BRIEFING SHEET FOR PRIMARY CARE
METOLAZONE FOR ADULTS

INTRODUCTION
This briefing sheet is intended to give general practitioners information on the use of Metolazone in heart failure and fluid overload in renal impairment/failure. Metolazone is a thiazide-like diuretic. Metolazone has an established role in the treatment of resistant oedema in heart failure where it is combined with a loop diuretic. The combination of metolazone and a loop diuretic is much more potent and needs to be initiated carefully by someone experienced in it's use and needs careful monitoring of renal function and electrolytes. It is routinely used in patients with renal impairment who do not respond to a loop diuretic.

TRAFFIC LIGHT CLASSIFICATION
Metolazone is classified as GREEN for this indication- it can be prescribed in primary care under the recommendation of a specialist in heart failure or nephrology. In clinically urgent cases the specialist team will need to prescribe.

DOSE
See the British National Formulary (please click here). An initial dosage of 2.5mg od or 5 mg alternate days to prevent a dramatic diuretic effect which is likely to occur when combined with the maximum dose of a loop diuretic.

SIDE EFFECTS
See the British National Formulary (please click here).

INTERACTIONS
See the British National Formulary (please click here).

BACKGROUND INFORMATION
Patients reaching the clinical point when they need metolazone treatment will usually have been under the Secondary Care Consultant Cardiologist, Renal team and/or Community Heart Failure Team. The decision to treat with this specialist treatment will either be made during an inpatient hospital stay or via the community heart failure team with clinical support from Secondary Care cardiologists or nephrologist. The specialist teams can be contacted as per details below if further advice is needed regarding ongoing management.

Sanofi-Aventis discontinued the UK licensed metolazone preparation in 2012 for commercial reasons and there were no safety or efficacy concerns noted for the withdrawal from the market. Until Jun 2022, metolazone was only available as an unlicensed special order imported product (Zaroxolyn®) that is indicated as a diuretic and antihypertensive. However, a licensed preparation, Xaqua ® is now available **and it is has up to two-fold difference in bioavailability compared to other (unlicensed, imported) metolazone preparations** Therefore, it is not interchangeable. Further information is available on the Specialist Pharmacy Service (SPS) website Differences between metolazone preparations and safety considerations – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice.
In addition the Medicines safety support: metolazone (Xaqua ®) guidance has been produced to support the switch locally.
Within Suffolk and North East Essex, the drug is approved for use in combination with a loop diuretic as a second line agent for the small number of refractory heart failure patients who have not responded to standard therapy at optimum dosage.

INFORMATION PROVIDED TO PATIENT BY THE SPECIALIST TEAM

- Ensure the patient is aware of the signs of over diuresis or worsening symptoms, when to seek medical advice from their GP and other professionals involved in the patient's care.
- Discuss the benefits and side effects of treatment with the patient and document that the patient has given informed consent to the unlicensed use of metolazone.
- Inform the patient on how they will receive regular reviews for their disease and continued need for metolazone therapy.
- Confirm if the patient is on the licensed preparation Xaqua ® and prescribe by brand.

Contact details

ESNEFT- IPSWICH HOSPITAL	
Heart Failure Dr Sanjay Jeyasseelan Sanjay.Jeyaseelan@esneft.nhs.uk Dr Naveed Razvi Naveed.Razvi@esneft.nhs.uk **Heart Failure Nurse Specialists** Anne Jones Ann.Jones@esneft.nhs.uk Mel Deal Mel.Deal@esneft.nhs.uk	Tel: 01473 703754 Email: HeartFailure.Team@ipswichhospital.nhs.uk Cardiology.HeartF@ipswichhospital.nhs.uk
Renal Dr. Brian Camilleri Dr Gerald Glancey Dr. Praveen Ande Dr Richard Smith Richard.Smith@esneft.nhs.uk	Tel: 01473 704117 Email: Renal.Nurses@esneft.nhs.uk
ESNEFT- COLCHESTER HOSPITAL	
Heart Failure Team ACE Community Heart Failure team Colchester Hospital Switchboard	Tel: (01255) 206244 Tel: (01206) 747474
Renal Dr Gabor Cserep Gabor.Cserep@esneft.nhs.uk Dr Dimitrios Kirmizis Dimitrios.Kirmizis@esneft.nhs.uk Dr Sabina Karimi Sabina.Karimi@esneft.nhs.uk Dr Prashant Khawnekar Prashant.Khawnekar@esneft.nhs.uk	Tel: 01206 74 4203
WEST SUFFOLK FOUNDATION TRUST	
Cardiology Dr Seth Dockerill Dr Lelioudis Konstantinos Dr Mariela Marinescu Dr Liam Ring Dr Pegah Salahshouri	Tel: 01284 713049 Tel: 01284 713176 Tel: 01284 713571 Tel: 01284 713389 Tel: 01284 712676 Email: CardiologySecretaries@wsh.nhs.uk
Renal Dr William Petchey Dr Vivian Yiu Dr Hsu Pheen Chong	Tel: 01284 713148 or 01284 713163

