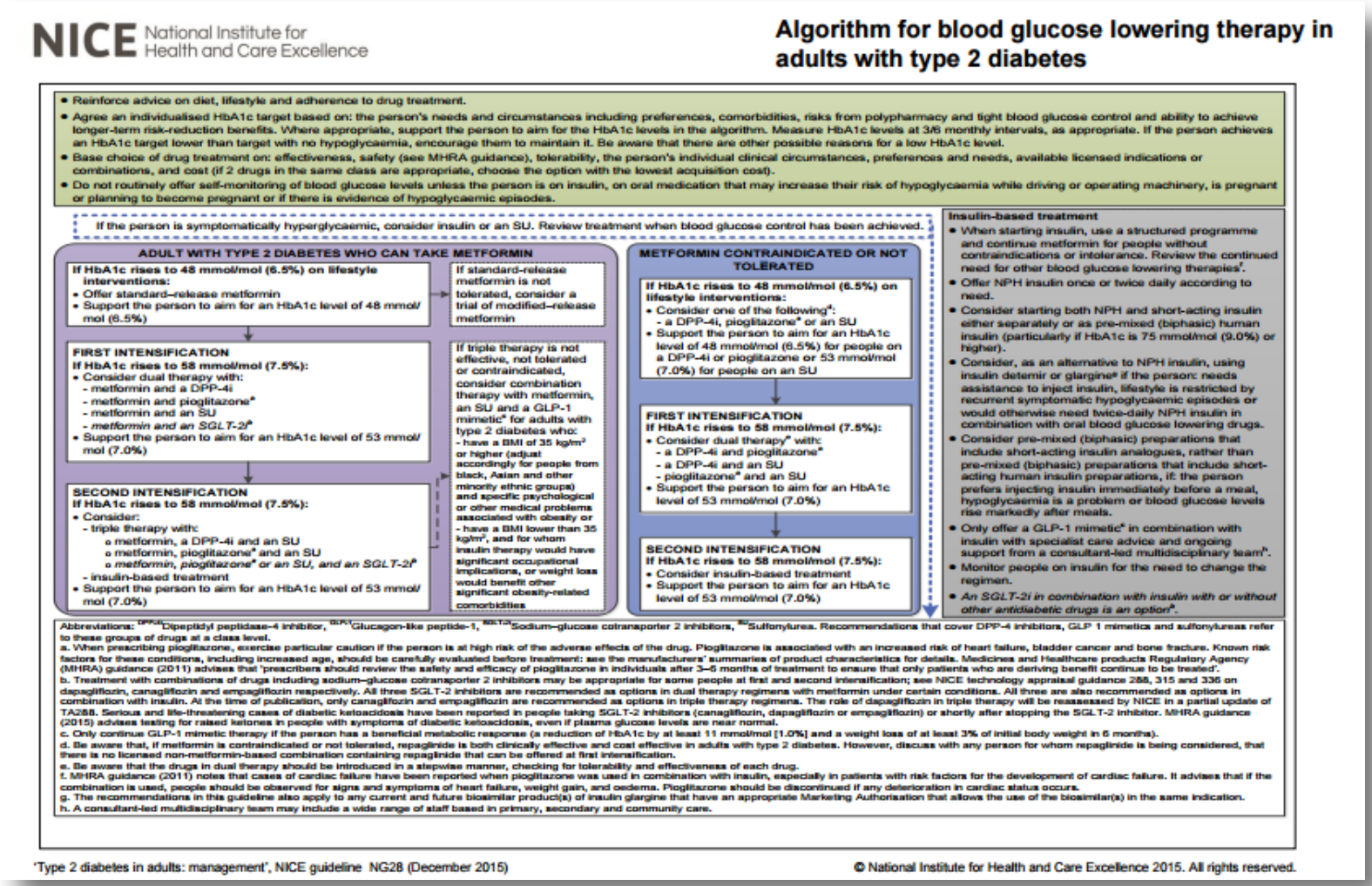
How do we apply MO to diabetes?

- We have a huge range of drugs which means we should be able to select the best option for each patient's individual factors
- There are multiple drugs in each class so adverse effects and safety can be minimised and choices can be changed
- Diabetes has a huge evidence base so decisions can be based on guidelines and best practice

NICE Guidance

- New NICE guidelines published in 2015 covering type 1 and type 2 diabetes, pregnancy, children and footcare
- Multiple technology appraisals for individual new drugs
- How do we understand all of these and fit them all together?

