Lokelma®
(sodium zirconium cyclosilicate)
powder for oral suspension

Formulary pack for the National Health Service (NHS)

This document has been provided by AstraZeneca UK Ltd and its aim is to support healthcare professionals and/or any other relevant NHS stakeholders in the completion of formulary applications, submissions, decision making and guideline development for the use of Lokelma in the UK. The Formulary Support Pack does not include all the information from the Summary of Product Characteristics (SmPC). Before prescribing Lokelma, please consult the full SmPC for further information (For Lokelma Prescribing Information, please click here or refer to Section 11).

Lokelma is indicated for the treatment of hyperkalaemia in adult patients.[1]

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Document overview and intended use

This document has been developed by AstraZeneca as a support resource to provide the type of information required for a local formulary application for Lokelma.

The information provided in this document is not intended as a substitute for local data regarding patients and services but provides additional information to support applications for local implementation.

The National Institute for Health and Care Excellence (NICE) have produced a medicines practice guideline on developing and updating local formularies.[2] This formulary pack has been developed in line with these recommendations.

It is not anticipated that the formulary application form as it stands should be submitted nor that any AstraZeneca personnel complete applications on behalf of healthcare professionals or other relevant NHS stakeholders who are completing a formulary application.

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2. Executive summary

Drug: Lokelma® (sodium zirconium cyclosilicate).[1]

Indication: Treatment of hyperkalaemia in adults.[1]

Proposed use: As aligned to the updated NICE recommendation for Lokelma (Technology Appraisal (TA)1148, published on the 29th April 2026), for the treatment of persistent hyperkalaemia in adults with chronic kidney disease (CKD) stage 3b to 5 or heart failure (HF) with a confirmed serum potassium (sK) level of ≥5.5 mmol/L, who are not taking an optimised dose of renin-angiotensin-aldosterone system inhibitors (RAASi) (due to hyperkalaemia), and are not on dialysis.[3]

Lokelma is also licensed and reimbursed for the treatment of hyperkalaemia in adults when used in emergency care for acute life-threatening hyperkalaemia alongside standard care.

Scope of formulary request: Although Lokelma is licensed and reimbursed for both acute and persistent hyperkalaemia, this formulary pack focuses on the use and reimbursement of Lokelma for the treatment of persistent hyperkalaemia to reflect the recent NICE reimbursement update lowering the sK threshold for initiation from ≥6.0 mmol/L to ≥5.5 mmol/L and removing the need for specialist initiation, allowing for increased flexibility of use across care settings and increasing patient access.

Place in therapy: Lokelma is a potassium binder, reimbursed for the management of persistent hyperkalaemia, from a sK level of ≥5.5 mmol/L in cardiorenal patients. The intended place in clinical practice is as a first-line sustainable treatment option to facilitate maintenance and optimisation of RAASi therapy, reflective of the products' licensing principles, and the treatment and management principles of persistent hyperkalaemia outlined in the 2026 NICE recommendation (TA1148) and the current Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for CKD.[1, 3, 4]

Dose and administration: 10 g three times daily during correction, usually for 24–48 hours and up to 72 hours if needed; then 5 g once daily maintenance, titrated up to 10 g once daily or down to 5 g alternate days as needed to maintain normal potassium level. Oral suspension.[1]

Clinical evidence: Trial data show rapid potassium reduction and long term sustained normokalaemia and potassium control in populations including patients with CKD, HF, diabetes and RAASi use.[1] Across a real-world evidence programme, treatment with Lokelma was associated with a greater likelihood of maintaining RAASi therapy following hyperkalaemia compared to no binder.[5] Similar trends observed in long-term open label studies showed Lokelma use is associated with high rates of RAASi maintenance following hyperkalaemia.[6, 7]

Safety: Most common side effects, worsening of pre-existing HF, hypokalaemia, oedema and constipation. Worsening of pre-existing HF during treatment was reported as a very common adverse reaction (frequency of ≥ 1/10) where most cases were resolved with appropriate clinical management without withdrawing Lokelma.[1]

Formulary request: Request approval for initiation and prescribing in both primary and secondary care. Proposed formulary classification: green or local equivalent. This reflects the updated NICE recommendation and the unmet need for an earlier intervention in the community, where many eligible patients are already monitored. Allowing primary care initiation may reduce avoidable referral and accident and emergency (A&E) admissions, improve access to treatment, support maintenance of RAASi, and enable a more integrated and preventative approach to chronic hyperkalaemia management which is aligned with the NHS 10-year Health Plan "Fit for Future".