MONITORING

On-going monitoring will be transferred from the specialist to the GP after the specialist has stabilised the patient on treatment

	Parameter	Frequency	
	In addition to absolute values for haematological indices, a rapid fall or rise and a consistent upward or downward trend in any value should prompt caution and extra vigilance		
Specialist	Urea & Electrolytes (U&Es) including creatinine Blood pressure / Weight	• Baseline levels taken prior to starting treatment. • Urea and electrolytes (U&Es) and creatinine within 7 days of starting treatment. • Recheck every 7–14 days, depending on the person's stability. • Patients should be weighed or encouraged to self-weigh daily. Aim for a daily weight loss of 0.5 Kg. • Blood pressure every clinic visit. • If diuresis is extensive, consider earlier testing of renal function.	
	Parameter	**Frequency**	**Action to take if abnormal result**
Specialist or GP (once care is transferred)	Urea & Electrolytes (U&Es) including creatinine	• Monthly	**Creatinine levels or eGFR** • If the serum creatinine level increases by more than 20% of baseline or the eGFR decreases by more than 15% of baseline - re-measure renal function within 2 weeks. • An increase of serum creatinine less than 30% from baseline does not normally require action. • If creatinine increases by 30–50% (or to greater than 200 micromol/L) or eGFR is less than 30 ml/min/1.73m^2 - review volume status and then reduce dose or stop diuretics (if the person is hypovolaemic). Re-measure renal function within 1 week. • If creatinine increases by more than 50% or to greater than 256 micromol/L (eGFR approximately 20–25 mL/min/1.73 m2) – assess volume status, check blood pressure and review other renal function tests, including electrolytes and proteinuria. If the patient is hypovolaemic, stop the diuretic. If there is any uncertainty, contact heart failure nurses / cardiologist urgently. **Potassium** If potassium level < 3 mmol/L (or 4 mmol/L in high-risk patients – below), 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 heart failure team if available. • If these options have been done, give potassium supplements; for example, Sando K (2 tablets) three times a day until potassium is >4mmol/l (usually for approximately 3 days and be aware 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. Patients at high risk of cardiac arrhythmias with even mild hypokalaemia include: • Those taking digoxin or drugs that prolong the QT interval (such as amiodarone). • Those with paroxysmal arrhythmias, unstable angina, or chronic liver disease. • If potassium concentration < 2.5 mmol/L (or <3.5 mmol/L in high-risk people) – seek urgent advice and consider admission to hospital for urgent potassium replacement. **Sodium** • If a sodium level of <131mmol/L is reported, repeat level next day and contact heart failure nurses for advice as soon as results are available. Consider reduction in diuretic therapy if clinically stable.
	Blood pressure / Weight	**Blood pressure:** every clinic visit **Weight:** patient monitoring and at every clinic visit	**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 heart failure nurses. • Daily weight loss in excess of approximately 0.5-1kg – consider reducing dose.
	Symptom monitoring (ask patient at each visit)	**Action to take if symptoms occur**	
	Increased dyspnoea, fatigue, oedema, weight gain)	• Contact heart failure nurses/Specialist to discuss increasing dose	