MEDICINES SAFETY SUPPORT: METOLAZONE (XAQUA ®) GUIDANCE

Summary

- A new licensed preparation of metolazone 5mg is available (Xaqua®).
- Xaqua® and current unlicensed preparations of metolazone are not equivalent and Xaqua is reported to be up to twice as potent.
- New patients starting metolazone should be prescribed Xaqua®.
- Patients currently on metolazone should be switched to the new preparation
- The specified guidance below should be followed on switching patients to Xaqua® with advice and monitoring provided to the patient.
- Xaqua® must always be prescribed by brand name.
- Vigilance must be exercised by healthcare professionals to ensure patients are not inadvertently switched between the metolazone preparations.

BACKGROUND

Xaqua®, a new 5mg scored tablet preparation of metolazone, was launched in July 2022. Whereas previously only unlicensed, imported versions of metolazone have been available in the UK, Xaqua® is licensed in the UK for hypertension and oedema related to kidney diseases and congestive heart failure. Clinicians should be aware that Xaqua® tablets are NOT INTERCHANGABLE with other metolazone preparations, due to the potential up to two-fold difference in bioavailability compared to other metolazone products. The manufacturer recommends that a dose adjustment may be necessary and individualised titration based on patient's response and tolerability is advised if switching from Xaqua® tablets to another metolazone product, or vice versa. See SPC and the SPS guidance for further details.

INDICATION

Metolazone is indicated for hypertension and for concomitant use with loop diuretics to increase fluid loss in fluid overloaded patients e.g. in heart failure or renal failure.
Metolazone shares thiazide like diuretic-properties. It has been found to be a potent thiazide diuretic. Metolazone can cause profound diuresis, hypokalaemia, hyponatraemia and dehydration.

PRESCRIBING INFORMATION

- Metolazone is classified **Green** on the Joint Prescribing Formulary and can be recommended or initiated by a specialist team in heart failure, cardiology or renal disease.
- New patients starting metolazone should be prescribed Xaqua®
- Ensure to prescribe Xaqua® by BRAND name.
- Confirm which preparation of metolazone existing patients have been taking. Switch to Xaqua® if the patient is on an alternative preparation.
- Consider dosage adjustment when switching to Xaqua® (refer to Table 1 below).
- Monitor for urea and electrolytes, creatinine, weight, blood pressure and for signs of dehydration after 3-5 days. Compare results to patient's baseline.
- Provide the advice to patients/carers as below.

ADVICE FOR SWITCHING BETWEEN METOLAZONE PREPARATIONS

Cardiology and renal consultants have agreed the following advice for clinicians:
Primary care clinicians should avoid prescribing metolazone generically and refer patients back to secondary care. If prescribing is unavoidable, prescribers should refer to the prescribing advice below for the indication related to the patient and 'Responsibilities of clinicians prescribing metolazone' section.

Existing patients with Heart Failure

- Specialist heart failure team should review appropriateness of continuing metolazone and stop if no longer indicated.
- Review diuretic therapy and consider alternative heart failure treatment options (as per local heart failure guidelines (see links below). Alternative treatment options may include:

Developed in collaboration with: East Suffolk and North Essex Foundation Trust (ESNFT), Suffolk and North East Essex (SNEE) Integrated Care Board (ICB)- Ipswich and East Suffolk Alliance and North East Essex Alliance. Version 1 SNEE Integrated Medicines Optimisation Committee approved 21/02/2023 ESNEFT MGG approved 15/02/2023 Review February 2026

- Increased dose of loop diuretic
- Replacement with thiazide diuretic e.g. indapamide 2.5mg in the morning
- Addition of SGLT2 inhibitor if within license and NICE technology appraisial.
- Addition of aldosterone antagonist e.g. spironolactone, eplerenone
- If metolazone therapy remains appropriate, heart failure team should review patient for a switch to Xaqua® and follow 'Responsibilities of clinicians prescribing metolazone'

