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 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 for Oedema

The details of side-effects, cautions, contraindications and interactions are not a complete list and the current BNF (MedicinesComplete — CONTENT > BNF > Drug: Metolazone) and the Drug Monograph (https://products.sanofi.ca/en/zaroxolyn.pdf) remain authoritative.

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	• It is licensed for the treatment of oedema and hypertension. • Zaroxolyn (the brand of metolazone used at BNHFT) is a quinazoline diuretic, with properties generally similar to the thiazide diuretics. The action of Zaroxolyn result 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	• 5-10mg daily orally. The dose should be taken in the morning, increased if necessary to 20mg daily. • In resistant oedema, the dose can be increased to a maximum of 80mg daily. • The tablets are available as 2.5mg and 5mg tablets.
Cautions and Contraindications	**Contraindications:** • Addison's disease • Hypercalcaemia • Hyponatremia • Refractory hypokalaemia • Symptomatic hyperuricaemia • Severe hepatic impairment • Anuria **Cautions:** • Diabetes • Gout • Risk of hypokalaemia • Systemic lupus erythematosus • Mild to moderate hepatic impairment **Cautions – Further Information:** **Existing conditions:** • Thiazides and related diuretics can exacerbate diabetes, gout, and system 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.
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:** • The amount present in milk is too small to be harmful. • Large doses may supress lactation.
Adverse Drug Reactions	**Common or very common:** • Alkalosis hypochloraemic; constipation; diarrhoea; dizziness; dry mouth; electrolyte imbalance; erectile dysfunction; fatigue; headache; hyperglycaemia; hyperuricaemia; nausea; postural hypotension; skin reactions. **Uncommon:** • Agranulocytosis; aplastic anaemia; leucopenia; pancreatitis; photosensitivity reaction; thrombocytopenia; vomiting **Rare or very rare:** • Paraesthesia **Frequency not known:** • Appetite decreased; arthralgia; asthenia; chest discomfort; chills; drowsiness; gastrointestinal discomfort; glycosuria; gout aggravated; haemoconcentration; hepatic disorders; hypoplastic anaemia; hypovolaemia; muscle complaints; palpitations; peripheral neuropathy; psychotic depression; severe cutaneous adverse reactions (SCARs); syncope; vasculitis; venous thrombosis; vertigo; vision blurred. • 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 (which will more than likely be performed by the hospital team or the community heart failure team). • Monitor U&Es fortnightly for 1 month, then 3-6 monthly 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.

Contact names and details

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References

- BNF (2021) Metolazone https://www.medicinescomplete.com/#/content/bnf/_915981306 Accessed 17th December 2021.
- Sanofi-Aventis Product Monograph - Zaroxolyn (2018) https://products.sanofi.ca/en/zaroxolyn.pdf Accessed 17th December 2021.

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Development Process

This guidance has been produced by Lauren Clarke, Senior Pharmacist - Interface following an AMBER-G classification status of Metolazone by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by the cardiologists and was ratified by the Area Prescribing Committee on 9th February 2022.