



## Intolerance and contraindications to metformin



This page contains additional content about the article *Pioglitazone (Actos) for type 2 diabetes mellitus*, published in NPS RADAR, April 2008.

### Gastrointestinal adverse effects

Diarrhoea, nausea and abdominal bloating are common with metformin<sup>15</sup> and are dose related.

Often transient: although they are reported to occur in 20–30% of patients, fewer than 5% of patients need to discontinue metformin.<sup>15</sup>

Minimise by:

- administering metformin with food, and
- starting with a low dosage (e.g. metformin 250–500 mg once daily), gradually increasing the dosage according to effect and tolerance.<sup>30</sup>

### Renal impairment

Opinions vary on the degree of renal impairment at which metformin should not be used.

Estimating an individual's creatinine clearance is a more accurate measure of renal function than serum creatinine concentration. Use the Cockcroft—Gault equation to estimate creatinine clearance:

Creatinine clearance (mL/min) =	(140 – age [years]) ( bodyweight (kg)
	815 ( serum creatinine (mmol/L)

Use either actual or ideal bodyweight, whichever is lower. For females, multiply the result of the equation by 0.85. This approach is invalid in severe renal insufficiency or with rapidly changing renal function.

Metformin should be avoided or discontinued when creatinine clearance is < 30 mL/min, and used with extreme caution when creatinine clearance is 30–50 mL/min (the dosage should not exceed 1 g/day in these patients).<sup>31</sup>

## Lactic acidosis

Lactic acidosis is a rare adverse effect of metformin (three cases per 100,000 patient–years<sup>32</sup> but serious when it does occur with fatality in up to 50% of cases.<sup>30,31</sup>

A Cochrane review did not find a single case of lactic acidosis reported in trials (n = 206) with more than 47,000 patient–years of metformin use despite many of the trials including some patients with at least one contraindication to metformin use.<sup>33</sup>

In most cases of lactic acidosis with metformin reported to the Australian Adverse Drug Reactions Advisory Committee, known risk factors were identified.<sup>30</sup> Risk factors for lactic acidosis include:

- reduced renal function (including that due to surgery, dehydration or use of contrast media)
- old age
- metformin doses in excess of 2 g daily
- cardiac or hepatic impairment.<sup>32</sup>

## References

References for this article are found on the page *Pioglitazone (Actos) for type 2 diabetes mellitus*, from NPS RADAR April 2008. URL: [http://nps.clients.squiz.net/health\\_professionals/publications/nps\\_radar/issues/current/april\\_2008/pioglitazone](http://nps.clients.squiz.net/health_professionals/publications/nps_radar/issues/current/april_2008/pioglitazone)

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