Cambridgeshire & Peterborough Integrated Care System

NHS Cambridgeshire and Peterborough

Metolazone (Xaqua®) for oedema in congestive heart failure and renal disease

Prescribing Support Document

What is it?

Metolazone is a sulphonamide with thiazide-like diuretic properties. It works by obstructing the re-absorption of sodium in the ascending branch of the loop of Henle and in the proximal tubules, which leads to excretion of approximately equivalent amounts of sodium and chloride.

Metolazone may be prescribed for:

- Oedema in congestive heart failure.
- Oedema in renal disease (when a high dose of a loop diuretic with or without another thiazide has failed to control fluid retention adequately).

Until recently metolazone was supplied to the UK as an unlicensed import from other countries in which it held a licence. A UK licensed product became available in March 2022: Xaqua® 5mg tablets.

There are significant differences in bioavailability between Xaqua® and alternative unlicensed imported metolazone preparations and the MHRA published a Drug Safety Update.

Xaqua® tablets have up to approximately twice the bioavailability of unlicensed imports. Patients unintentionally switched between products may experience toxicity or subtherapeutic effects as a result of the difference in bioavailability. For further information please see Metolazone preparation differences and safety considerations - Specialist Pharmacy Service.

Please refer to the Cambridgeshire and Peterborough system-wide formulary for links to local and national guidance.

NO SCG Specialist initiation without shared care guidance.

Licensed indications and prescribing good practice

Which health professional will prescribe?

New patients

The specialist team will be responsible for initiating and prescribing Xaqua® for new patients until the patient is stabilised. Primary care clinicians will be asked to continue prescribing thereafter.

Existing patients

Existing patients should NOT be transferred over to the new licensed product without specialist review. The specialist team will be responsible for reviewing patients taking the metolazone unlicensed import and transferring them over to Xaqua® if appropriate, and continue to prescribe the new product until the patient is stabilised. Primary care clinicians will be asked to continue prescribing thereafter.

Preparations and Dosage

Preparation

Metolazone (Xaqua®) 5mg tablets – ***prescribe by brand name***.

For patients taking the metolazone unlicensed import, continue prescribing this and refer the patient to the specialist team for review. Patients should NOT be transferred over to Xaqua® without specialist review.

Excipients

Xaqua® contains lactose (at the time of document publication). Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine. Prescribers should consult the Summary of Product Characteristics (SPC) for full list of excipients.

Dosage and Administration

The recommended dose of Xaqua® for oedema related to congestive heart failure and kidney disease is 2.5mg to 5mg daily (Xaqua® 5mg tablets can be divided into equal halves). The tablet should always be taken at the same time in relation to food. The dose may be adjusted according to the individual response of the patient.

An off-label dose of 1.25mg may be recommended by the specialist team for congestive heart failure. In these circumstances, the specialist team will advise the patient to use the 2.5mg dose (half a tablet) on alternate days (Xaqua® 5mg tablets can be divided into equal halves).

For patients with swallowing difficulties, the tablets can be crushed and mixed with water for administration (unlicensed).

Contraindications and precautions for use

Contraindications

- Hypersensitivity to the active substance, sulfonamides, thiazides or to any of the excipients.
- Anuria.
- Hepatic coma or precomatose conditions.
- Severe disturbances of the electrolyte balance.

Special warnings and precautions for use

- Renal impairment: Use with caution in severe renal impairment and continuously monitor renal function during thiazide therapy.
- Hepatic impairment: Hypokalaemia caused by diuretics can precipitate encephalopathy in severe hepatic impairment. There is an increased risk of hypomagnesaemia in patients with alcoholic cirrhosis.
- Elderly: Regular ongoing monitoring and blood tests are recommended in elderly patients and patients who are on long term treatment. *Prescription potentially inappropriate (Screening Tool of Older Persons' Prescriptions (STOPP) criteria): with current significant hypokalaemia (serum potassium less than 3 mmol/L), hyponatraemia (serum sodium less than 130 mmol/L) or hypercalcaemia (corrected serum calcium greater than 2.65 mmol/L)—hypokalaemia, hyponatraemia and hypercalcaemia can be precipitated by a thiazide diuretic with a history of gout (gout can be precipitated by a thiazide diuretic).*
- Electrolyte imbalance: Thiazides can cause fluid or electrolyte imbalance. Warning signs of fluid and/or electrolyte imbalance are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pain or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea or vomiting.

Drug interactions

Prescribers should consult the latest edition of the British National Formulary (BNF) or Summary of Product Characteristics (SPC).

Adverse effects

Undesirable effects

Common

- Metabolism and nutrition disorders: hypokalaemia, hyponatraemia, hypomagnesemia, hypochloremia, hypochloremic alkalosis, hyperuricemia, hyperglycemia, azotemia, hypotension, orthostatic hypotensionglycosuria, increased serum urea (BUN) and serum creatinine.
- Nervous system disorders: headache, dizziness, fatigue.
- Vascular disorders: hypotension, orthostatic hypotension.
- Gastrointestinal disorders: nausea, vomiting, constipation, diarrhoea.
- Musculoskeletal and connective tissue disorders: Muscle pain, muscle cramps.

Pregnancy and contraception

Pregnancy

Thiazide diuretics and related diuretics may pass over to the foetus and cause electrolyte imbalance. Cases of neonatal thrombocytopenia have been reported. Therefore, metolazone must not be administered during the last trimester of pregnancy unless absolutely necessary, and then with the lowest recommended dose. Seek advice from the

specialist team if needed. Patients planning a pregnancy should be referred to their specialist team.

Breast-feeding

Metolazone passes over to the breast milk in such an amount that there is a risk for the infant even at therapeutic doses. Large doses may suppress lactation.

For full details on cautions, contraindications, drug interactions and adverse effects, prescribers should consult the latest edition of the British National Formulary (BNF) or Summary of Product Characteristics (SPC).

Primary care responsibility

- Provide regular prescriptions as agreed with the specialist team.
- Monitor for adverse side effects.
- Ensure clear documentation in patient record of intended brand and dose. Check the patient is aware of the intended brand, dose, frequency and arrangements for monitoring.
- Inform the specialist if metolazone is stopped.
- *Monitoring: check serum creatinine, urea and electrolytes at regular intervals and observe for clinical signs of fluid and/or electrolyte imbalance. The frequency of monitoring is based on the individual patient and will be communicated by the specialist team to the primary care clinician.*

References

- Xaqua 5 mg Tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
- Metolazone - BNF | NICE
- Xaqua (metolazone) 5mg tablets: exercise caution when switching patients between metolazone preparations - GOV.UK (www.gov.uk)
- Metolazone preparation differences and safety considerations – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice
- NEWT Guidelines - Drug Monographs - Metolazone

Document ratification details

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