NG28: Treatment Guidance



NICE National Institute for Health and Care Excellence

Algorithm for blood glucose lowering therapy in adults with type 2 diabetes

- Reinforce advice on diet, lifestyle and adherence to drug treatment.
- Agree an individualised HbA1c target based on: the person's needs and circumstances including preferences, comorbidities, risks from polypharmacy and tight blood glucose control and ability to achieve longer-term risk-reduction benefits. Where appropriate, support the person to aim for the HbA1c levels in the algorithm. Measure HbA1c levels at 3/6 monthly intervals, as appropriate. If the person achieves an HbA1c target lower than target with no hypoglycaemia, encourage them to maintain it. Be aware that there are other possible reasons for a low HbA1c level.
- Base choice of drug treatment on: effectiveness, safety (see MHRA guidance), tolerability, the person's individual clinical circumstances, preferences and needs, available licensed indications or combinations, and cost (if 2 drugs in the same class are appropriate, choose the option with the lowest acquisition cost).
- Do not routinely offer self-monitoring of blood glucose levels unless the person is on insulin, on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery, is pregnant or planning to become pregnant or if there is evidence of hypoglycaemic episodes.

If the person is symptomatically hyperglycaemic, consider insulin or an SU. Review treatment when blood glucose control has been achieved.

ADULT WITH TYPE 2 DIABETES WHO CAN TAKE METFORMIN

If HbA1c rises to 48 mmol/mol (6.5%) on lifestyle interventions:
- Offer standard-release metformin
- Support the person to aim for an HbA1c level of 48 mmol/mol (6.5%)

If standard-release metformin is not tolerated, consider a trial of modified-release metformin

FIRST INTENSIFICATION
If HbA1c rises to 58 mmol/mol (7.5%):
- Consider dual therapy with:
  - metformin and a DPP-4i
  - metformin and pioglitazone[a]
  - metformin and an SU
  - *metformin and an SGLT-2i*[b]
- Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)

SECOND INTENSIFICATION
If HbA1c rises to 58 mmol/mol (7.5%):
- Consider:
  - triple therapy with:
    - metformin, a DPP-4i and an SU
    - metformin, pioglitazone[a] and an SU
    - *metformin, pioglitazone[a] or an SU, and an SGLT-2i*[b]
  - insulin-based treatment
- Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)

If triple therapy is not effective, not tolerated or contraindicated, consider combination therapy with metformin, an SU and a GLP-1 mimetic[c] for adults with type 2 diabetes who:
- have a BMI of 35 kg/m² or higher (adjust accordingly for people from black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity or
- have a BMI lower than 35 kg/m², and for whom insulin therapy would have significant occupational implications, or weight loss would benefit other significant obesity-related comorbidities

METFORMIN CONTRAINDICATED OR NOT TOLERATED

If HbA1c rises to 48 mmol/mol (6.5%) on lifestyle interventions:
- Consider one of the following[d]:
  - a DPP-4i, pioglitazone[a] or an SU
- Support the person to aim for an HbA1c level of 48 mmol/mol (6.5%) for people on a DPP-4i or pioglitazone or 53 mmol/mol (7.0%) for people on an SU

FIRST INTENSIFICATION
If HbA1c rises to 58 mmol/mol (7.5%):
- Consider dual therapy[e] with:
  - a DPP-4i and pioglitazone[a]
  - a DPP-4i and an SU
  - pioglitazone[a] and an SU
- Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)

SECOND INTENSIFICATION
If HbA1c rises to 58 mmol/mol (7.5%):
- Consider insulin-based treatment
- Support the person to aim for an HbA1c level of 53 mmol/mol (7.0%)

Insulin-based treatment
- When starting insulin, use a structured programme and continue metformin for people without contraindications or intolerance. Review the continued need for other blood glucose lowering therapies[f].
- Offer NPH insulin once or twice daily according to need.
- Consider starting both NPH and short-acting insulin either separately or as pre-mixed (biphasic) human insulin (particularly if HbA1c is 75 mmol/mol (9.0%) or higher).
- Consider, as an alternative to NPH insulin, using insulin detemir or glargine[g] if the person: needs assistance to inject insulin, lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes or would otherwise need twice-daily NPH insulin in combination with oral blood glucose lowering drugs.
- Consider pre-mixed (biphasic) preparations that include short-acting insulin analogues, rather than pre-mixed (biphasic) preparations that include short-acting human insulin preparations, if: the person prefers injecting insulin immediately before a meal, hypoglycaemia is a problem or blood glucose levels rise markedly after meals.
- Only offer a GLP-1 mimetic[c] in combination with insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team[h].
- Monitor people on insulin for the need to change the regimen.
- *An SGLT-2i in combination with insulin with or without other antidiabetic drugs is an option*[b].

