NHS
Kent and Medway

Metolazone (Xaqua®) in Kent and Medway ICB

Document History

Title		Prescribing Metolazone (Xaqua®) in Kent and Medway ICB
Version	Date	Main changes comments
Draft 1.0	19/04/2024	-
Draft 1.1	13/05/2024	Inclusion of heart failure and renal specialists only

Document distribution

Version	Clinical committee	Date agreed	Comments
Draft 1.0	Formulary working group (FWG)	7/05/2024	1. Substitute Cardiology services with Heart Failure services
	Integrated Medicines Optimisation Steering Group (IMOSG)	15/05/2024	2. A request to include a dose equivalence table
Draft 1.1	Integrated Medicines Optimisation Committee (IMOC)	20/06/2024	1. Approved.

Approved by: IMOC
Approval Date: June 2024
Review Date: June 2026

Kent & Medway ICB Position Statement

Prescribing Metolazone (Xaqua®) in Kent and Medway ICB

- **Metolazone should always be prescribed by the preferred licensed brand, Xaqua® across Kent and Medway ICB ***
- **New patients starting metolazone should be initiated on Xaqua® and at any points of transfer of care this should be clearly documented***
- **Patients currently on metolazone need to be safely switched to Xaqua® by their specialist service in a secondary care or community setting and subsequent prescriptions should be brand specific- at any points of transfer of care this should be *clearly requested and documented*.**
- **In the scenario where Xaqua® is inappropriate for a patient and the specialist's decision is to continue a prescription for an unlicensed form of Metolazone, the expectation is that this prescribing remains with the specialist, in order to have better control over the product/dose the patient will receive. This should be clearly documented in the patient notes.**

  **** This decision has been taken due to safety concerns attributed with varying bioavailability between metolazone products***

Metolazone is a thiazide-like diuretic used for the treatment of fluid retention related to the heart and kidney. Historically Metolazone has only been available in the UK as an imported unlicensed version, but the MHRA has since licensed Xaqua® - metolazone 5mg tablets.

The bioavailability of Xaqua® is understood to be *approximately* two-fold greater than unlicensed imported forms of metolazone**

Dose of Xaqua (mg)	~Estimated equivalent dose of unlicenced import of Metolazone (Metenix)(mg)
2.5mg	5mg
5mg	10mg

** The figures in the table above are based on comparative bioavailability studies reported by the manufacturer of Xaqua® which have shown that the bioavailability of Xaqua® may differ significantly (up to approximately 2-fold) from the originator product Metenix (a formerly licenced product, which was withdrawn in the UK in March 2012 for commercial reasons). The bioavailability of Xaqua® has not been compared to any other unlicensed metolazone products (this data remains unknown) so any switch should consider that differences in bioavailability may or may not be apparent. Switching from the unlicensed (imported) product to Xaqua® may or may not require dose adjustments and individualised titration based on patient's response and tolerability.

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Xaqua® is the only licensed preparation of Metolazone in the UK.

The recommendations in this position statement are aimed at reducing the prescribing and dispensing of unlicensed/generic preparations of metolazone across Kent and Medway ICB, due to safety concerns around (known and unknown) significant variations in bioavailability between preparations.

The advice to reduce the prescribing of generic Metolazone prescribing is based on the following recommended reading sources:

1. Medicines and Healthcare products Regulatory Agency (MHRA) Drug safety update Xaqua (metolazone) 5mg tablets: exercise caution when switching patients between metolazone preparations [2023]

2. SPS - Specialist Pharmacy Service – The first stop for professional medicines advice: Differences between metolazone preparations and safety considerations

3. British National Formulary (BNF) - Important safety information - Metolazone | Drugs | BNF | NICE

4. EMC. Xaqua 5mg Tablets. Renascience Pharma Ltd. Xaqua 5 mg Tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

5. The Marketing Authorisation Holder for Xaqua have circulated a letter to healthcare professionals to reinforce key messages about initiating metolazone treatment or switching to Xaqua.

Healthcare professionals are advised to always consider the following points:

For NEW PATIENTS:

- Prescribe licensed formulation by brand, Xaqua®
- Xaqua® is only available as 5mg tablets - divisible as 2.5mg [half tablet] or 5mg [whole tablet] strength.
- Xaqua® 5mg tablets should only be initiated by service specialists in the heart failure or renal team.
- Only use as an addition to high dose loop diuretics for fluid overload in heart failure and renal disease
- At points of transfer of care e.g. when requesting the GP to continue prescribing – it should be **clearly** requested and documented that Xaqua® is to be prescribed.

For EXISITING PATIENTS:

- The risk in existing patients is that they could be dispensed a different Metolazone product each time

- Service specialists should manage the switching of existing metolazone patients from unlicensed imported metolazone products to Xaqua®

- If switching to Xaqua is appropriate, the dose of metolazone provided as Xaqua may need to be adjusted to take account of individual patient factors, and the difference in bioavailability between Xaqua and the metolazone preparation being replaced (where that information is available).

- In the absence of comparative bioavailability data to inform a dose recommendation, an option may be to reduce the dose by half (from unlicensed metolazone to Xaqua) and/or adjust the frequency of dosing of Xaqua (for example, from unlicensed metolazone daily to Xaqua on alternate days). The dose can then be titrated upwards under increased monitoring, if necessary.

- Do not divide Xaqua tablets into quarters – when it is necessary to split tablets, this should be only into halves using the tablet score-line.
- Patients need to be made fully aware of the change and the reasons for it. K&M ICB have developed a patient information leaflet to support prescribers and patients.
- Monitor patients to assess the clinical impact of the switch – monitoring should be done on an individual basis after an assessment of the patient's risk, and should include assessment of blood pressure, urea & electrolytes, degrees of oedema and breathlessness, creatinine, and weight.

Advice and Guidance

For primary care clinicians, advice and guidance should be sought by contacting the heart failure or renal advice service via ERS Advice and Guidance or email as appropriate.