Financial/resource impact: List prices are £156.00 for 5 g x 30 sachets, £31.20 for 10 g x 3 sachets, and £312.00 for 10 g x 30 sachets. Local budget impact should be assessed using the NICE resource impact template and local assumptions. Primary care initiation may reduce local costs, simplify pathways and reduce resource burden on emergency and secondary care services.

Recommendation to Area Prescribing Committee: Update the status of Lokelma® on your formulary to be in line with NICE TA1148 for the treatment of adults with CKD stage 3b to 5 or HF and sK level of ≥5.5 mmol/L and amend local prescribing status to allow primary and secondary care initiation/prescribing for eligible adults with persistent hyperkalaemia.

3. Summary of the condition and unmet need

3.1. Description of hyperkalaemia

Hyperkalaemia is a common, potentially life-threatening electrolyte disorder characterised by elevated sK, which is particularly prevalent in adults with CKD and/or HF.[8-10]

In these cardiorenal patients, hyperkalaemia should be recognised as a predictable consequence of impaired renal potassium excretion and/or use of guideline-directed RAASi therapy (angiotensin-converting enzyme inhibitor (ACEi)/ angiotensin II receptor blocker (ARB)/ angiotensin receptor-neprilysin inhibitor (ARNi)/ mineralocorticoid receptor antagonist (MRA)).[11] Cardiorenal conditions in and of themselves, and RAASi therapies, carry an inherent risk of hyperkalaemia through altering of potassium homeostasis and ultimately reducing urinary potassium excretion.[11]

Despite chronically elevated mild to moderate sK levels (≥5.0-6.0) often being asymptomatic, it imposes a substantial barrier to individuals receiving the guideline recommended doses of RAASi therapy in order to confer the greatest cardiorenal protection.[3, 12]

As sK levels approach severe thresholds (≥6 mmol/L) the individual becomes increasingly vulnerable to the rapid manifestation of serious symptoms and cardiac complications including arrhythmia and cardiopulmonary arrest.[12-14] In UK practice, thresholds that trigger intervention vary; however, outcome data consistently show meaningful risk escalation of major adverse cardiac events (MACE), hospitalisations, death and increased resource utilisation from sK 5.5 mmol/L.[15]

The most up to date relevant guidance (UK Kidney Association (UKKA), British Society of Heart Failure (BSH), as well as the international guidelines KDIGO) recognise 5.5 mmol/L as the threshold at which active intervention is warranted.[4, 12, 16] Indeed, other international guidelines, including the European Society of Cardiology (ESC) and the International Society of Nephrology (ISN) advocate for even earlier intervention with potassium lowering treatments at thresholds from >5.0 mmol/L, specifically in patients with chronic or recurrent hyperkalaemia on RAASi therapy.[17, 18]

Together this well recognised international literature and guidance reflect the principle that hyperkalaemia should be managed proactively, with earlier intervention aimed at sustained potassium control, to facilitate RAASi therapy optimisation to protect this high-risk population from cardiac decompensation, accelerated renal decline and increased mortality due to inadequate RAASi blockade.

3.2. Disease burden

Up to 42% of patients with CKD stages 3–5 and 25% of patients with HF experience hyperkalaemia within the first year of diagnosis, with the incidence rising as high as 48% in patients with comorbid HF and CKD.[19, 20] In addition, RAASi therapy is associated with an almost two-fold increased risk of hyperkalaemia versus those with cardiorenal disease not receiving RAASi.[21]

Whilst severe hyperkalaemia has been variously defined as serum potassium in excess of 6.0 or 6.5 mmol/L, several published literature sources have consistently reported that the association between serum potassium and mortality have been observed as a U-shaped curve, with mortality risk progressively increasing in individuals with either hypo- (sK+ less than 4.0 mmol/L) or hyperkalaemia (sK+ greater than 5.0 mmol/L).[9, 14, 22-25]

