Wye Valley NHS Trust

Medicines Optimisation Team

NHS Herefordshire Clinical Commissioning Group

Metformin Guidance

July 2016

Room for more metformin?

Lifestyle interventions are key in the prevention and treatment of type 2 diabetes.

When blood glucose is inadequately controlled with these, **metformin** is the first-line hypoglycaemic drug of choice in all patients, particularly those who are overweight (BMI >25kg/m^2).

It is the only oral hypoglycaemic agent that has been shown to reduce macrovascular complications and death. It is also associated with fewer hypoglycaemic attacks than sulfonylureas and does not cause weight gain.

For people in whom metformin is contraindicated or not tolerated, and in patients who are not overweight, a sulphonylurea eg gliclazide standard release is a suitable first-line alternative.

Metformin works mainly by decreasing gluconeogenesis and by increasing peripheral utilisation of glucose. Metformin is only effective if there are some residual functioning pancreatic islet cells. Newer hypoglycaemic drugs are all usually second line options and although effective at reducing HbA1c levels, many lack robust clinical outcome data, particularly around their cardiovascular effects and long term safety in people with type 2 diabetes. Improvements in surrogate markers (e.g. HbA1c levels) do not automatically confer benefits on patient mortality or morbidity and risks may become apparent only over time when these agents have more widespread use in a diverse patient population.

There is large variation of metformin prescribing across Herefordshire GP practices. A national and local QIPP target is to reduce prescribing variation and increase metformin and sulfonylurea use.

Metformin Prescribing tips

- First line choice of treatment for the vast majority of patients with type 2 diabetes
- Consider in all patients with diabetes with residual functioning islet cells
- Reduces cardiovascular events
- Less than 5% of people discontinue metformin because of adverse effects
- Diarrhoea occurs in up to 20%, is dose dependent and may resolve with dose reduction
- The combination of insulin with metformin is associated with significantly less weight gain than seen with twice daily insulin injections or insulin combined with sulfonylureas

Dosing advice

⇒ Start at low dose (500mg daily with or after food) increase by 500mg per day each week to highest tolerated dose up to usual maximum 1g twice daily

⇒ Always advise patient to take tablets with or after food

⇒ If gastrointestinal side effects, reduce back to previously tolerated dose

Modified release metformin may be better tolerated compared to immediate release metformin formulations by some patients.

If patients have persistent GI side effects in spite of slow introduction of the standard formulation, a short trial of modified release metformin ie Sukkarto SR should be considered before using alternative treatments.

The NHS Atlas of Variation shows Herefordshire CCG in the lower 2nd quartile for metformin prescribing across England measured by cost/ATROPU 2015. CCG and practice graphs available

eGFR ml/minute/1.73-m^2	**Action – with respect to renal function in primary care**
< 30	STOP metformin & sulfonylurea
30-45	metformin dose max 1000 mg/day
45+	metformin dose max 2000 mg/day
Information for patients undergoing contrast media investigation	
>60 and **normal** serum creatinine **<60 & high** serum creatinine	No need to stop metformin Any decision to stop for 48hrs to be discussed with referring clinic
Surgery : CONTINUE* * If contrast medium is to be used and eGFR less than 50 mls/min/1.73m2, metformin should be omitted on the day of the procedure and for the following 48 hours.	

Metformin	Strengths Pack size	£ 28 days May 2016	Herefordshire Formulary	Notes / advice
Take with or immediately after a meal to increase insulin sensitivity **May need to stop metformin at times of intercurrent illness i.e. pneumonia and D&V**				
Tablets *Once, twice or three times daily*	**500mg** 28 tabs **850mg** 56 tabs	£0.86 £1.30	Yes	NICE metformin dose stepped up gradually over several weeks to minimise the risk of GI adverse effects (NICE 2015) CKS recommends starting dose of 500mg once a day (with breakfast), increasing by 500mg at intervals of 1–2 weeks according to response. **The recommended daily dosage of metformin is 2g (in divided doses), higher doses provide no additional benefit.**
Modified Release Tablets **Sukkarto SR®** *Once or twice daily* ***(Sukkarto brand costs 35% less than generic MR)***	**500mg** 56 tabs **1g** 56 tabs	£3.46 £5.54	Yes	If gastrointestinal adverse effects prevent the person from continuing metformin treatment, NICE recommends considering a trial of modified release metformin, ie Sukkarto® SR [NICE, 2015]: Weak evidence suggests that switching from standard to modified release metformin may reduce the frequency of gastrointestinal adverse effects
Metformin Solution (Sugar Free)	**500mg/5ml** 150ml	£17.24	Yes	**Reserved** for patients with swallowing difficulties or those with enteral tubes.
Crushing tablets	**Do not crush tablets** since oral solution available or Seek advice from Medicines Information Wye Valley Trust ☎ 01432 364017			

Could this Patient Decision Aid help your discussion with type 2 diabetes patients? NICE NG 28 type 2 diabetes see link

Medicines to help control your blood glucose	**What does taking it Involve?**	**Can it cause hypoglycaemia (hypos)?**	**What is its effect on weight?**	**Other Issues**
Metformin	1 tablet usually taken 2 or 3 times a day	Metformin does not usually make you more or less likely to get hypos. But anyone with type 2 diabetes can get hypos.	Usually no effect or small weight loss	♦ Digestive problems such as nausea, vomiting, diarrhoea, abdominal pain and loss of appetite have been seen in more than 100 people in every 1000 who take metformin. Not everyone gets these problems. They most often happen at the beginning of the treatment and then usually go away. ♦ Changes in the sense of taste have been seen in 10 to 100 people in every 1000 who take it. But 900 to 990 people in every 1000 do not get this problem. ♦ Very rarely, metformin can cause a **blood problem** called lactic acidosis. This may affect fewer than 1 in 10,000 people who take it. Most people do not get this but it is very serious if it occurs. The risk is higher for people with liver or kidney problems, uncontrolled diabetes, prolonged fasting, or dehydration

Review points

➔If patients have had metformin stopped, e.g. after a temporary reduction in renal function whilst in hospital, consider restarting it when appropriate in primary care.

➔If patients have not tolerated metformin, review starting dose of 500mg once a day (with breakfast), increasing by 500mg at intervals of 1–2 weeks according to response or try the modified release preparation Sukkarto® SR.

➔MR preparations can be taken once daily to improve concordance Sukkarto® SR is bioequivalent to Glucophage® SR, at the respective tablet strengths.

➔Prescribing slow release MR metformin by brand Sukkarto® SR costs 35% less than generic MR and can save Herefordshire CCG £50k per year. Generically written prescriptions for metformin MR tablets are charged at the premium Drug Tariff Price.

➔Patients who only take metformin do not need to test their blood glucose and therefore should not be issued with a meter or blood glucose testing strips.

➔Latest guidelines and patient decision aid available at: http://www.herefordshireccg.nhs.uk/diabetes

➔Review patients prescribed glibenclamide (not recommended) and gliclazide MR (on the LPT list) switch to standard release gliclazide [MR 30mg is approx. equivalent to 80mg standard release gliclazide]