Abbreviations: DPP-4 Dipeptidyl peptidase-4 inhibitor, GLP-1 Glucagon-like peptide-1, SGLT-2 Sodium–glucose cotransporter 2 inhibitors, SU Sulfonylurea. Recommendations that cover DPP-4 inhibitors, GLP-1 mimetics and sulfonylureas refer to these groups of drugs at a class level.

a. When prescribing pioglitazone, exercise particular caution if the person is at high risk of the adverse effects of the drug. Pioglitazone is associated with an increased risk of heart failure, bladder cancer and bone fracture. Known risk factors for these conditions, including increased age, should be carefully evaluated before treatment: see the manufacturers' summaries of product characteristics for details. Medicines and Healthcare products Regulatory Agency (MHRA) guidance (2011) advises that 'prescribers should review the safety and efficacy of pioglitazone in individuals after 3–6 months of treatment to ensure that only patients who are deriving benefit continue to be treated'.

b. Treatment with combinations of drugs including sodium–glucose cotransporter 2 inhibitors may be appropriate for some people at first and second intensification; see NICE technology appraisal guidance 288, 315 and 336 on dapagliflozin, canagliflozin and empagliflozin respectively. All three SGLT-2 inhibitors are recommended as options in dual therapy regimens with metformin under certain conditions. All three are also recommended as options in combination with insulin. At the time of publication, only canagliflozin and empagliflozin are recommended as options in triple therapy regimens. The role of dapagliflozin in triple therapy will be reassessed by NICE in a partial update of TA288. Serious and life-threatening cases of diabetic ketoacidosis have been reported in people taking SGLT-2 inhibitors (canagliflozin, dapagliflozin or empagliflozin) or shortly after stopping the SGLT-2 inhibitor. MHRA guidance (2015) advises testing for raised ketones in people with symptoms of diabetic ketoacidosis, even if plasma glucose levels are near normal.

c. Only continue GLP-1 mimetic therapy if the person has a beneficial metabolic response (a reduction of HbA1c by at least 11 mmol/mol [1.0%] and a weight loss of at least 3% of initial body weight in 6 months).

d. Be aware that, if metformin is contraindicated or not tolerated, repaglinide is both clinically effective and cost effective in adults with type 2 diabetes. However, discuss with any person for whom repaglinide is being considered, that there is no licensed non-metformin-based combination containing repaglinide that can be offered at first intensification.

e. Be aware that the drugs in dual therapy should be introduced in a stepwise manner, checking for tolerability and effectiveness of each drug.

f. MHRA guidance (2011) notes that cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for the development of cardiac failure. It advises that if the combination is used, people should be observed for signs and symptoms of heart failure, weight gain, and oedema. Pioglitazone should be discontinued if any deterioration in cardiac status occurs.

g. The recommendations in this guideline also apply to any current and future biosimilar product(s) of insulin glargine that have an appropriate Marketing Authorisation that allows the use of the biosimilar(s) in the same indication.

h. A consultant-led multidisciplinary team may include a wide range of staff based in primary, secondary and community care.

'Type 2 diabetes in adults: management', NICE guideline NG28 (December 2015)

Key guidance

- Type 2 diabetes is main focus of primary care; NG28 is the key guideline for treatment
- TAs mainly relate to SGLT2 class
- PH35 and PH38 also important – key recommendations for prevention and at risk populations
- BNSSG formulary

Insulin Safety

- 5 key principles for safe insulin prescriptions:
  - the date of prescription is clearly written
  - the prescriber's signature and contact details are included
  - both the word 'insulin' and the brand name are written in full
  - the word 'units' is written in full with no abbreviations
  - the form of dosage, ie cartridge, pen or vial, is clearly written.

- How many of these are included on prescriptions in primary care?

Insulin Dosing

- How often do you see 'As required' or 'As directed' on a prescription?
- Who does this help?

