Frimley Health and Care

National shared care protocol for metolazone (Xaqua® brand only) for chronic heart failure in adult services	
Adapted and adopted for use in NHS Frimley	
Agreed by NHS Frimley Medicines Optimisation Group	November 2024
Ratified by NHS Frimley Medicines Board	November 2024
Review date	November 2027

Shared care protocol:

Metolazone (Xaqua® brand only) for chronic heart failure

The content of this shared care protocol was correct as of the date of approval. As well these protocols, please ensure that summaries of product characteristics (SPCs), British national formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites are reviewed for up-to-date information on any medicine.

Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate and optimise treatment as outlined in section 5. Prescribe the maintenance treatment for at least 4 weeks and until optimised.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information (section 13).

- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the required monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- Check local formulary status and, if accepted, prescribe ongoing treatment as detailed in the specialists request and as per section 5, taking into any account potential drug interactions in section 7.
- Adjust the dose prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in section 9. Communicate any abnormal results to the specialist.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.
- Stop treatment as advised by the specialist.

Patient and/or carer responsibilities

- Take medication as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
- Attend regularly for monitoring and review appointments with primary care and specialist, and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter medications to their prescriber and be aware they should discuss the use of specialist medication with their pharmacist before purchasing any OTC medicines.
- Not to drive or operate heavy machinery if medication affects their ability to do so safely.
- Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant

Background

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Metolazone (Xaqua) is a quinazoline diuretic, with properties generally similar to the thiazide diuretics. It acts by interfering with the renal tubular mechanism of electrolyte reabsorption, i.e. primarily inhibits sodium reabsorption at the cortical diluting site and to a lesser extent in the proximal convoluted tubule.[1]

Metolazone is used in combination with loop diuretics to achieve diuresis in patients with refractory heart failure who have not responded to standard therapy at optimum dosage.

A licensed form of metolazone is now available in the UK as the brand Xaqua. This shared care document applies to this licensed brand only.

Metolazone can produce a profound diuresis and electrolyte disturbances when utilised with loop diuretics, so patients on metolazone treatment must be managed carefully.

Indications

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[2]

The licensed indications covered by the document are:

- For use in combination with loops diuretics to achieve diuresis in patients with refractory heart failure who have not responded to standard therapy at optimum dosage.

This shared care protocol applies from the age of 18 years old.

Metolazone is classified as Amber with Shared Care and so can be prescribed in primary care in line with this document.

[3]

Locally agreed off-label use

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[4] Nil

Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC)and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

Contraindications:

- Hypersensitivity to any ingredient in the product
- Addison's disease; hypercalcaemia; hyponatraemia; refractory hypokalaemia; symptomatic hyperuricaemia, severe liver disease.

Cautions:

- Diabetes; gout; risk of hypokalaemia; systemic lupus erythematosus, nephrotic syndrome, malnourishment, moderate hepatic impairment.
- Lower initial doses of diuretics may be necessary in the elderly because they are particularly susceptible to the side-effects.
- Acute porphyrias.

5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after at least 4 weeks, and when the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
- Termination of treatment will be the responsibility of the specialist.

Initial stabilisation:

The starting dose of metolazone is usually 2.5mg (half a 5mg tablet) once or twice weekly; with dose titration in accordance with clinical response and effect on urea and electrolytes levels. Dose could be increased to a maximum of 5mg daily with the aim of achieving a daily weight loss of 0.5kg. Patients should weigh themselves daily to ensure they are maintaining their target weight or achieving acceptable weight loss.

The loading period must be prescribed by the initiating specialist.

Maintenance dose (following initial stabilisation):

Once on a stable dose, shared care can be requested and prescribing can move into primary care.

6. Pharmaceutical aspects

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Route of administration:	Oral
Formulation:	Xaqua 5mg tablets
Administration details:	The tablets have a single score line, allowing it to be broken into equal halves of containing 2.5mg. If necessary, the tablets can be crushed and mixed with water for administration. This is an off-license method of administration.
Other important information:	Xaqua is a licensed product in the UK. Products that are unlicensed or that are not licensed in the UK should no longer be used. All initiations should be for Xaqua and people prescribed other formulations should converted following advice from their Heart Failure Team.

7. Significant medicine interactions

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The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

Interacting Drug	Action to be taken
Lithium	• Monitor lithium levels, reduce dose of lithium if necessary
Theophylline	• Monitor potassium levels
Disopyramide	• Monitor potassium levels
Amisulpiride	• Monitor potassium levels
Atomoxetine	• Monitor potassium levels
Cardiac glycosides	• Monitor potassium levels
NSAIDS	• Avoid in HF

8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

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Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

Baseline investigations:

- U&Es including an assessment of renal function.
- Blood pressure (systolic blood pressure needs to above 90mmHg)

Initial monitoring (including frequency):

- Check urea and electrolytes (U&Es) and creatinine within 7 days of starting treatment. Then recheck every 7 to 14 days until dose stable.
- Patient should be weighed or encouraged to self-weigh daily. Aim for a daily weight loss of 0.5kg. If diuresis is extensive, consider earlier testing of renal function.

Ongoing monitoring (including frequency):

The specialist will retain the responsibility for monitoring the patient's ongoing response to treatment and advise if a dose change or treatment cessation is appropriate.

After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.

9. Ongoing monitoring requirements to be undertaken by primary care

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See section 10 for further guidance on management of adverse effects/responding to monitoring results. Funding for monitoring in primary care has been agreed from 1st July 2024 onwards.

