

## BNF case study

A 57 year old man is being treated for type 2 diabetes, heart failure, and stable angina. Over the last 3 years he has managed to lose 15kg in weight and now has a body mass index of 26kg/m<sup>2</sup>. His U & Es and renal function are normal.

Blood pressure = 120/78mmHg  
HbA<sub>1c</sub> = 9.1%  
Fasting blood glucose = 7.9mmol/litre

His medication regimen is:  
Aspirin 75 mg daily  
Isosorbide mononitrate MR 60 mg daily  
Simvastatin 40 mg each night  
Ramipril 1.25 mg daily  
Furosemide 80 mg each morning  
Metformin 1 g twice daily  
Gliclazide 160 mg twice daily  
Glyceryl trinitrate spray as required

He is committed to taking his drug treatment and you do not suspect non-compliance. In the past he has been unable to tolerate acarbose.

### Is it reasonable to add pioglitazone or rosiglitazone to this patient's drug therapy?

This patient's glycosylated haemoglobin concentration and fasting blood glucose concentrations remain high despite maximum doses of metformin and gliclazide.

The prescribing notes in section 6.1.2.3, BNF 55, state that inadequate response to a combination of metformin and sulphonylurea may indicate failing insulin release; the introduction of pioglitazone or rosiglitazone has a limited role in these circumstances and the initiation of insulin is more appropriate. Long-term benefits of the thiazolidinediones have not yet been demonstrated.

BNF 55 provides a summary of the MHRA/CHM's cardiovascular safety advice on these drugs. Pioglitazone and rosiglitazone are contra-indicated in this patient with heart failure. Furthermore, rosiglitazone may be associated with a small increased risk of cardiac ischaemia and is not recommended in this patient who also has stable angina.

### How should this patient's type 2 diabetes be treated?

The long-term safety and benefits of new drugs such as exenatide are unclear. A long-acting insulin such as insulin glargine or insulin detemir should be prescribed—weight gain is minimised if the insulin is administered at night. In this patient who is overweight, gliclazide and metformin should be continued initially with a view to reducing the dose of gliclazide and eventually withdrawing gliclazide.

**Ramipril and furosemide were started in this patient 4 months ago following a diagnosis of left ventricular systolic dysfunction. His left ventricular ejection fraction at the time was 32%. Today he is complaining of breathlessness 20 minutes after walking and finds it difficult to walk up hills.**

**How can you optimise this patient's treatment of heart failure?**

The patient is still taking the starting dose of ramipril. The prescribing notes on Heart Failure in section 2.5.5, BNF 55, advise that the ACE inhibitor should be titrated to a 'target dose' (or the maximum tolerated dose if lower). The ramipril monograph shows that the dose should be increased gradually at intervals of 1–2 weeks to a target dose of 10 mg daily if tolerated. The blood pressure must be monitored regularly as the dose is increased. Renal function and electrolytes should also be monitored during treatment.

**The ramipril is titrated gradually to 5 mg twice daily. The patient is no longer complaining of breathlessness. Which other drug should be added to his medication regimen for heart failure?**

The prescribing notes on Heart Failure in section 2.5.5, BNF 55, recommend that the beta-blockers, bisoprolol or carvedilol, are of value in any grade of stable heart failure and left ventricular systolic dysfunction. While his heart failure appears stable, he should be started on either bisoprolol or carvedilol cautiously.

**How should you initiate bisoprolol in this patient?**

Bisoprolol should be started at a very low dose and titrated very slowly over a period of weeks or months. Symptoms may deteriorate initially, calling for adjustment of concomitant therapy. His heart rate, blood pressure, and clinical status should be reviewed after each titration. Full details of the dose regimen can be found in the drug monograph.

**What impact might bisoprolol have on this patient's stable angina?**

The prescribing notes on Angina in section 2.6, BNF 55, advise that beta-blockers are effective in the treatment of stable angina. A long-acting nitrate is used if the beta-blocker is not tolerated or contra-indicated. As the bisoprolol is gradually titrated to a target dose of 10 mg daily, you should try to discontinue the isosorbide mononitrate.

**What impact might bisoprolol have on this patient's diabetes?**

The prescribing notes on Beta-blockers, in section 2.4, BNF 55, do not contra-indicate them in diabetes; however, they can lead to a small deterioration of glucose tolerance and interference with metabolic and autonomic responses to hypoglycaemia. This is less likely to happen with cardio-selective beta-blockers such as bisoprolol.