

Prescribing tip for actioning by Practice

Metformin and reduced vitamin B12 levels: new advice for monitoring patients at risk



Decreased vitamin B12 levels are a known consequence of long-term treatment with metformin. The mechanism is currently thought to be multifactorial, comprising altered intestinal motility, bacterial overgrowth and reduced uptake of vitamin B12 within the small intestine.

This is an especially common side-effect in those receiving a [higher dose or longer treatment duration and in those with existing risk factors](#). The MHRA are therefore advising checking vitamin B12 serum levels in patients being treated with metformin who have symptoms suggestive of vitamin B12 deficiency and that periodic monitoring for patients with risk factors for vitamin B12 deficiency should be considered.¹

Risk factors for vitamin B12 deficiency:

- baseline vitamin B12 levels at the lower end of the normal range
- conditions associated with reduced vitamin B12 absorption (such as elderly people and those with gastrointestinal disorders such as total or partial gastrectomy, Crohn's disease and other bowel inflammatory disorders, or autoimmune conditions)
- diets with reduced sources of vitamin B12 (such as strict vegan and some vegetarian diets)
- concomitant medication known to impair vitamin B12 absorption (including proton pump inhibitors or colchicine)
- genetic predisposition to vitamin B12 deficiency, such as intrinsic factor receptor deficiency (Imerslund-Gräsbeck syndrome) and transcobalamin II deficiency

Symptoms of vitamin B12 deficiency - Patients with a vitamin B12 deficiency can be asymptomatic or they can present with symptoms of megaloblastic anaemia or neuropathy or both. Other [symptoms of low vitamin B12 levels](#) may include mental disturbance (depression, irritability, cognitive impairment), glossitis (swollen and inflamed tongue), mouth ulcers, and visual and motor disturbances. It is important for patients with anaemia or neuropathy caused by vitamin B12 deficiency to be diagnosed and treated as soon as possible to avoid the development of permanent symptoms.

Advice for healthcare professionals:

- metformin can commonly reduce vitamin B12 levels in patients, which may lead to vitamin B12 deficiency
- the risk of low vitamin B12 levels increases with higher metformin dose, longer treatment duration and in patients with risk factors for vitamin B12 deficiency
- test vitamin B12 serum levels if deficiency is suspected (for example, in patients presenting with megaloblastic anaemia or new-onset neuropathy) and follow current clinical guidelines on investigation and management of vitamin B12 deficiency (for example, see [Clinical Knowledge Summary from NICE](#))
- consider periodic vitamin B12 monitoring in patients with risk factors for vitamin B12 deficiency (see list of risk factors in article)
- administer corrective treatment for vitamin B12 deficiency in line with current clinical guidelines; continue metformin therapy for as long as it is tolerated and not contraindicated
- report suspected adverse drug reactions associated with metformin on a [Yellow Card](#)

Advice for healthcare professionals to give to patients and carers:

- if you are taking metformin, seek medical advice if you develop new or worsening symptoms of extreme tiredness, a sore and red tongue, pins and needles, or pale or yellow skin – these can be signs of low vitamin B12 levels
- you may need blood tests to find out the cause of your symptoms; these symptoms can also be caused by diabetes or other unrelated health issues
- you can keep taking metformin while vitamin B12 levels are being corrected
- do not stop your treatment without first discussing this with your doctor

Reference 1. [Metformin and reduced vitamin B12 levels: new advice for monitoring patients at risk - GOV.UK \(www.gov.uk\)](#) accessed 22/6/22.

To contact the Medicines Optimisation Team please phone 01772 214302

If you have any suggestions for future topics to cover in our prescribing tips please contact Nicola.schaffel@nhs.net

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