



METFORMIN - SAFE PRESCRIBING - FIRST-LINE, GO FOR IT!

- REVIEW DOSES REGULARLY; INCREASE DOSES SLOWLY
- CONSIDER METFORMIN FOR PATIENTS WITH STABLE RENAL FUNCTION
- WITHHOLD METFORMIN PRE AND POST-OPERATIVELY
- MONITOR VITAMIN B₁₂ STATUS IF WARRANTED

Metformin is generally considered first-line for people with type 2 diabetes¹ and is recommended for people with prediabetes.^{2,3} Metformin should be used as an adjunct, not an alternative to lifestyle improvements.¹⁻³

Metformin lowers blood glucose without altering insulin secretion so hypoglycaemia is not a concern and routine blood glucose monitoring is not necessary if metformin is used as monotherapy.⁴

REVIEW DOSES REGULARLY; INCREASE DOSES SLOWLY

When initiating metformin, gradually titrate upwards from a starting dose of 500mg once¹ or twice daily. Emphasise the importance of taking each dose with food to reduce gastrointestinal side effects. Twice daily dosing (rather than three times) is usually more acceptable for compliance. Most people will be adequately controlled with a total daily dose of less than 2g per day,¹ some may require up to 2.5g per day.

Gastrointestinal (GI) intolerance, such as diarrhoea, nausea, vomiting, is the most frequently reported adverse effect, occurring in 5 to 20% of people taking metformin,⁶ especially during the initial treatment period.⁵ These symptoms generally resolve spontaneously, and are usually reduced if metformin is taken with meals or if the dose is increased slowly.^{1,3} A temporary dose reduction can be considered if symptoms are particularly troublesome.⁵

CONSIDER METFORMIN FOR PATIENTS WITH STABLE RENAL FUNCTION

Patients with mild-to-moderate renal impairment may still be prescribed metformin, providing they are considered stable,^{7,8} and metformin is prescribed at reduced dose with renal function monitored closely (3-6 monthly).⁵

- eGFR below 60mL/min/1.73m² reduce metformin dose¹
- eGFR below 30mL/min/1.73m² discuss with a nephrologist or diabetes specialist¹
- eGFR below 15mL/min/1.73m² metformin contraindicated^{5,9}

Review treatment during acute conditions which can alter renal function, such as dehydration, severe infection, or shock.¹⁰ Advise to either temporarily withhold metformin in these circumstances, or to seek advice from their GP.

Note: Recent evidence suggests that metformin is not associated with an increased risk of lactic acidosis compared to other antihyperglycemic treatments.^{8,11}

WITHHOLD METFORMIN PRE AND POST-OPERATIVELY

Because surgery and fasting for surgery can lead to dehydration and hypoxaemia⁵ it is advisable to withhold metformin temporarily.

For elective surgery, metformin should be withheld on the day of surgery, and restarted when eating and drinking has resumed.¹⁰ For radiological studies, metformin should be withheld from 48 hours prior to the procedure until 2 days after. For emergency procedures, stop metformin on admission and reinstate when renal function returns to normal.⁵

Monitor glucose levels closely in the post-operative period; short-term insulin therapy may be needed.⁵

MONITOR VITAMIN B₁₂ STATUS IF WARRANTED

Vitamin B_{12} deficiency is associated with diabetes, and long term use of metformin can also reduce B_{12} absorption.⁵ If there are concerns, or symptoms of anaemia or peripheral neuropathy occur, check vitamin B_{12} levels.¹² If a deficiency is detected, consider vitamin B_{12} supplementation.¹³

1





METFORMIN

Metformin during pregnancy and breastfeeding

Pregnancy catergory C

Abnormal blood glucose levels during pregnancy can lead to congenital abnormalities. Insulin may be used to maintain blood glucose levels as close to normal as possible,⁵ but oral options are usually more acceptable. Metformin is increasingly being used in clinical practice now there is data to support its use.^{14,15}

NICE guidelines for diabetes in pregnancy recommend that metformin should be offered to women with gestational diabetes if blood glucose targets are not met using changes in diet and exercise within 1-2 weeks. Insulin should be offered if metformin is contraindicated or unacceptable.¹⁶

Note: Women with gestational diabetes should discontinue their hypoglycaemic treatment after giving birth.^{10,16}

Use in lactation

Metformin is excreted into breast milk, but the amounts seem to be clinically insignificant.¹⁷ NICE guidelines recommend that pregnant women taking metformin with *pre-existing* type 2 diabetes, may continue with it immediately following birth even if they are breastfeeding.¹⁶ Metformin should be used with caution if breastfeeding premature infants due to their immature renal function ACKNOWLEDGEMENTS We wish to thank Dr Catherine McNamara and Dr Rick Cutfield, Diabetes Specialists, and Elizabeth Brookbanks, Clinical Pharmacist, at Waitemata DHB for their valuable contribution to this bulletin.

