Amber with Guidance (Amber-G) = To be recommended or initiated by a specialist with follow up prescribing and monitoring by primary care clinicians.*
**Specialist is defined by the APC as a clinician who has undertaken an appropriate formal qualification or recognised training programme, or who has the appropriate knowledge and competencies within the described area of practice.*

NHS Barnsley Hospital NHS Foundation Trust | NHS South West Yorkshire Partnership NHS Foundation Trust | NHS Barnsley Clinical Commissioning Group

Metolazone (Xaqua®) for Oedema

Please note that Xaqua® holds a UK product license and should be product of choice for new patients.

Whilst this guideline replaces the previous guideline for the use of Zaroxolyn® and Metenix® (unlicensed imports), the doses of the preparations are not interchangeable and patients should be maintained on their usual brand where possible. Contact specialist teams and/or Medicines Information if advice is need on switching brands.

Background Information	• A specialist should initiate metolazone the treatment of oedema and supply the first prescription. It should then be communicated to primary care in writing via the discharge letter or clinic letter.
BNF therapeutic class	• Thiazides and related diuretics.
Indication	• Metolazone is licensed for the treatment of oedema and hypertension. • As a quinazoline diuretic, it has properties generally similar to the thiazide diuretics. The action of metolazone results from interference with the renal tubular mechanism of electrolyte reabsorption. When it is given, diuresis and saluresis usually begin within one hour and persist for 24 hours depending on the dose. The effect may be prolonged beyond 24 hours particularly at higher recommended dosages.
Dosage and administration	Once the desired therapeutic effect has been achieved, it is recommended to reduce the maintenance dose if possible. **Xaqua®** • 2.5mg – 5mg daily orally. The dose should be taken in the morning. • Xaqua® is available as 5mg tablets. **Zaroxolyn® and Metenix®** • 5-10mg daily orally. The dose should be taken in the morning, increased if necessary to 20mg daily. • Zaroxolyn® is available as 2.5mg and 5mg tablets. • Metenix® is available as 5mg tablets (may be difficult to obtain)
Cautions and Contraindications	**Contraindications:** • Hypersensitivity to the active ingredients, sulphonamides, thiazides or any of the listed excipients. • Anuria • Hepatic coma or precomatose conditions • Severe electrolyte disturbances **Cautions:** • Diabetes • Gout • Addison's disease • Risk of electrolyte imbalances • Elderly patients • Severe renal impairment • Severe hepatic impairment

	Cautions – Further Information: **Existing conditions:** • Thiazides and related diuretics can exacerbate diabetes, gout, and systemic lupus erythematosus **Potassium loss:** • Hypokalaemia can occur with thiazides and related diuretics. • Hypokalaemia is dangerous in severe cardiovascular disease and in patients also being treated with cardiac glycosides. Often the use of potassium-sparing diuretics avoids the need to take potassium supplements. • In hepatic impairment, hypokalaemia caused by diuretics can precipitate encephalopathy. **Elderly:** • Manufacturer advises lower initial doses of diuretics may be necessary in the elderly because they are particularly susceptible to the side-effects. The dose should be then adjusted according to renal function. **Prescription potentially inappropriate (STOPP criteria):** • With current significant hypokalaemia (serum potassium less than 3mmol/L), hyponatremia (serum sodium less than 130mmol/L) or hypercalcemia (corrected serum calcium greater than 2.65mmol/L) – hypokalaemia, hyponatraemia and hypercalcemia can be precipitated by a thiazide diuretic. • With a history of gout (gout can be precipitated by a thiazide diuretic). **Renal Impairment:** • In general, manufacturers advise cation in mild to moderate impairment (risk of electrolyte imbalance and reduced renal function) • The manufacturer advises metolazone remains effective if eGFR is less than 30mL/minute/1.73m2 but is associated with a risk of excessive diuresis. **Hepatic Impairment:** • In severe hepatic impairment, hypokalaemia caused by diuretics can precipitate encephalopathy. • In patients with alcoholic cirrhosis there is an increased risk of hypomagnesaemia.
Pregnancy and breast feeding	**Pregnancy:** • Thiazides and related diuretics should not be used to treat gestational hypertension. They may cause neonatal thrombocytopenia, bone marrow suppression, jaundice, electrolyte disturbances, and hypoglycaemia; placental perfusion may also be reduced. Stimulation of labour, uterine inertia, and meconium staining have also been reported. **Breast feeding:** • Metolazone passes into breast milk in such an amount that there is a risk for the baby, even at therapeutic doses. • Diuretic treatment may supress lactation.
Adverse Drug Reactions	**Common or very common:** • Alkalosis hypochloraemic; constipation; diarrhoea; dizziness; dry mouth; electrolyte imbalance; fatigue; headache; hyperglycaemia; hyperuricaemia; nausea; vomiting; azotaemia; glycosuria; increased serumm creatinine and blood urea nitrogen (BUN); postural hypotension; muscle pain/cramps. **Uncommon:** • Leucopenia; exanthema (including urticaria); vasculitis; joint pain; gout.