- Community pharmacy can contribute by keeping updated records of doses in the PMR
  - This could be accessible by multiple HCPs eg district nurses, GPs, secondary care
  - It can also assist patients especially those that have had a dose change in hospital

Transfer of Care

- Community pharmacy is rapidly becoming a hub of information related to medicines in the transfer of care process

- The use of MURs and NMS reviews mean that the patient and relevant professionals have key interventions highlighted

PharmOutcomes

- Specialist non-medical prescribing teams at BRI will refer patients to community pharmacies directly
- A patient is seen in clinic and/or discharged from an inpatient stay and the diabetes team will share the clinical information with a community pharmacy of the patient's choice, with their consent
- An online referral is completed and it will be up to the community pharmacist as to what to do with the referral.
- What will you do with that referral??

- This can drive a MUR or NMS session. You can check:
  - understanding of indication
  - technique
  - compliance
  - emergence of adverse effects

- But can also:
  - advise on stock/supply/storage to the patient's medicines
  - advise on use of blood glucose monitors etc.

- The referral on the PharmOutcomes system will direct you to a series of questions about the actions you took i.e. Did you conduct an MUR? Where there any adverse effects? Did you raise a yellow card report? These will be no different to the 'standard' transfer of care receipt that you complete already

- Hopefully the referral process will start in the next few months

Breakout Session One

- A patient has been referred to you via PharmOutcomes
- You receive their discharge summary with the following information:
  - Patient AB is 75 years old and has had diabetes for 4 years. He was admitted following a fall and whilst in hospital was referred to the diabetes team as he was having regular hypoglycaemic episodes
  - On admission he was treated with metformin 1g BD, gliclazide 80mg BD and Insulatard 40units ON
  - His prescription has been altered to metformin 1g BD and Insulatard 25 units BD. The gliclazide has been stopped.
  - His insulin has been changed from a 3ml cartridge to a Kwikpen
  - His blood pressure is normal and he has mild renal impairment (eGFR = 50ml/min/1.72m^2)

Breakout Session Two

- A patient has been referred to you via PharmOutcomes
- You receive their clinic letter with the following information:
  - Patient CD is 65 years old and has had diabetes for 8 years. She was seen in secondary care as she has difficult to control type 2 diabetes and has poor control with a HbA1c of 81 mmol/mol
  - Her medication on referral was metformin 850mg TDS, gliclazide 160mg BD and sitagliptin 100mg OM
  - She has high blood pressure (150/96 mmHg) that is not controlled with ramipril 10mg OM and a high BMI (38 kg/m^2). Her renal function is normal
  - At her first visit the diabetes team have decided to switch her sitagliptin to empagliflozin 10mg OM

- What will you do now?
- Do you need any further information to proceed?
- What are the key safety messages to deliver?
- What needs to be documented?
- What CPD do you feel you need to complete to be ready?

