Pending CCG approval

NHS
Pan Mersey
Area Prescribing Committee

SODIUM ZIRCONIUM CYCLOSILICATE powder for oral suspension (Lokelma® ▼) for persistent hyperkalaemia

The Pan Mersey Area Prescribing Committee recommends the prescribing of SODIUM ZIRCONIUM CYCLOSILICATE powder for oral suspension (Lokelma® ▼) for persistent hyperkalaemia in adults following initiation by a specialist in accordance with NICE TA599.

AMBER following specialist initiation

Sodium zirconium cyclosilicate is licensed for the treatment of hyperkalaemia in adult patients.[1] NICE technology appraisal TA599[2] (04 September 2019) recommends sodium zirconium cyclosilicate as an option for treating hyperkalaemia in adults only if used:

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

Sodium zirconium cyclosilicate is recommended only if the company provides it according to the commercial arrangement (see cost section for further information).

Clinical trials show that sodium zirconium cyclosilicate lowers serum potassium when used in outpatient care, but there is no clinical evidence that it extends life or improves quality of life. Sodium zirconium cyclosilicate may allow people to stay on RAAS inhibitors for longer. Staying on these drugs may extend life and improve quality of life.[2]

For persistent treatment in the clinic setting, treatment must be initiated by a specialist (see local implementation recommendations below). During the titration phase multiple medication changes and blood test monitoring are required. The aim of this titration is to optimise RAAS inhibitor therapy whilst achieving an acceptable serum potassium.

Prescribing and monitoring of sodium zirconium cyclosilicate must be retained by the specialist for at least one month after the patient is stabilised on the optimum RAAS inhibitor therapy / sodium zirconium cyclosilicate combination, with stable urea and electrolytes.

Sodium zirconium cyclosilicate should be stopped if RAAS inhibitors are no longer suitable.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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Effectiveness[1,2]

Sodium zirconium cyclosilicate is a non-absorbed, non-polymer inorganic powder with a uniform micropore structure that preferentially captures potassium in exchange for hydrogen and sodium cations. It captures potassium throughout the entire gastrointestinal (GI) tract and reduces the concentration of free potassium in the GI lumen, thereby lowering serum potassium levels and increasing faecal potassium excretion to resolve hyperkalaemia.[1]

The NICE appraisal committee considered evidence from trials ZS003, ZS004 and ZS005 and acknowledged that all trials showed that sodium zirconium cyclosilicate treatment reduced serum potassium level from baseline. However, there were no data on whether sodium zirconium cyclosilicate, compared with standard care, allowed more patients to continue on RAAS inhibitors. The committee concluded that the company had not provided any data comparing sodium zirconium cyclosilicate with current NHS treatments to correct hyperkalaemia and maintain normal serum potassium levels in outpatient care (that is, management of RAAS inhibitors). Without these data, it could not determine whether sodium zirconium cyclosilicate is more clinically effective than current standard care in the NHS for treating chronic hyperkalaemia. The appraisal committee concluded that sodium zirconium cyclosilicate was a cost-effective use of NHS resources for treating chronic hyperkalaemia in outpatient care, with an ICER less than £20,000 per QALY gained compared with standard care for people with hyperkalaemia who have either chronic kidney disease or heart failure, once the PAS discount was applied.[2]

Safety[1]

Sodium zirconium cyclosilicate is not absorbed or metabolised by the body, therefore no drug interactions are expected. Sodium zirconium cyclosilicate can transiently increase gastric pH and therefore should be administered at least 2 hours before or 2 hours after oral medications with clinically meaningful gastric pH dependent bioavailability, e.g. azole antifungals (ketoconazole, itraconazole and posaconazole), antiretroviral drugs (atazanavir, nelfinavir, indinavir, ritonavir, saquinavir, raltegravir, ledipasvir and rilpivirine) and tyrosine kinase inhibitors (erlotinib, dasatinib and nilotinib).

The most commonly reported adverse reactions in clinical trials were hypokalaemia (4.1%) and oedema related events (5.7%). No events of intestinal perforation have been reported with sodium zirconium cyclosilicate however, since intestinal perforation has been reported with polymers that act in the gastrointestinal tract, specific attention should be paid to signs and symptoms related to intestinal perforation.

There is no evidence for the effectiveness or safety of sodium zirconium cyclosilicate beyond one year.

Refer to SPC for full safety information.

Cost[3]

The NHS list price per 30-sachet pack of sodium zirconium cyclosilicate is: 5g - £213.60; 10g - £472.20. However, a PAS discount and primary care rebate are available so the actual cost incurred will be less than NHS list price. NICE considers the use of sodium zirconium cyclosilicate to be cost-effective use of NHS resource once this discount is applied.