The SPARK study investigated the impact of sK levels on clinical outcomes (all-cause mortality, all-cause hospitalisation, MACE and health care resource utilisation).[15] SPARK is a UK specific, retrospective, observational study that provides a comprehensive evaluation of hyperkalaemia using a large, real-world dataset encompassing over 500,000 eligible patients with CKD or HF. The study identified that sK below 6 mmol/L are not a benign range, confirming the adverse relationship between sK levels >5.0 mmol/L and all-cause mortality,

recognised by international guidelines (ESC, KDIGO) and previously reported literature.[4, 15, 17]

All-cause mortality risk was found to meaningfully and significantly increase in CKD and HF patients as sK exceeded ≥5.5 mmol/L, increasing by 1.5 and 1.7- fold, respectively, compared to the reference range (sK 4.5-5.0 mmol/L).[15] Consistent U-shaped relationships were observed for all measured clinical outcomes, where meaningful increases in the risk of the outcome were observed from sK ≥5.5 mmol/L (See Section 6.1, for further information).

Hyperkalaemia is often a recurrent condition in these individuals, with successively shorter time intervals between each episode.[26][1] In a real world evidence study, repeated hyperkalaemia within 45 days of a first event occurred in 56% of individuals with CKD (stages 3-4) and 56% of patients with HF and CKD (stage 3-4).[27]

In addition to the well characterised adverse outcomes associated with elevated sK levels, persistent hyperkalaemia indirectly worsens outcomes in these patients through the down-titration, interruption or discontinuation of RAASi therapy, thereby limiting the established cardioprotective benefits these medicines afford.[28, 29] RAASi therapy is often not re-instated following an episode of hyperkalaemia at or following discharge, further exacerbating the loss of cardiorenal protection.[17, 29-32] In an observational study of UK clinical practice research datalink (CPRD) and hospital episode statistics (HES) data between January 2006-2015, the mean duration of RAASi discontinuation exceeded 2.4 years in patients with CKD and 1.9 years in patients with HF.[28, 29, 33]

3.3. Cost burden

In addition to the substantial impact of persistent hyperkalaemia on mortality and morbidity, there is also a significant economic burden associated with persistent hyperkalaemia in terms of increased healthcare utilisation and the costs associated with this resource use.[34]

A retrospective cohort analysis aimed to characterise healthcare resource use associated with hospitalisations attributed to hyperkalaemia in patients with cardiovascular (CV) and renal comorbidities in the UK.[34] Between 2003 and 2018, 536,678 unique patients were eligible for study inclusion, and their hospital admissions related to hyperkalaemia were analysed from CPRD data and healthcare resource use was estimated using mean length of hospital stay and applying an average cost of a mean inpatient day for a severe hyperkalaemia event as £727. The mean length of stay was 17.0 days for CKD patients and 17.6 days for HF patients. The total cost over the period was £76,578,466 and £32,245,605 for CKD and HF patients, respectively.[34]

3.4. Unmet need

The most up to date relevant guidelines consistently emphasise that hyperkalaemia should not be a barrier to optimisation of RAASi therapy.[4, 12, 17] However, despite this evidenced based principle, down-titration or discontinuation remains the most commonly utilised clinical strategy to manage elevated potassium levels. Patients with CKD and HF receiving less than 50% of recommended RAASi doses have been reported to experience approximately 5.5-fold and 7-fold higher mortality rates respectively, compared with those maintained on at least 50% of target dose.[29]

Importantly, the development of hyperkalaemia should not be interpreted as representing ‘maximally tolerated’ or optimised RAASi therapy.[4, 12, 17] The longstanding perception that RAASi optimisation ends where hyperkalaemia begins is increasingly inconsistent with modern cardiorenal care pathways, in which proactive potassium management and targeted potassium lowering therapies are available and enable continuation and optimisation of guideline-directed, life-prolonging treatment.

