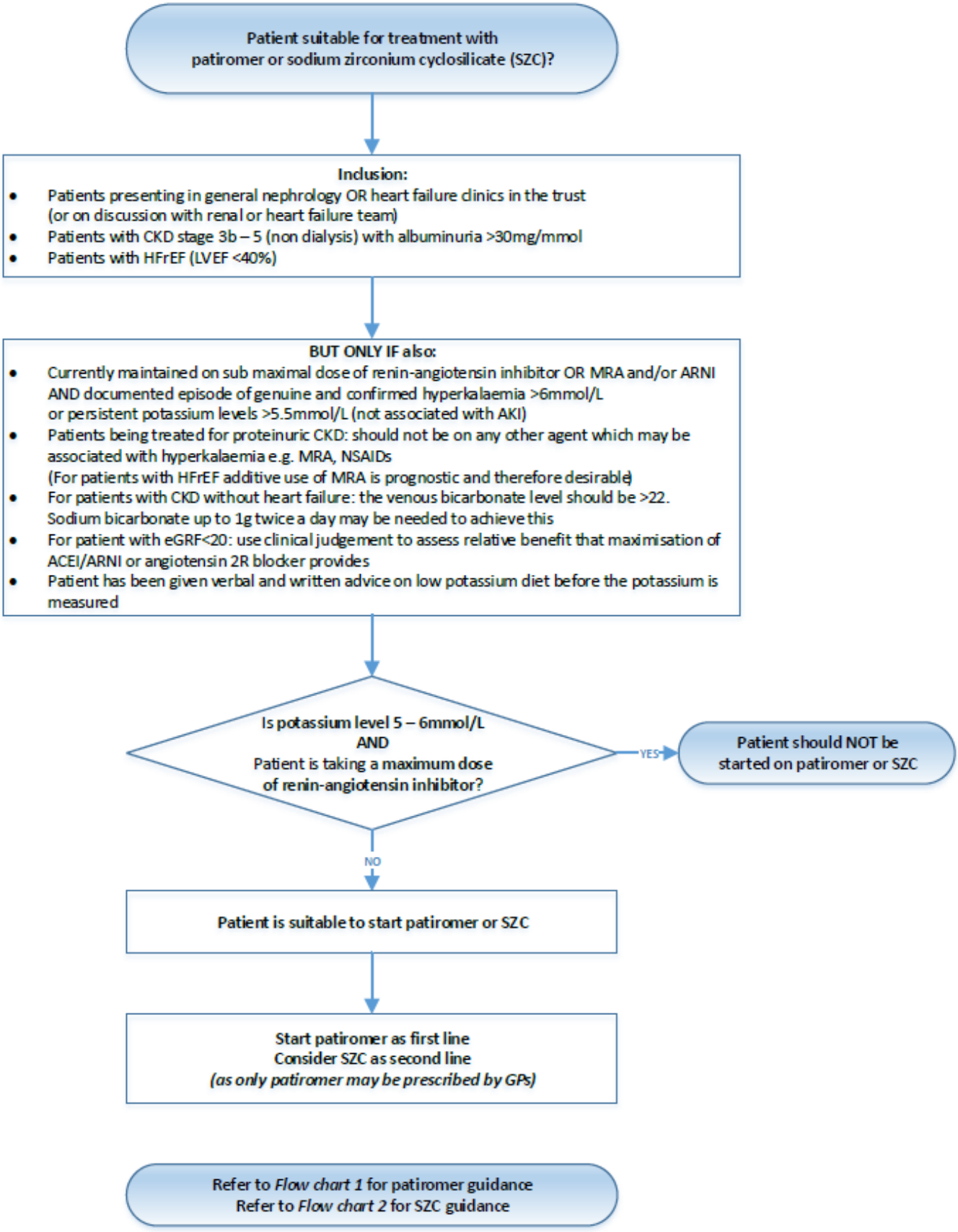
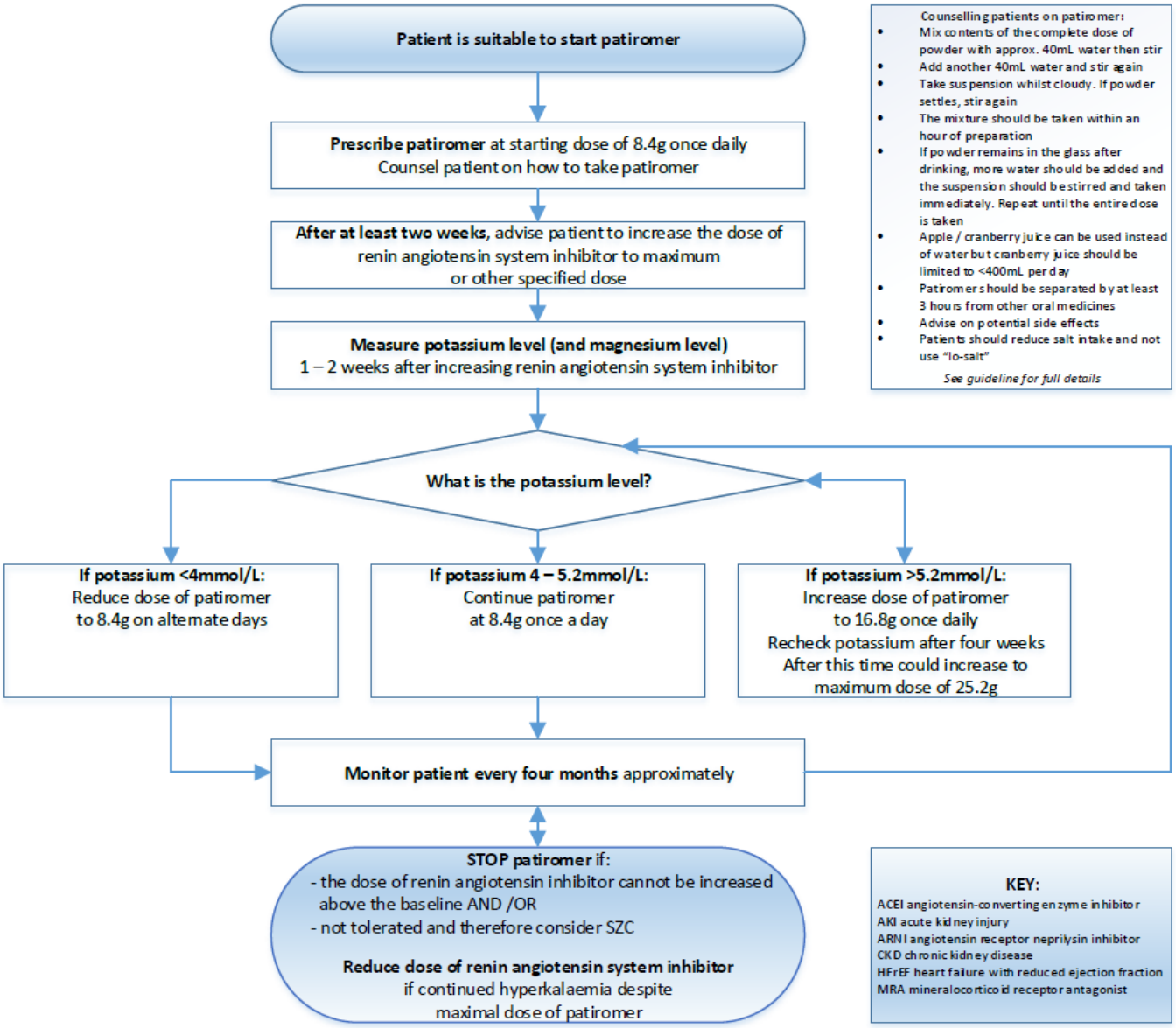
CLINICAL GUIDELINE TITLE	Patiromer and sodium zirconium cyclosilicate (SZC): use in adults with chronic hyperkalaemia