	Rare or very rare: • Allergic reactions (including anaphylaxis); aplastic or hypoplastic anaemia; agranulocytosis; thrombocytopenia; hypercalcaemia; hypophosphataemia; neuropathy, vertigo; paraesthesia; lethargy; drowsiness; weakness; restlessness; apathy; seizures; hepatic encephalopathy; transient blurred vision; tachycardia; chest pain; palpitations; syncope; dehydration; haemoconcentration; venous thrombosis; abdominal pain; anorexia; abdominal bloating; hepatitis; intrahepatic cholestasis; pancreatitis; toxic epidermal necrolysis (TEN); Stevens-Johnson syndrome (SJS); purpura; photosensitivity; renal insufficiency; oliguria; erectile dysfunction; chills; increased LDL cholesterol; increase triglycerides. **Choroidal effusion, acute myopia and secondary angle-closure glaucoma** Sulfonamide or sulfonamide derivative drugs can cause an idiosyncratic reaction resulting in choroidal effusion with visual field defect, transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of drug initiation. Untreated acute angle-closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue drug intake as rapidly as possible. Prompt medical or surgical treatments may need to be considered if the intraocular pressure remains uncontrolled. Risk factors for developing acute angle-closure glaucoma may include a history of sulfonamide or penicillin allergy. **Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme: www.mhra.gov.uk/yellowcard**
Monitoring	• Electrolytes should be monitored, particularly with high doses and long-term use. • U&Es should ideally be checked three days after any dose adjustment, and then fortnightly for 1 month (which will be performed by the hospital team or the community heart failure team). • Monitor U&Es **every 3-6 months** once the patient is stabilised on treatment. • Rarely, the rapid onset of severe hyponatremia and/or hypokalemia has been reported following the initial dose, when symptoms consistent with severe electrolyte imbalance appear rapidly, the drug should be discontinued and supportive measures should be initiated immediately.
Interactions	• Common interactions can be found in the links to the BNF and drug monograph above.
Additional information	**Patient advice:** • Warning signs of electrolyte imbalance irrespective of cause are: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia and gastrointestinal disturbances such as nausea and vomiting. • Patients experiencing eye pain and/or reduced visual acuity should seek urgent medical advice.

Contact names and details

Contact Details	Telephone number	Email
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BHNFT Medicines Information team	01226 432857	medicine.information1@nhs.net

References

- BNF Metolazone
- Xaqua SmPC accessed online via Xaqua 5 mg Tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
- Zaroxolyn SmPC (Canada) accessed online via zaroxolyn (sanofi.ca)

https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

Development Process

This guidance has been produced by Gillian Turrell, Lead Pharmacist, Medicines Information and Cardiology following an AMBER-G classification status of Metolazone by the Barnsley Area Prescribing Committee. This guideline was ratified by the Area Prescribing Committee on 12th June 2024.