In UK clinical practice, patients with hyperkalaemia may be managed in primary care, or secondary care settings, dependent on patient status, their sK level and whether their hyperkalaemia is acute or persistent in nature.[12] Epidemiological data demonstrates that the majority of patients with CKD and HF experiencing persistent, mild to moderate hyperkalaemia are receiving ongoing care in a primary care setting.[12] According to Prescribing Episode Statistics (PES) data, between February 2025 and January 2026, a potassium binder

[1] Retrospective, observational cohort study utilizing UK primary and secondary care data from Clinical Practice Research Datalink and linked Hospital Episode Statistics, respectively (between January 1, 2003 and June 30, 2018)

was prescribed to 12,930 patients in a primary care setting across NHS England.[35] Primary care clinicians are therefore already demonstrating that they are well-positioned to manage chronic hyperkalaemia as part of integrated chronic disease management.[3]

Despite this, red or amber formulary positioning limit the ability of primary care clinicians to initiate sodium zirconium cyclosilicate in a timely manner, creating a potential barrier to proactive potassium management and RAASi optimisation in the community. Enabling primary care initiation would support earlier intervention for chronic hyperkalaemia, improve access to an appropriate treatment within a familiar and routinely accessed care setting, ultimately allowing for greater autonomy within primary care to drive more efficient medicines optimisation.

Therefore, a green formulary classification could support a more integrated and preventative approach to chronic hyperkalaemia management by expanding therapeutic options available to primary care, reducing avoidable referrals solely for binder initiation, and potentially decreasing secondary care utilisation associated with downstream serious cardiorenal events attributable to suboptimal RAASi therapy use following hyperkalaemia.

4. Medicine details

Non-proprietary (Generic) Name:	Sodium zirconium cyclosilicate
Brand name	Lokelma®
Marketing authorisation holder	AstraZeneca
Formulation & strength[1]	Lokelma® 5 g powder for oral suspension Lokelma® 10 g powder for oral suspension
Licensed indication[1]	Lokelma is indicated for the treatment of hyperkalaemia in adult patients.
License status	Marketing authorisation was received in March 2018. **Marketing Authorisation Numbers:** PLGB 17901/0331 PLGB 17901/0332
Method of administration[1]	**For oral use.** The entire contents of the sachet(s) should be emptied in a drinking glass containing approximately 45 ml of water and stirred well. The tasteless liquid should be drunk while still cloudy. The powder will not dissolve. If the powder settles, the liquid should be stirred again and taken. If needed, rinse the glass with more water to ensure that all of the content is taken.
Posology[1]	**Correction phase** The recommended starting dose of Lokelma is 10 g, administered three times a day orally as a suspension in water. When normokalaemia is achieved, the maintenance regimen should be followed (see below). Typically, normokalaemia is achieved within 24 to 48 hours. If patients are still hyperkalaemic after 48 hours of treatment, the same regimen can be continued for an additional 24 hours. If normokalaemia is not achieved after 72 hours of treatment, other treatment approaches should be considered. **Maintenance phase** When normokalaemia has been achieved, the minimal effective dose of Lokelma to prevent recurrence of hyperkalaemia should be established. A starting dose of 5 g once daily is recommended, with possible titration up to 10 g once daily, or down to 5 g once every other day, as needed, to maintain a normal potassium level. No more than 10 g once daily should be used for maintenance therapy. sK levels should be monitored regularly during treatment.
Innovation type	Revision to the NICE recommendation for Lokelma in TA1148:[3] • For persistent hyperkalaemia, Lokelma is reimbursed from a sK of ≥5.5 • Reimbursement no longer restricted to specialist care allowing initiation in primary care
Duration of treatment	Chronic management

5. National guidance

5.1. UK and international clinical guidelines

There are multiple guidelines which advise on the management of hyperkalaemia, including the UKKA NICE accredited Clinical Practice Guidelines,[12] and international guidelines such as the ESC clinical practice guideline,[17] American Heart Association (AHA) HF guideline,[32] and KDIGO guidelines.[4] These all recommend RAASi as the first-line therapy to delay disease progression and emphasise the importance of maximising RAASi therapy to the maximum tolerated dose. They recommend the use of K^+ binders as the preferred option to manage persistent hyperkalaemia instead of RAASi down-titration or discontinuation:

- The UKKA Clinical Practice Guidelines recommends initiating K^+ binders at an sK level of ≥5.5 mmol/L;[12]
- The 2021 ESC HF guidelines recommend initiating K^+ binders as soon as sK exceeds 5.0 mmol/L and note that K^+ binders enable continuation of RAASi treatment;[17]
- The 2024 KDIGO guidance recommends initiating K+ binders at an sK level of ≥5.5 mmol/L, and state that potassium binders may help facilitate essential use of RAASi/MRA. The guidance states that RAASi down-titration or discontinuation should be a last resort for treating hyperkalaemia in CKD patients.[4]

The UKKA guidelines specifically recommend Lokelma as an option in the out-patient setting for the management of persistent hyperkalaemia with a confirmed sK ≥6.0 mmol/L.[12] However, this guidance was last updated in 2023 and are in misalignment to NICE TA1148 (2026) which now recommends the use of Lokelma to treat persistent hyperkalaemia from sK level of ≥5.5 mmol/L (see Section 5.2).[3] An update to the UKKA guidelines is expected in October 2026.[12] The ESC guidelines for HF also specifically recognise Lokelma as effective in normalising elevated potassium levels, maintaining normokalaemia over time and preventing the recurrence of hyperkalaemia, and recommend that Lokelma can be considered for the management of patients with chronic or recurrent hyperkalaemia on RAASi therapy.[17]

5.2. HTA Guidance

NICE

On the 29th April 2026, the NICE TA Guidance (TAG) for Lokelma (TA1148) for treating hyperkalaemia in adults was broadened to be used to treat persistent hyperkalaemia from sK level of ≥5.5 mmol/L. The revised recommendation no longer restricts reimbursement to a specialist setting, enabling primary care initiation and expanding the role of primary care beyond the current continuation and long-term management of hyperkalaemia.[3]

There are two potassium binders which have a NICE recommendation for the management of hyperkalaemia, including Lokelma and Veltassa (Table 1).[3, 36] However, currently Lokelma is the only potassium binder to be recommended for the treatment of persistent hyperkalaemia from sK level of ≥5.5 mmol/L in patients with HF or CKD.[3]

Scottish Medicines Consortium (SMC)

There are two potassium binders which have a SMC recommendation for the management of hyperkalaemia, including Lokelma and Veltassa (Table 1).[37, 38] A reassessment of Lokelma for the treatment of hyperkalaemia in adult patients is currently ongoing with the SMC.[39]

Table 1. Summary of the Health Technology Appraisal (HTA) recommendations for the management of hyperkalaemia

	Lokelma	Veltassa
NICE	TA1148 (updated April 2026): Sodium zirconium cyclosilicate can be used as an option for treating hyperkalaemia in adults only if used: • in emergency care for acute life-threatening hyperkalaemia alongside standard care or • for people with persistent hyperkalaemia and CKD stage 3b to 5 or HF, if they: ○ have a confirmed sK level of **at least 5.5 mmol/L** and ○ because of hyperkalaemia, are not taking an optimised dosage of RAASi and ○ are not on dialysis.	TA623: Veltassa is recommended as an option for treating hyperkalaemia in adults only if used: • in emergency care for acute life-threatening hyperkalaemia alongside standard care or • for people with persistent hyperkalaemia and stages 3b to 5 CKD or HF, if they: ○ have a confirmed sK level of **at least 6.0 mmol/L** and ○ are not taking, or are taking a reduced dosage of, a RAASi because of hyperkalaemia and ○ are not on dialysis.
SMC	SMC2288: Patients with hyperkalaemia (defined as a sK >6.0 mmol/L) with CKD stage 3b to 5 and/or HF, who would otherwise need to down-titrate or discontinue their RAASi therapy to maintain a clinically acceptable sK level (normokalaemia). **An appraisal to update the SMC Advice for Lokelma is ongoing (SMC2884).**	SMC2381: Patients with hyperkalaemia (defined as a sK >6.0 mmol/L) with CKD stage 3b to 5 and/or HF, who would otherwise need to down-titrate or discontinue their RAASi therapy to maintain a clinically acceptable sK level (normokalaemia).