NICE estimates the cost of implementing both this TA and TA623 (Patiromer for treating hyperkalaemia) as £5,096 per 100,000 population in 2020/21, rising to £15,172 per 100,000 population by end of 2023/24. NICE assumes an equal split in prescribing costs between sodium zirconium cyclosilicate and patiromer.

Patient factors[1]

No changes from the normal doses are required for patients with renal or hepatic impairment.

Safety and efficacy in children and adolescents (< 18 years) have not been established.

There are no data from use in pregnancy. Sodium zirconium cyclosilicate can be used during breastfeeding.

Sodium zirconium cyclosilicate is considered high in sodium (approximately 400 mg sodium per 5g). This should be taken into consideration particularly for those on a low salt diet.

Prescribing information[1,2]

- The recommended starting dose is 10g three times a day, administered orally as a suspension in water, taken with or without food. When normokalaemia has been achieved, the minimal effective dose to prevent recurrence of hyperkalaemia should be established. For maintenance, a starting dose of 5g once daily is recommended, titrated up to 10g once daily, or down to 5g once every other day, as needed to maintain a normal potassium level. No more than 10g once daily should be used for maintenance therapy.
- If a patient misses a dose they should be instructed to take the next usual dose at their normal time.
- If severe hypokalaemia occurs, discontinue sodium zirconium cyclosilicate and re-evaluate the patient.
- Sodium zirconium cyclosilicate should be stopped if RAAS inhibitors are discontinued.
- Sodium zirconium cyclosilicate is considered high in sodium (approximately 400 mg sodium per 5g). This should be taken into consideration particularly for those on a low salt diet.

Local Implementation recommendations

- Within the Pan Mersey health economy, the term 'specialist' for the purposes of this prescribing statement is understood to be a consultant physician specialising in acute medicine, nephrology or cardiology, a cardiology GPSi or a prescribing member of the specialist team with experience of treating persistent hyperkalaemia and who has access to the relevant specialist multidisciplinary renal or heart failure team.
- The specialist is responsible for initiation, dose titration, monitoring and patient review until the patient is stabilised on the optimal RAAS inhibitor therapy / sodium zirconium cyclosilicate combination. Specialist review is expected to be frequent during the titration phase until the patient is stable, when standard regular review can resume according to clinical need.
- Prescribing and monitoring of sodium zirconium cyclosilicate must be retained by the specialist until the patient has been stable for at least one month.
- Any specialist starting sodium zirconium cyclosilicate must write to the patient's GP to inform them that it is being initiated within the specialist service. The patient's GP should be advised at this stage that advice from the specialist team should be sought before making any changes to the patient's current medication which may affect the patient's serum potassium including (but not limited to) diuretics, RAAS inhibitors and aldosterone antagonists.
- Once the patient is considered stable (for at least one month) on optimal RAAS inhibitor therapy / sodium zirconium cyclosilicate combination, with stable urea and electrolytes, the patient's GP will be requested to take on the ongoing prescribing of sodium zirconium cyclosilicate. Treatment with sodium zirconium cyclosilicate is likely to be lifelong, unless there is a clinical need for discontinuation.
- Clear written communication from the specialist team is required to request transfer of prescribing, including how to contact the specialist team for advice. The patient must receive an adequate further supply of sodium zirconium cyclosilicate from the specialist team to allow the safe transfer of prescribing to primary care, this is expected to be a minimum of 2 weeks' supply.
- Serum potassium should be monitored when clinically indicated, including after changes are made to medicinal products that affect the serum potassium concentration (e.g. renin-angiotensin-aldosterone system (RAAS) inhibitors or diuretics) and after dose titration. Once stabilised, monitoring is unlikely to be any more frequent than current practice in this group of patients.
- If, after stabilisation, changes are required to medicines that may affect serum potassium then the specialist team should be contacted for advice. This includes (but is not limited to) changes to diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs) and aldosterone receptor antagonists.

References

1. AstraZeneca UK Limited. Summary of Product Characteristics: Lokelma 10g powder for suspension, 15 April 2021. Accessed 20 May 2021.
2. National Institute for Health and Care Excellence. Technology Appraisal 599: Sodium zirconium cyclosilicate for treating hyperkalaemia, 04 September 2019. Accessed 20 May 2021.
3. NHS Business Services Authority. Dictionary of medicines and devices (dm+d) browser. Accessed 20 May 2021.