Existing Patients with Chronic Renal Disease CKD4/5

- Review appropriateness of continuing metolazone.
- Review diuretic therapy and consider alternative treatment options
- If metolazone therapy remains appropriate, renal team should review patient for a switch to xaqua® and follow 'responsibilities of clinicians prescribing metolazone'

ADVICE TO BE GIVEN TO PATIENTS/CARERS

The following advice must be given by the prescribing clinician. Ensure that patients/carers are advised to:

- Be aware that the brand of metolazone should not be switched, unless advised by their healthcare professional.
- Be aware of the change in their current dosing regimen, if applicable. Take daily weights, check for swelling of ankles, shortness of breath.
- Contact the specialist team (e.g. heart failure or renal team) if symptoms are exacerbated
- Be aware of the signs and symptoms of electrolyte disturbance. Be aware of need for blood tests.

Prescribed dose of unlicensed metolazone	**Suggested dose of Xaqua® (licensed metolazone) Note: 5mg tablets can be halved**
5mg in the morning	2.5mg in the morning
2.5mg in the morning	2.5mg alternate morning
2.5mg alternate morning	2.5mg twice a week
2.5mg in the morning three times a week	2.5mg twice a week
2.5mg in the morning twice a week	2.5mg in the morning once a week

ADVICE AND GUIDANCE

For advice and guidance for primary care clinicians, please contact the cardiologist or renal advice service via ERS Advice and Guidance or email as appropriate. Information to contact the relevant teams are as below:

<table>
<tr><td rowspan="4">Renal</td><td colspan="2">ESNEFT Ipswich Site</td></tr>
<tr><td>Dr. Brian Camilleri
Dr Richard Smith
Dr. Praveen Ande</td><td>Team Tel: 01473 704117
Email Nurses: Renal.Nurses@esneft.nhs.uk</td></tr>
<tr><td colspan="2">ESNEFT Colchester Site</td></tr>
<tr><td>Dr Gabor Cserep
Dr Dimitrios Kirmizis
Dr Jeff Eberhard
Dr Inaam Mohammed</td><td>Email: chu-ftr.renalsecretaries@nhs.net
Tel: 01206 742612</td></tr>
<tr><td rowspan="3">Heart Failure</td><td colspan="2">ESNEFT Ipswich Site</td></tr>
<tr><td>Dr Sanjay Jeyaseelan- Consultant Heart Failure Lead for Ipswich Hospital, ESNEFT

Heart Failure Nurse Specialists
Ann Jones
Anne Foley Smith</td><td>Ipswich Hospital Heart Failure Team
• Tel: 01473 703754
• Email: HFteam@nhs.net
Ipswich Community Heart Failure Team
• Tel: 0300 123 2425
Email: suffolkcommunityhealthcare.referrals@nhs.net</td></tr>
<tr><td colspan="2">ESNEFT Colchester Site</td></tr>
</table>

	NEECS Community Heart Failure team Colchester Hospital Switchboard Dr Duncan Field and Dr Allan Harkness	NEECS gateway number 0300 003 2144 Tel: (01206) 747474

REFERENCES

1. Specialist Pharmacy Services, Differences between metolazone preparations and safety considerations. Published 7 September 2022. Last updated 13 September 2022. Accessed on 14 November 2022 via https://www.sps.nhs.uk/articles/differences-between-metolazone-preparations-and-safety-considerations/
2. JAC/Wellsky accessed 11/01/2023
3. NHS Business Services Authority. Drug Tariff January 2023. Accessed 04/11/2022
4. Renascience Pharma Ltd. Summary of Product Characteristics; Xaqua 5 mg Tablets. Accessed online 11/01/2023.

RELATED GUIDANCE

SNEE Metolazone GP factsheet Final v2 Jan2023

This document has been adapted from the Buckinghamshire, Oxfordshire and Berkshire West Integrated Care System Metolazone (Xaqua®) Guidance v1 November 2022 with permission and thanks.