Abbreviations: CKD: chronic kidney disease; HF: heart failure; RAASi: renin-angiotensin-aldosterone system inhibitor; sK: serum potassium
Source: SMC (2021), SMC (2020), SMC (2026), NICE (2026) and NICE (2020).[3, 36-39]

6. Supporting evidence

6.1. Real World Evidence

SPARK

The SPARK study was used prominently in the 2026 NICE reappraisal, to demonstrate the clinical need to manage hyperkalaemia at serum potassium levels below 6 mmol/L.[15] SPARK addresses the unmet need around hyperkalaemia in and of itself, irrespective of RAASi therapy or the underlying condition. The study confirms that hyperkalaemia is an independent risk factor for all-cause mortality, MACE, all-cause hospitalisation, and healthcare resource utilisation (HCRU).

It was a retrospective, population-based database analysis using the UK CPRD Aurum and GOLD databases, linked with HES and Office for National Statistics mortality data. It was designed to evaluate the epidemiology of hyperkalaemia and the relationship between serum potassium levels, clinical outcomes HCRU, and associated costs in the general population and in patients with CKD and/or HF.[15]

The SPARK study was conducted in alignment with the NICE Real World Evidence framework. The study controls for a comprehensive set of 38 measured confounders, including age, sex, comorbidities, RAASi use amongst other covariates, reducing the likelihood of major residual confounding. In addition, the sensitivity analysis used E-values to quantify the strength of unmeasured confounding required to explain away the observed observation.[15]

A total of 4,789,407 patients were included in the outcomes analysis, of whom 631,934 (13.2%) had CKD and/or HF. Mean age in the overall cohort was 57.5 years and 45.4% were male.[15]

The study demonstrated there was a U-shaped association between sK and outcomes: both hypokalaemia and hyperkalaemia were linked to higher rates of MACE, all-cause mortality, and all-cause hospital admissions compared to the 4.5–5.0 mmol/L reference range. Risks increased stepwise at the extremes and were consistent in CKD and HF subgroups. In HF (without CKD), all-cause mortality incidence rose to 1.7-fold (95% CI 1.5–1.8) at sK 5.5–<6.0 mmol/L and 3.2-fold (95% CI 2.7–3.8) at sK ≥6.0 mmol/L versus reference. In CKD, all-cause mortality incidence rose to 1.5-fold (95% CI 1.4–1.6) at sK 5.5–<6.0 mmol/L and 2.8-fold (95% CI 2.3–3.1) at sK ≥6.0 mmol/L versus reference.[15]

Increased HCRU and costs were also observed in patients with serum potassium ≥5.0 to <5.5 mmol/L, ≥5.5 to <6.0 mmol/L, and >6.0 mmol/L compared with the reference group.[15]

ZORA

ZORA is a global observational study programme that investigated the management and consequences of hyperkalaemia in patients with CKD and/or HF in routine clinical practice.[5]

A multi-country comparative cohort analysis, utilised hospital records and medical claims from the US, Japan, and Spain to evaluate the likelihood of maintaining (stabilised/up-titrated) RAASi therapy at 6 months following a hyperkalaemia episode in 2 cohorts: patients treated with Lokelma for at least 120 days vs those with no K+ binder prescription during the 180-day follow-up. This analysis was pertinent to the recent NICE reappraisal for Lokelma, and utilised as the most relevant data source to demonstrate that Lokelma use is associated with higher RAASi maintenance, offering a clinically meaningful pathway by which intervention at 5.5–5.9 mmol/L can preserve lifesaving, disease modifying therapy.[5]

Propensity score (PS) matching (1:4) was applied to balance the Lokelma cohort to the no K+ binder cohort on baseline characteristics. Logistic regression analysis was performed to compare the odds of maintained RAASi therapy at 6 months in the Lokelma versus no K+ binder cohorts.[5]

The PS-matched Lokelma cohort included 1,397 patients, ~74% of the patients maintained RAASi therapy compared to ~54% (N=4900) of patients in the no K+ binder cohort at 6 months, equating to a 2.56 greater odds [(95% CI 1.92–3.41); P < .0001] of maintaining RAASi therapy at 6 months on Lokelma vs no K+ binder. The outcome favouring Lokelma was observed regardless of geography or comorbidity.[5]