Monitoring and advice	Frequency
• U&Es and renal function	Each month **The exact frequency of monitoring to be communicated by the specialist in all cases**.
• Blood pressure	Each month
• Body weight	Each month

If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.

Adverse effects and other management

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Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For information on incidence of ADRs see relevant summaries of product characteristics

Result	Action for primary care
As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance	
Daily weight loss in excess of approximately 0.5-1kg	Consider dose reduction
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
Serum creatinine increases by 30–50% (or to greater than 200 micromol/L) or eGFR is less than 30 mL/min/1.73 m2	Review volume status and then reduce dose or stop diuretics (if the person is hypovolaemic). Re-measure renal function within 1 week
Serum 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 person is hypovolaemic, stop the diuretic. If there is any uncertainty, contact heart failure nurses / cardiologist urgently.
Potassium level < 3 mmol/L or 4 mmol/L in high-risk people: People 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.	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 24mmol (2 tablets) 3x daily 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.
Sodium level of <131mmol/L	Repeat level next day. Clinical evaluation of volume status is particularly important to decide whether a reduction or increase in

	diuretics is needed. Contact heart failure team for advice when results are available.
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 team
Worsening symptoms of heart failure: increased dyspnoea, fatigue, oedema, weight gain	Contact heart failure team for advice

Advice to patients and carers

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The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:

- Patient should be encouraged to weigh themselves regularly as requested by the specialist or GPs. Report any adverse effects to the Secondary Care Specialist or GP; whilst taking metolazone therapy.
- Report signs of over diuresis, such as weight loss of more than 0.5kg – 1kg a day, any dizziness, light headedness, fatigue or uraemia; or any signs of worsening symptoms.

The patient should be advised:

- To discuss with the heart failure specialist about the risks and benefits of metolazone treatment. Make an informed decision about treatment options based on information provided by the heart failure specialist.
- Once agreed to treatment, MUST attend blood test as arranged by the specialist or GPs.

Patient information resources:

https://patient.info/medicine/metolazone-a-diuretic-xaqua

Pregnancy, paternal exposure and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

12.

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.

Breastfeeding:

Specialist sources indicate that levels in milk have not been determined, but are likely to be too low to affect the infant. Large doses may suppress lactation.

Specialist contact information

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Name	Speciality	Telephone No.	Email address
In Hours			
Advice and Guidance via eRS			
Cardiology Consultant of the Week	Cardiology Consultant (Frimley Park Hospital) (Wexham Park Hospital)	Via switchboard	
Annabel Sturges	Heart failure nurse specialist (Frimley Park Hospital)	01276 526969	
Elaine Catu	Heart failure nurse specialist (Wexham Park Hospital)	07785996702	
Stephanie Murray	Heart failure nurse specialist (Wexham Park Hospital)	01753 634791/ 07775404609	
Lex Kirke	Cardiology pharmacist (Frimley Park Hospital)	03006133740	
Preya Fakira	Cardiology pharmacist (Wexham Park Hospital)	Via switchboard	
Out of Hours			
Medical Registrar on call	Frimley Park Hospital Wexham Park Hospital	Via switchboard	

Additional information

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Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement should be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

References

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- Metolazone | Drugs | BNF | NICE
- Xaqua 5 mg Tablets - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)
15. - 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure (escardio.org)
- North Cumbria - NECS Medicines Optimisation (necsu.nhs.uk) North Cumbria Metolazone Prescribing and Monitoring Guidelines

Other relevant national guidance

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16. - https://www.sps.nhs.uk/articles/metolazone-preparation-differences-and-safety-considerations/
- Overview | Chronic heart failure in adults: diagnosis and management | Guidance | NICE

Local arrangements for referral

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17. Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

Contact details for specialist given in section 13.

The GP may contact the specialist team for advice at any time if there are concerns.

During normal working hours (Monday to Friday, 9am-5pm) the Heart Failure Specialist Nurse Team or Consultant Cardiologist of the Week can be contacted to offer advice regarding clinical parameters and blood tests. GPs are responsible for arranging the blood test to be done. Out-of-hours and over the weekend, the prescriber may be required to make a clinical decision based upon the received blood results and clinical presentation of patient; or the relevant Medical Registrar on call may be contacted for advice.

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*:* *[insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed *Frimley* shared care protocol for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

If you are in agreement, please undertake monitoring and treatment from *[insert date]*
NB: date must be at least 1 month from initiation of treatment.

The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

Please respond to this request for shared care, in writing, within 14 days of the request being made where possible.

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*
Patient *[insert Patient's name]*
NHS Number *[insert NHS Number]*
Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: _____Date: _____

Primary Care Prescriber address/practice stamp

Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

Re:

Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety NHS *Frimley,* in conjunction with local acute trusts have classified *[insert medicine name]*as a Shared Care drug, and requires a number of conditions to be met before transfer can be made to primary care.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

		Tick which apply
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care** As the patients primary care prescriber I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.**	
2.	**The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	

3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.***	
5.	**Shared Care Protocol not received** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed. For this reason I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England ‘Responsibility for prescribing between Primary & Secondary/Tertiary care’ guidance (2018) states that “when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and

the dissemination of sufficient, up-to-date information to individual GPs." In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible

Yours sincerely

Primary Care Prescriber signature: _____
Date: _____

Primary Care Prescriber address/practice stamp