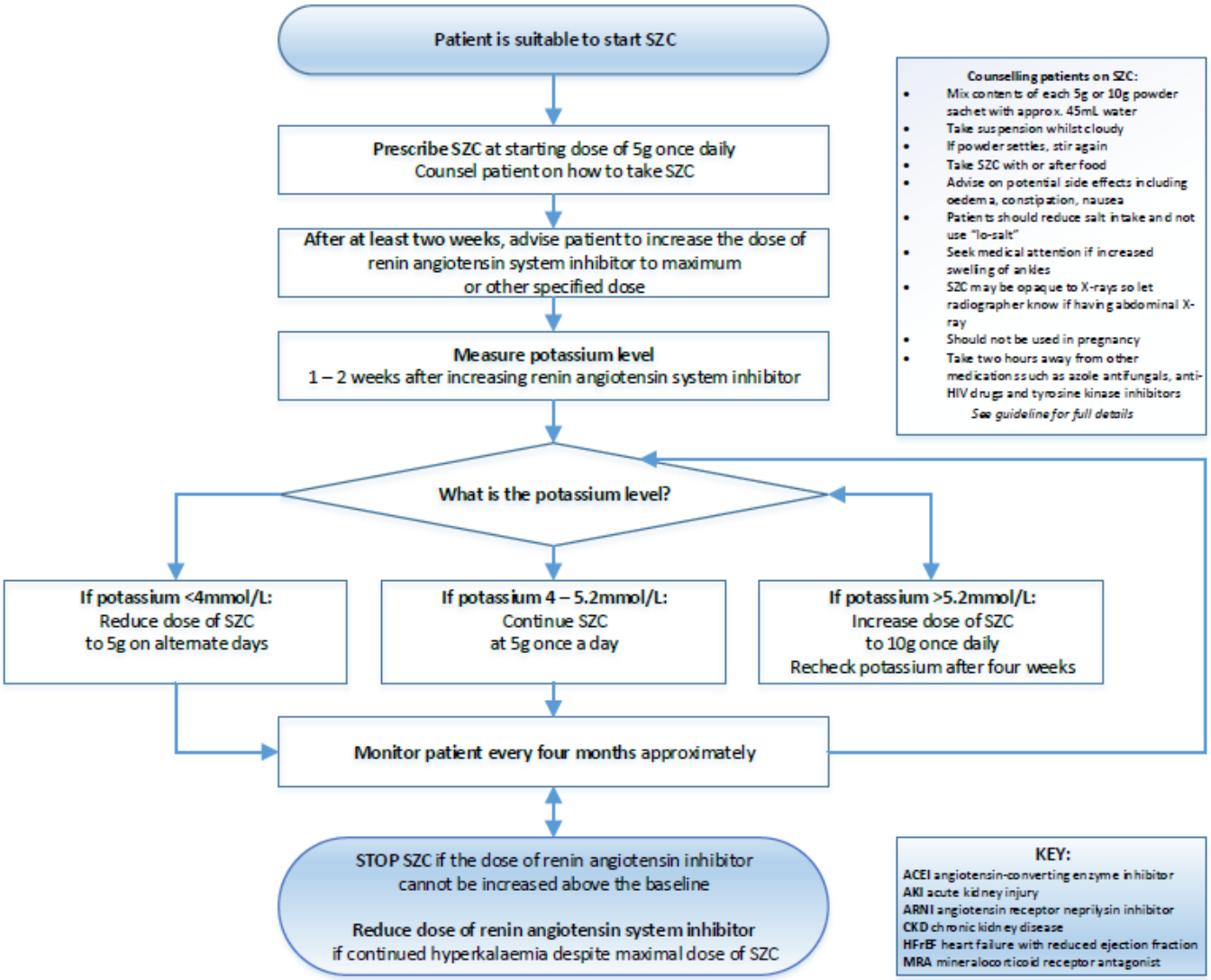
1) SUMMARY



Flow chart 1: Treatment with patiromer



Flow chart 2: Treatment with sodium zirconium cyclosilicate



2) INTRODUCTION

Patiromer and sodium zirconium cyclosilicate (SZC) are both indicated for use in patients with chronic kidney disease or heart failure with reduced ejection fraction who cannot tolerate maximal doses of renin-angiotensin system blockade because of persistent serum potassium >5.5mmol/L.