6.2. Efficacy and Safety Studies

Three studies tested the initial effect of Lokelma to correct hyperkalaemia during a 48-hour period, with two studies also testing maintenance of normokalaemia effect obtained. The maintenance studies included patients with CKD (58%), HF (10%), diabetes mellitus (DM) (62%) and prescribed RAASi therapy (68%).[1]

Two further, open-label maintenance studies tested long-term safety and sustained potassium control with Lokelma for up to 12 months.[6, 7]

These five registrational studies included 1760 patients given doses of Lokelma; 507 exposed for at least 360 days.[1] In the studies, Lokelma reduced sK and maintained normal sK levels regardless of the underlying cause of hyperkalaemia, age, sex, race, comorbid disease or concomitant use of RAASi. No dietary restrictions were imposed; patients were instructed to continue their usual diet without any specified alterations.[1]

Harmonize and Harmonize 11-month Extension

A multi-phase, placebo-controlled maintenance study with an additional open-label phase[1, 7, 40]

In the correction phase of the study, 258 patients with hyperkalaemia (baseline average 5.6, range 4.1–7.2 mmol/L) received 10 g of Lokelma administered three times daily for 48 hours.[1] Reductions in potassium were observed 1 hour after the first 10 g dose of Lokelma. Median time to normokalaemia was 2.2 hours with 66% of patients achieving normokalaemia at 24 hours and 88% at 48 hours. Responses were larger in patients with more severe hyperkalaemia when compared to patients with non-severe hyperkalaemia; for example, sK fell 0.8, 1.2 and 1.5 mmol/L in patients with baseline sK <5.5, 5.5–5.9 and ≥6 mmol/L, respectively.[1, 40]

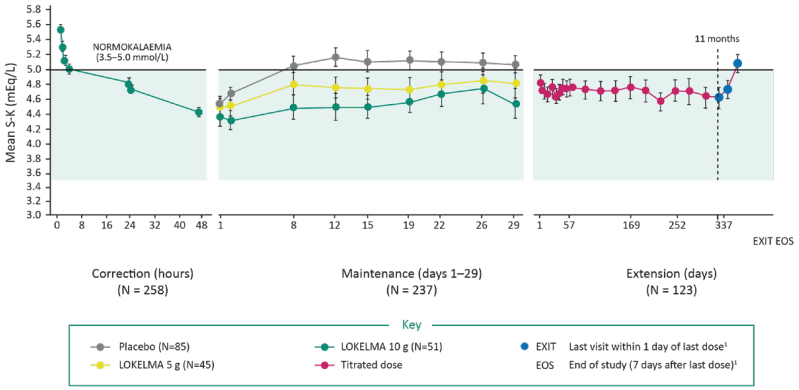
Patients who achieved normokalaemia (potassium levels between 3.5 and 5 mmol/L) were randomised in a double-blind fashion to one of three doses of Lokelma [5 g (n=45), 10 g (n=51), or 15 g (n=56), (noting that 15 g is not licensed for use in patients not on haemodialysis)] or placebo (n=85) administered once daily for 28 days (the double-blind randomised withdrawal phase).[1]

The proportion of subjects with average sK <5.1 mmol/L from Study Day 8 to 29 (3-week period) was greater at the 5 g, 10 g and 15 g once-daily doses of Lokelma (80%, 90% and 94%, respectively), compared with placebo (46%).[1] There was a mean decrease in sK of -0.77 mmol/L, -1.10 mmol/L, -1.19 mmol/L and -0.44 mmol/L, respectively and the proportion of subjects who remained normokalaemic was 71%, 76%, and 48% in the 5 g, 10 g, once-daily doses of Lokelma and placebo groups, respectively.[1]

Maintenance phase with Lokelma titration (open-label) results: 123 patients entered the 11-month open-label phase.[1] The proportion of subjects with average sK <5.1 mmol/L was 88%, the average sK level was 4.66 mmol/L and the proportion of sK measurements below 3.5 mmol/L was less than 1%; between 3.5 and 5.1 mmol/L was 77%; or between 3.5 and 5.5 mmol/L was 93%, irrespective of other factors that might influence the sK. Treatment was discontinued on study exit (Day 365).[1]

Figure 1 illustrates the mean sK over the correction and maintenance phases of the study.