New Medications

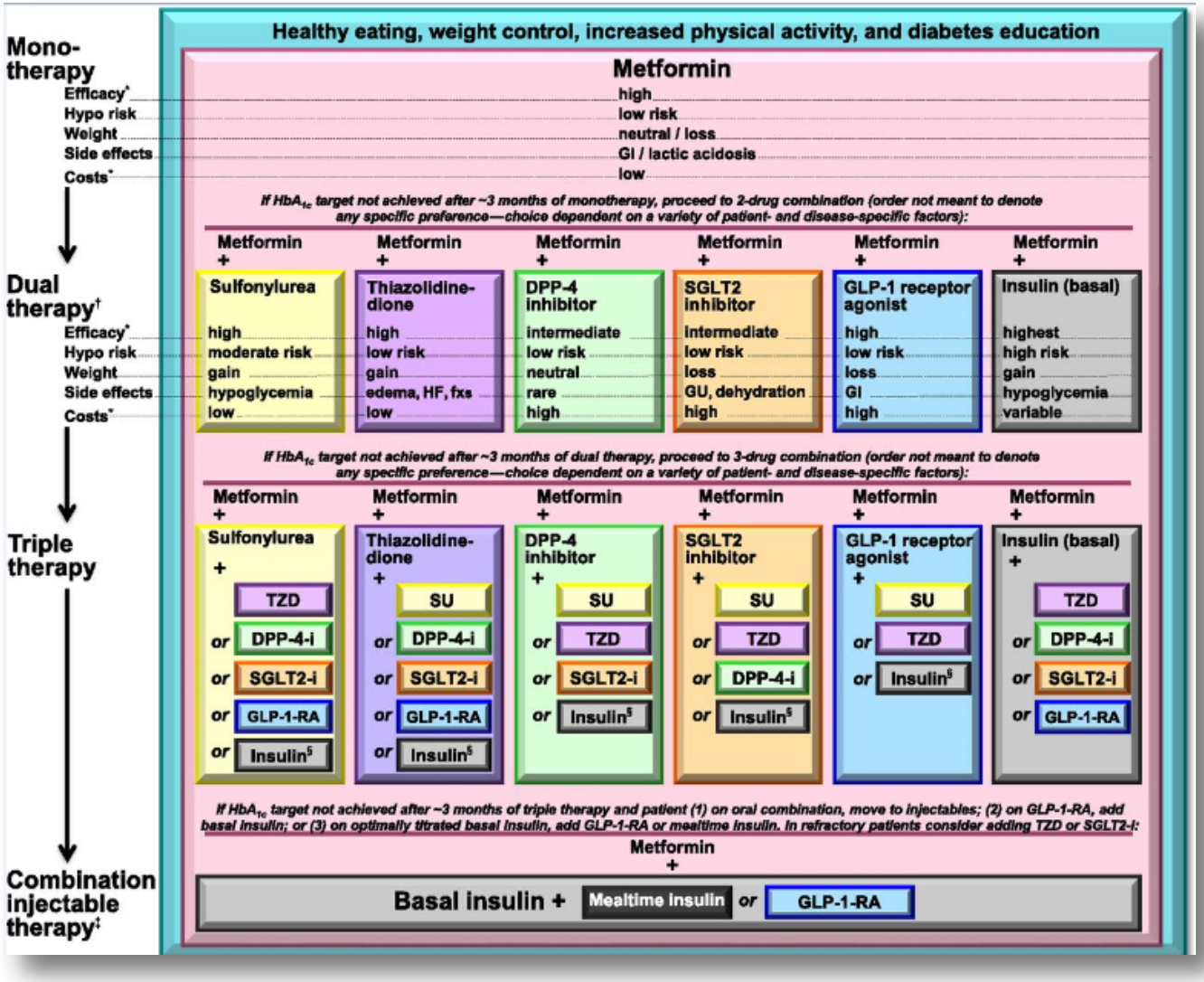
- Since 2010 12 new drugs have been launched including 1 new drug class and 5 new insulins, including 3 concentrated insulin products

- Can you name all of these?
- How relevant is this knowledge to your current practice?
- Would this help to make diabetes treatments safer?

Choosing treatments

- Diabetes is very varied and does not fit an algorithm well (such as with blood pressure)
- Increased medication choice allows individualised decisions to be made
- Medicines optimisation is IDEAL for diabetes and allows us to take account of patient factors at each stage of treatment