This guidance is designed to define how patiromer and SZC are used chronically to maximise the use of inhibitors of the renin angiotensin system in patients with proteinuric renal disease or reduced ejection fraction heart failure where this is limited by hyperkalaemia. This guidance needs to be seen in conjunction with separate guidelines for the acute management of hyperkalaemia.

3) DEFINITIONS

See below

4) SCOPE

Renal Services and Heart Failure Services

5) FULL GUIDELINE

5.1 Background

NICE Technology appraisal guidance published on patiromer on 13th February 2020: https://www.nice.org.uk/guidance/ta623/chapter/1-Recommendations has made the following recommendations relating to the use of patiromer for the treatment of hyperkalaemia.

NICE Technology appraisal guidance published on SZC on 4 September 2019: www.nice.org.uk/guidance/ta599 has made the following recommendations relating to the use of Sodium zirconium cyclosilicate (SZC) for the treatment of hyperkalaemia.

Patiromer or SZC are recommended as an option for treating hyperkalaemia in adults only if used:

1. in emergency care for acute life-threatening hyperkalaemia alongside standard care or
2. in outpatient care for people with persistent hyperkalaemia and chronic kidney disease stage 3b to 5 or heart failure with reduced ejection fraction, if they:
   a. have a confirmed serum potassium level of at least 6.0mmol/litre
   b. are not taking an optimised dosage of renin-angiotensin-aldosterone system (RAAS) inhibitor because of hyperkalaemia and
   c. are not on dialysis.

This guidance document is aimed at supporting the use of patiromer and SZC in the outpatient environment in order to support the care for people with persistent hyperkalaemia in association with chronic proteinuric kidney disease and heart failure with reduced ejection fraction (HFrEF).

A separate guidance note has been produced in relation to the use of this agent for the treatment of life-threatening hyperkalaemia.

5.2 Patients to be included

Inhibitors of the renin angiotensin system have significant prognostic benefit in patients with proteinuric chronic kidney disease and HFrEF. In addition, mineralocorticoid receptor antagonsists and combination RAAS & neprilysin inhibitors (ARNI) also have significant prognostic benefit in HFrEF.

Furthermore, data relevant to each of these indications highlights that the greatest benefit is seen in patients who are able to receive maximal dose of these drugs.

Unfortunately, some patients who would benefit from maximal therapy are unable to achieve this for a number of reasons. Hyperkalaemia is just one of those reasons and this guidance aims to optimise the treatment of individuals who would most benefit from maximisation of the inhibitors the renin-angiotensin system but where this cannot be achieved solely because of hyperkalaemia.

Patients suitable for treatment with patiromer or SZC include:

a) Patients attending the general nephrology or heart failure clinics at Imperial College Healthcare NHS Trust (*patients in other specialities who might be considered appropriate for this treatment should be discussed with the renal or heart failure team*)

b) Patients with CKD stage 3b to 5 (non dialysis) with albuminuria greater than 30mg/mmol

c) Patients with HFrEF (LVEF <40%)

BUT ONLY IF they also are:

a) currently maintained on a sub maximal dose of an inhibitor to the renin-angiotensin system/MRA and/or ARNI

b) AND have had a documented episode of genuine hyperkalaemia (>6mmol/L) or persistent potassium levels >5.5mmol/L which has occurred separately from an episode of acute kidney injury

c) for patients being treated for proteinuric CKD they should not be on any other agent that may be associated with hyperkalaemia MRA, NSAIDs etc. For patients with HFrEF the additive use of MRA is prognostic and therefore desirable.

d) for patients with CKD without heart failure there should have been correction of acidosis up to a maximum dose of sodium bicarbonate 1 g BD

e) for patients with an eGFR <20 clinical judgement should be used to assess the relative benefits that maximisation of ACEI / ARNI or Angiotensin 2R blocker provides.

Patients should have been given verbal and written advice on a low potassium diet prior to their potassium being measured when a decision is made to start patiromer or SZC.

Patients should NOT be started on patiromer or SZC if their potassium level is 5.0 to 6 mmol/L and they are taking a maximum dose of renin-angiotensin inhibitor. In this case patiromer or SZC are not indicated and the current max dose of renin-angiotensin system blocker can continue.