REFERENCES

- Moore P. Improving glycaemic control in people with type 2 diabetes: Expanding the primary care toolbox. Best Practice Journal 2013;53:6-15 <u>www.bpac.org.nz/BPJ/2013/</u> <u>June/diabetes.aspx</u> (Accessed 03-03-16)
- Ministry of Health. Pre-diabetes advice 2013. <u>www.hiirc.org.nz/page/41850/prediabetes-advice-a-summary-of-current/</u> [Accessed 27-07-16]
- Auckland Regional Health Pathways. Prediabetes. <u>http://aucklandregion.</u> <u>healthpathways.org.nz/index.htm</u> (Accessed 27-07-16)
- Self monitoring blood glucose (SMBG) for type 2 diabetes. Best Practice Advisory Centre, New Zealand. <u>www.bpac.org.nz/resources/reports/2010/bpac_smbg_report_2010.pdf</u> (Accessed 15-03-16)
- Mylan New Zealand Limited. Metformin hydrochloride, film coated tablets. Data Sheet. 18-01-16. <u>www.medsafe.govt.nz/profs/datasheet/m/MetforminMylantabs.pdf</u> (Accessed 04-03-16)
- Dury P. HbA1c targets in people with type 2 diabetes do they matter? Best Practice Journal 2010;30:8-15 <u>www.bpac.org.nz/magazine/2010/august/docs/BPJ_30_hba1c_pages8-15_pf.pdf</u> (Accessed 15-03-16)
- Inzucchi SE, Bergenstal RM, Buse JB et al. 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;38-140-49 <u>http://care.diabetesjournals.org/content/ diacare/38/1/140.full.pdf</u> [Accessed 12-08-16]
- Lu WR, Defilippi J, Braun A. Unleash metformin: reconsideration of the contraindication in patients with renal impairment. Annals of Pharmacotherapy 2013;47[11]:1488-97
- New Zealand Medicines and Medical Devices Safety Authority [Medsafe]. Metformin Renal impairment and risk of lactic acidosis. Prescriber Update 2015;36(4):56-7 <u>www.medsafe.govt.nz/profs/puarticles/December2015/Metformin.htm</u> [Accessed 15-03-16]
 New Zealand Cardina Medical Devices in budge obligition unconfigure of an article 15-03-16]
- New Zealand Formulary. Metformin hydrochloride <u>www.nzf.org.nz/nzf_3715.</u> <u>html?searchterm=metformin</u> [Accessed 15-03-16]
 Chloride CD, Orende CD, Orende CD, Chloride CD, Chloride CD, Orende CD, Chloride CD, Orende CD, Chloride CD, Chloride
- Salpeter SR, Greyber E, Pasternak GA, Salpeter EE. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. Cochrane Database of Systematic Reviews 2010; Apr 14(4):CD002967 <u>www.cochrane.org/CD002967/END0C</u><u>risk-of-fatal-and-nonfatal-lactic-acidosis-with-metformin-use-in-type-2-diabetesmellitus</u> [Accessed 12-08-16]
- Gow D, Moore P. Assessing diabetic peripheral neuropathy in primary care. Best Practice Journal 2014;61:36-47 <u>www.bpac.org.nz/BPJ/2014/June/diabetic-peripheral-neuropathy.aspx</u> (Accessed 15-03-16)
- Houghton L. Vitamins and minerals: dietary sources, supplements and deficiencies. Best Practice Journal 2008;15:32-41 <u>www.bpac.org.nz/magazine/2008/august/docs/</u> <u>bpj15_vitamins_pages_32-41_pf.pdf</u> (Accessed 15-03-16)
- Rowan JA, Hague WM, Gao W et al for the MiG Trial Investigators. Metformin versus insulin for the treatment of gestational diabetes. New England Journal of Medicine 2008;358:2003-15 <u>www.smschile.cl/documentos/NEJM/diabetes/articulo2.pdf</u> (Accessed 15-03-16)
- Balsells M, Garcia-Patterson, Sola I et al. Glibenclaminde, metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis. British Medical Journal 2015;350:h102. <u>www.bmj.com/content/350/bmj.h102</u> (Accessed 15-03-16)
- 16. Diabetes in pregnancy. Management of diabetes and its complications from preconception to the postnatal period. NICE (National Institute for Health and Clinical Excellence) Clinical Guidelines 2015. National Collaborating Centre for Women's and Children's Health. <u>www.nice.org.uk/guidance/ng3</u> (Accessed 15-03-16)
- Children's Health. <u>www.nice.org.uk/guidance/ng3</u> [Accessed 15-03-16]
 17. Briggs GG, Ambrose PJ, Nageotte MP, Padilla G, Wan S. Excretion of metformin into breast milk and the effect on nursing infants. Obstetrics and Gynecology. 2005;105(6):1437-41.

For further information on other high-risk medicines visit our website at: www.saferx.co.nz

No: 0182-01-096, Issued October 2016, Review October 2019

DISCLAIMER: This information is provided to assist primary care health professionals with the use of prescribed medicines. Users of this information must always consider current best practice and use their clinical judgement with each patient. This information is not a substitute for individual clinical decision making. Issued by the Quality Use of Medicines Team at Waitemata District Health Board, email: feedback@saferx.co.nz