NHS
North Cumbria Integrated Care
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# Prescribing and monitoring guidelines for METOLAZONE in patients with severe heart failure

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| **Indication** | **Metolazone is an unlicensed medication used in the treatment of heart failure.**<br><br>Patients with heart failure can gradually become resistant to oral loop diuretics e.g. furosemide or bumetanide despite increasing doses. In addition as heart failure progresses patients can develop renal dysfunction with decrease of GFR. Frequently patients need to be admitted to hospital to start IV diuretics. Hospitalisation is costly and distressing to the patients and their families.<br><br>Metolazone frequently succeeds in inducing diuresis, even at low GFR when given in combination with loop diuretics. In some scenarios it can prevent hospital admission.<br><br>The North of Tyne formulary recommends High dose bendroflumethiazide or intermittent metolazone, in combination with a loop diuretic such as furosemide in order to achieve a significant diuresis. Most Cardiologists and Physicians find metolazone an useful adjunct for provoking a diuresis in conjunction with a loop diuretic.<br><br>Ref: North of Tyne Heart Failure guidance http://www.northoftyneapc.nhs.uk/wp-content/uploads/sites/6/2017/04/Heart-Failure-GL-Revised-Mar-2017.pdf |
| **Dose & Administration** | Recommended starting dose is 2.5 mg orally once or twice a week and titrating to a maximum of 5mg/day **if** necessary. If changes in dose are necessary these are to be communicated to the GP via the community heart failure team.<br><br>**Please note: Metolazone is currently no longer available as a licensed product in the UK. Unlicensed imports of metolazone are available as a "special" but difficulties in obtaining supplies have been reported. Metolazone should be reserved for treatment following specialist advice and initiation with initial supply by secondary care.** |
| **Contra-indications** | • Refractory Hypokalaemia.<br>• Symptomatic hyperuricaemia.<br>• Severe Renal or Hepatic impairment.<br>• Acute porphyrias.<br>• Contraindicated in Pregnancy<br>• The British National Formulary states amount present in milk is too small to be harmful. Large doses may suppress lactation. |
| **Drug Interactions** | • Hypokalaemia caused by thiazides and related diuretics increases cardiac toxicity with cardiac glycosides, flecainide, lidocaine, disopyramide, sotalol.<br>• Hypokalaemia caused by diuretics increases risk of ventricular arrhythmias with amisulpride, atomoxetine, pimozide (avoid concurrent use with pimozide).<br>• Increased risk of hypokalaemia when given with reboxetine.<br>• Increased risk of hyponatraemia other sodium lowering medications.<br>• Increases the risk of hypersensitivity reactions when given with allopurinol.<br>• Increases the risk of hypercalcaemia when given with calcium salts, vitamin d substances and toriemifene.<br>• Hypokalaemia caused by thiazides and related diuretics antagonises action of lidocaine (less likely with topical lidocaine).<br>• Thiazides and related diuretics reduce excretion of lithium (increased plasma concentration and risk of toxicity).<br>• Enhanced hypotensive effect when diuretics given with ACE inhibitors, alpha-blockers, angiotensin-II receptor antagonists.<br>• Diuretics increase risk of nephrotoxicity of NSAIDs, also antagonism of diuretic effect. |
| **Adverse Effects** | • **Symptomatic Hypotension** (Systolic pressure < 90 mmHg associated with dizziness, fainting, confusion) - Check blood chemistry to exclude other causes for symptoms, consider reduction in diuretic therapy if clinically stable – discuss with |

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| | community heart failure team.<br>• **Worsening Symptoms** (increased dyspnoea, fatigue, oedema, weight gain) - contact community heart failure team to discuss increasing dose.<br>• **Hypovolaemia**- Consider reducing dose or most often stopping diuretics and discuss with community heart failure team.<br>• **Hypokalaemia-** If potassium level < 3 mmol/L (or <4 mmol/L in high-risk people), ensure patient is reviewed urgently to prevent potassium falling lower and requiring admission to hospital for urgent replacement. Consider increasing dose of ACE inhibitor or add spironolactone - discuss with community heart failure team if available. If these options have been done, give potassium supplements: Sando K 24mmol three times a day until potassium is >4mmol/l (usually for approximately 3 days and beware that levels will continue to rise once supplements have been discontinued). Potassium levels should be rechecked on a 24-48hourly basis until >4mmol/L. Then repeat U&Es within 7days.<br>• People at high risk of cardiac arrhythmias with even mild hypokalaemia include:<br>o Those taking digoxin or drugs that prolong the QT interval (such as amiodarone).<br>o Those with paroxysmal arrhythmias, unstable angina, or chronic liver disease.<br>**If potassium concentration < 2.5 mmol/L (or 3.5 mmol/L in high-risk people) – admit patient to hospital for urgent potassium replacement.**<br>• **Hyponatraemia- If** sodium less than 131mmol/L consider reduction in diuretic therapy and discuss with community heart failure team.<br>• **Worsening renal function** –<br>o If the serum creatinine level increases by more than 20% of baseline or the eGFR decreases by more than 15% of baseline<br>▪ **measure renal function within 3 days to ensure it has not deteriorated further.**<br>o If creatinine increases by 30–50% (or to greater than 200 micromol/L) or eGFR is less than 30 mL/min/1.73 m2 –<br>▪ **urgently review volume status**<br>▪ **reduce dose or stop diuretics (especially if the person is hypovolaemic**)<br>▪ **contact the community heart failure team.**<br>▪ **measure renal function within 3 days.**<br>o If creatinine increases by more than 50% (or to greater than 256 micromol/L) or eGFR approximately 20–25 mL/min/1.73 m2<br>▪ **Assess volume status (usually the person will be hypovolaemic in this scenario)**<br>▪ **check blood pressure**<br>▪ **review other renal function tests, including electrolytes and proteinuria**<br>▪ **stop the diuretic**<br>▪ **Contact community heart failure team urgently.** |
| **Monitoring** | **Before treatment:**<br>• Urea and electrolytes (U&Es), patient weight, blood pressure and creatinine.<br>**During treatment:**<br>• Urea and electrolytes (U&Es) and creatinine within 7 days of starting treatment and recheck every 7-14 days initially depending on the person's stability. Once treatment is stable, i.e. same renal function three weeks in a row measure renal function and serum electrolytes at least once every month. Patients on metolazone for palliative reasons need less frequent monitoring.<br>• Patients should be weighed or encouraged to self-weigh daily. Aim for weight loss 0.5-1 Kg/day. More than that should prompt decreasing dose and/or earlier checking of U & E.<br>•Blood pressure should be monitored and checked at least monthly.<br>**Blood tests will be carried by the patient's usual GP. Abnormal results will be reported to and discussed with the heart failure consultant (Dr Ibrahim) or cardiology consultant on call as appropriate/ available Tel: 01228 814034 or 814270 and/ or GP. Any changes made to medication or requests are to be communicated to the GP.** |