Episodes of hyperkalaemia > 6 mmol/L should where possible have been confirmed as genuine, since many such results are spurious (e.g. primary care bloods taking 12 hours to reach labs, or traumatic venepunctures).

5.2 Choice of treatment

Patiromer should be considered first line as SZC may not be prescribed by GPs due to the funding arrangements. SZC should therefore be considered as second choice.

The benefits and risks of administering patiromer should be carefully evaluated in patients with current or history of severe gastrointestinal disorders, before and during treatment (*see Summary of Product Characteristics for more details*).

Patiromer contains sorbitol and patients with the rare genetic disorder fructose intolerance should not be prescribed patiromer.

Patiromer contains calcium as part of the counter ion complex, some of which may be released part of which may be absorbed and therefore caution should be applied in patients at risk of hypercalcaemia.

5.3 Treatment Schedule

5.3.1 Patiromer

Eligible patients can be prescribed patiromer at a starting dose of 8.4 g once daily. After they have been on this medication for more than two weeks they can be advised to increase their renin angiotensin system inhibitor to a maximal or increased dose (clinical judgement). Potassium and magnesium should be measured 1 to 2 weeks after maximisation of inhibitor of the renin angiotensin system.

If on the first check the potassium <4mmol/L the dose of patiromer can be reduced to 8.4 g alternate days and repeat blood tests (see below) would not be expected for a further 3 to 4 months.
If the potassium remains above 5.2 mmol/L the dose of patiromer should increase to 16.8g once daily and the potassium rechecked four weeks later.

Patients should be monitored for their potassium and magnesium approximately four monthly and if their potassium level drops to <4mmol/L the dosage of patiromer should be reduced and if it is above 5.2mmol/L the dosage of patiromer could be increased to a maximum dose of 25.2g per day.

Dose changes should only be made at 8.4g increments or decrements.

If hypomagnesia develops consideration would need to be given to either supplementing the magnesium or reducing the dose of patiromer depending on the clinician's opinion.

If patients continue to suffer from hyperkalaemia despite the use of maximal dose patiromer the dosage of the inhibitor of the renin angiotensin system will need to be reduced and if the dose of the inhibitor the renin angiotensin system cannot be increased above the baseline dosage then patiromer should be stopped. If patiromer is stopped monitoring of the potassium level is required as the levels will rise.

5.3.2 Sodium zirconium cyclosilicate (SZC)

Eligible patients can be prescribed SZC at a starting dose of 5 g once daily. After they have been on this medication for more than two weeks they can be advised to increase their renin angiotensin system inhibitor to a maximal or increased dose (clinical judgement). Potassium should be measured 1 to 2 weeks after maximisation of inhibitor of the renin angiotensin system.

If on the first check the potassium <4mmol/L the dose of SZC can be reduced to 5 g alternate days and repeat blood tests would not be expected for a further 3 to 4 months.
If the potassium remains above 5.2 mmol/L the dose of SZC should increase to 10g once daily and the potassium rechecked four weeks later.

Patients should be monitored approximately four monthly and if their potassium level drops to <4mmol/L the dosage of SZC should be reduced and if it is above 5.2mmol/L the dosage could be increased to a maximum dose of 10 g per day.

If patients continue to suffer from hyperkalaemia despite the use of maximal dose SZC the dosage of the inhibitor of the renin angiotensin system will need to be reduced and if the dose of the inhibitor the renin angiotensin system cannot be increased above the baseline dosage then SZC should be stopped.

5.4 Patient advice

5.4.1 Patiromer

Patients should be advised on how to take patiromer according to the following steps:

- The dose should be mixed with approximately 40mLs of water and stirred well. Then add an additional 40mL of water and the suspension should be stirred again thoroughly.
- Apple juice can be substituted for water but this may not be appropriate if the patient has diabetes.
- The powder will not dissolve. More water may be added to the mixture as needed for the patient's desired consistency.
- The mixture should be taken within one hour of initial suspension. If powder remains in the glass after drinking more water should be added and the suspension stirred and taken immediately. This may be repeated as needed to ensure the entire dose is administered.

Administration of patiromer should be separated by at least 3 hours from other oral medications.

Patiromer can be taken with or without food. It should not be heated or microwaved, nor added to heated foods or liquids.