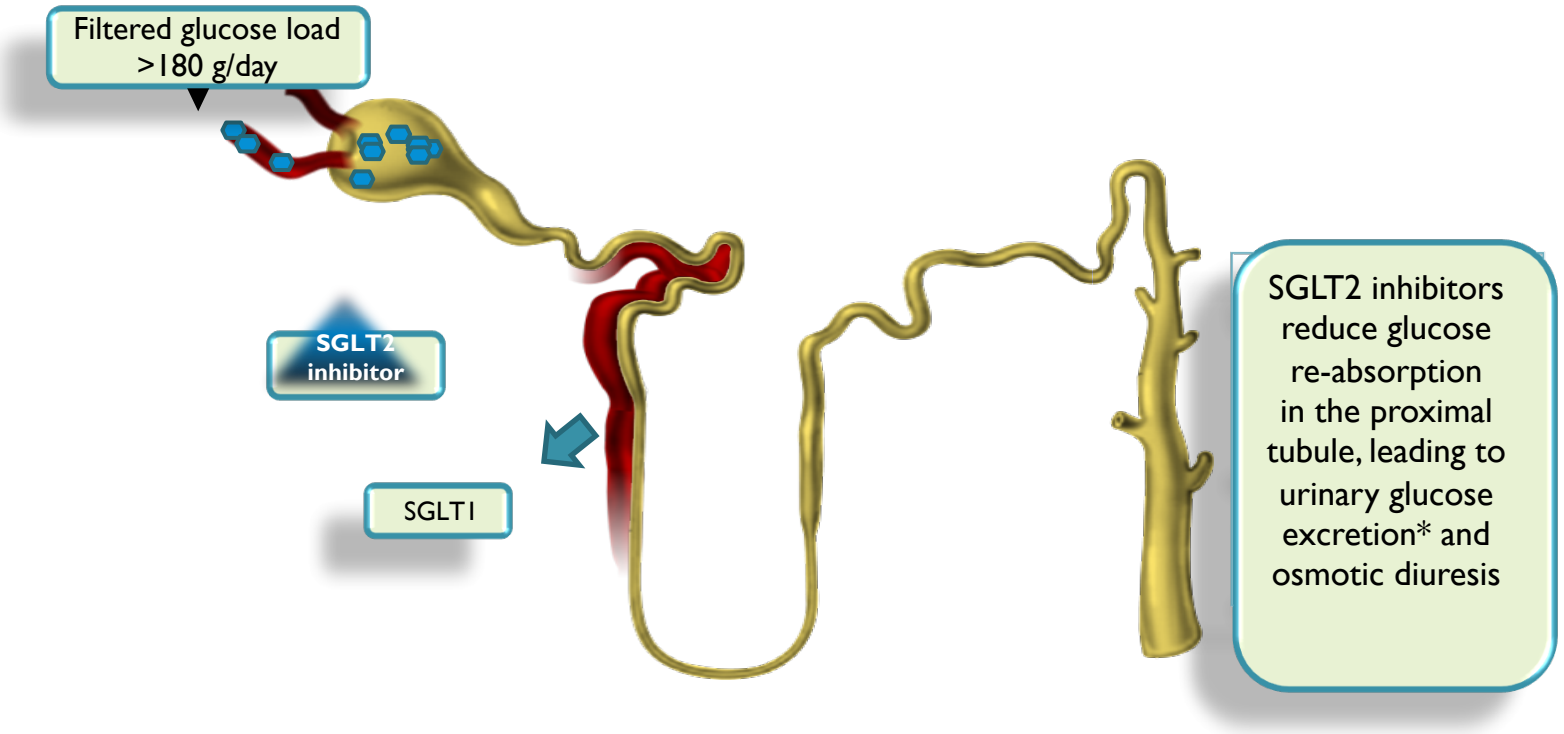
ADA/EASD Guidance



Inzucchi SE. Management of Hyperglycemia in Type 2 Diabetes, 2015: A Patient-Centered Approach: Update to a Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care, 2015; 38(1): 140-149.

SGLT-2 Inhibitors

- The newest class on the market
- Novel mode of action: Urinary glucose excretion via SGLT2 inhibition



Summary of SGLT-2 Inhibitors

	Empagliflozin[1]	Canagliflozin[2]	Dapagliflozin[3]
Recommended starting dose	10 mg once daily	100 mg once daily	10 mg once daily
Uptitration advice (if starting dose is tolerated)	25 mg once daily	300 mg once daily	N/A
Can combine with other standard Tx (& insulin)	Yes	Yes	Yes
Advice when adding to insulin or secretagogues	Consider reducing dose (to lower hypo risk)	Consider reducing dose (to lower hypo risk)	Consider reducing dose (to lower hypo risk)
Can be taken with or without	Yes (at any time of day with or without)	**No (take before 1st meal of day)**	Yes (at any time of day with or without food)
Advice if eGFR <60 mL/min/1.73m^2	Do not initiate Tx Reduce to 10 mg if pt tolerating Tx then falls persistently below	Do not initiate Tx Reduce to 100 mg if a pt tolerating Tx then falls persistently below	Do not initiate Tx **Discontinue if a pt tolerating Tx then falls persistently below**
Advice if eGFR <45 mL/min/1.73m^2	Not recommended	Not recommended	Not recommended
Use in the elderly	No dose adjustment **With caution in ≥75y** Not recommended ≥85y	No dose adjustment With caution in ≥65y	No dose adjustment Not recommended ≥75y

1. Jardiance (empagliflozin) summary of product characteristics; 2. Invokana (canagliflozin) summary of product characteristics; 3. Forxiga (dapagliflozin) summary of product characteristics.

New Insulins

- Concentrated insulin is now widely available:
  - Glargine U300 (Toujeo)
  - Lispro U200 (Humalog)
  - Degludec U200 (Tresiba)
  - Humulin U500 (Humulin R)
- Biosimilar insulin also available:
  - Glargine (Abasaglar)

- What checks are in place to ensure you are providing the correct insulin?

Local guidance

- BNSSG insulin formulary: http://www.bnssgformulary.nhs.uk/includes/documents/BNSSG_Insulin_Formulary%20v3%20update%20July16.pdf

- South west Academic Health Science Network (AHSN) is developing new projects to improve insulin safety

Summary

- This evening we have discussed key safety issues related to diabetes care and the contribution you can make
- We have outlined key guidance to help with making decisions related to diabetes
- We have discussed the latest class of drugs for type 2 diabetes and outlined the newest insulins on the market

Questions??