Patiromer should not be taken in its dry form.

Patients should be advised that potential side effects include hypomagnesia, constipation, diarrhoea, abdominal pain, flatulence.

Patiromer should not be used in women of childbearing age where pregnancy is a possibility

5.4.2 Sodium zirconium cyclosilicate

Patients should be advised on how to take SZC - Manufacturer advises mix the contents of each 5- or 10-g sachet of powder with approximately 45 mL of water and stir well. The powder will not dissolve and the suspension should be taken while it is cloudy; if the powder settles it should be stirred again. SZC can be taken with or without food.

Patients should be advised that potential side effects include oedema, constipation and nausea.

Patients should be advised to reduce salt intake (as would be the case for all patients in whom inhibitors of the renin angiotensin system are indicated) but not to use “lo-salt”.

Patients should be advised to seek medical attention if they develop increase swelling of their ankles.

Patients should be advised that SZC may be opaque to X-rays and if undergoing any abdominal x-ray they should let the radiographer know that they are on this drug.

SZC should not be used in women of childbearing age where pregnancy is a possibility

SZC should be taken two hours away from administration of the following medications – azole antifungals (ketoconazole, itraconazole and posaconazole), anti-HIV drugs (atazanavir, nelfinavir, indinavir, ritonavir, saquinavir, raltegravir, ledipasvir and rilpivirine) and tyrosine kinase inhibitors (erlotinib, dasatinib and nilotinib)

6) IMPLEMENTATION

Training required for staff	Yes
If yes, who will provide training:	*Dr Andrew Frankel for Renal* *Dr Carla Plymen for Cardiology*
When will training be provided?	Through regular Renal regular post grad meeting schedule Through Cardiology regular post grad meeting schedule
Date for implementation of guideline:	DATE

7) MONITORING / AUDIT

When will this guideline be audited?	October 2020
Who will be responsible for auditing this guideline?	Dr Andrew Frankel (Renal) Dr Carla Plymen (Cardiology)
Are there any other specific recommendations for audit?	To ensure that all patients being prescribed Lokelma meet initiation requirements To ensure that all patients being prescribed Lokelma meet maintenance requirements To assess the increased use of inhibitors of the renin angiotensin system in patients being prescribed SZC To assess for safety issues including episodes of hyperkalaemia

8) REVIEW

Frequency of review	**Please indicate frequency of review:** 3 years **Person and post responsible for the review:** Dr Andrew Frankel

9) REFERENCES

10) GUIDELINE DETAIL

Start Date:	**26th May 2020**
Approval Dates	Drugs and Therapeutics Committee 12th May 2020 (chair's action 12th May 2020)
Has all relevant legislation, national guidance, recommendations, alerts and Trust action plans been considered, and included as appropriate in the development of this guideline?	**Please list ALL guidance considered:** **NICE technology appraisal**
Have all relevant stakeholders been included in the development of this guideline?	**Please list all (name and role):** Renal Services General Nephrologists and Lead Pharmacist Cardiac Failure Services Consultants Advanced Practice Nurses Lead Pharmacist
Who will you be notifying of the existence of this guidance?	**Please give names/depts:** Renal Consultants Cardiac Failure Consultants and Advanced Practice Nurses
Related documents	
Author/further information	Dr Andrew Frankel (Renal) a.frankel@nhs.net
Document review history	**Next review due: 12th May 2023** V0.1 – first draft of new guideline V0.2 – updated guideline V0.3 – further updates V0.4 – amendments following DTC V0.5 – further changes to the title **V1.0 – finalised version**
THIS GUIDELINE REPLACES:	NA

11) INTRANET HOUSEKEEPING

Key words	Chronic hyperkalaemia; SZC; Lokelma; hyperkalaemia; sodium zirconium cyclosilicate; patiromer; Veltassa
Which Division/Directorate category does this belong to?	Renal and Cardiac services
Which specialty should this belong to when appearing on the Source?	renal; cardiology; endocrinology and diabetes

12) EQUALITY IMPACT OF GUIDELINE

Is this guideline anticipated to have any significant equality-related impact on patients, carers or staff? No