Figure 1: Mean sK levels across correction, maintenance and extension phases with 95% CI.[1, 7, 40]



Abbreviations: CI, confidence interval; EOS, end of study; sK , serum-potassium.
Source: Adapted from Kosiborod M, et al. (2014), Roger SD et al. (2019), and Lokelma SmPC (2026).[1, 7, 40]

Study-ZS005

A two-phase, multicentre, multi-dose, open-label safety and efficacy study[1, 6]

The long-term effects of Lokelma were assessed in this 12-month study in 751 subjects with hyperkalaemia (baseline average 5.59 mmol/L; range 4.3–7.6 mmol/L).[1, 6] Comorbid conditions included CKD (65%), DM (64%), HF (15%) and hypertension (83%). Use of diuretics and RAASi was reported by 51 and 70% of subjects, respectively. During the correction phase, 10 g of Lokelma was administered three times daily for at least 24 hours and up to 72 hours. Subjects who achieved normokalaemia (3.5–5.0 mmol/L, inclusive) within 72 hours entered the maintenance phase of the study. All subjects in the maintenance phase received Lokelma at a starting dose of 5 g once daily which could be increased in increments of 5 g once daily (to a maximum of 15 g once daily) or decreased (to a minimum of 5 g once every other day) based upon the titration regimen. The 15 g maintenance phase dose is not approved for use in non-haemodialysis patients.[1]

Normokalaemia was achieved in 494/748 (66%), 563/748 (75%) and 583/748 (78%) of subjects after 24, 48 and 72 hours of correction phase dosing with an average reduction in sK of 0.81 mmol/L, 1.02 mmol/L and 1.10 mmol/L at 24 (n=748), 48 (n=104) and 72 (n=28) hours, respectively.[1, 6] Normokalaemia was dependent on baseline potassium concentration, with subjects with the highest baseline sK concentrations having the most prominent decrease after starting the study drug but with the lowest proportion of subjects achieving normokalaemia. One hundred and twenty-six patients had a baseline sK ≥6.0 mmol/L (mean baseline potassium 6.28 mmol/L). These subjects had a mean reduction of 1.37 mmol/L at the end of the correction phase.[1]

Table 2: Correction phase (Study-ZS005): proportion of subjects with sK concentrations between 3.5 and 5.5 mmol/L, inclusive, by correction phase study day – intent-to-treat (ITT) population.[1]

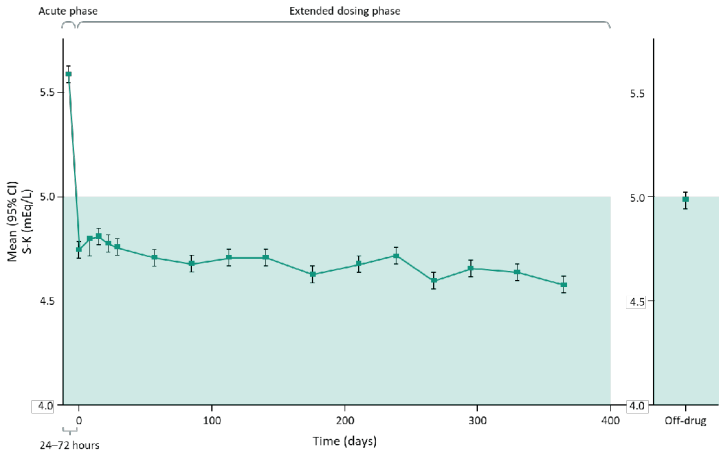
Correction phase (CP)	Lokelma 10 g three times daily (N=749)					
	sK 3.5–5.0 mmol/L inclusive			sK 3.5–5.5 mmol/L inclusive		
	n/N	Proportion	95% CI	n/N	Proportion	95% CI
CP at 24 hrs	494/748	0.660	0.625, 0.694	692/748	0.925	0.904, 0.943
CP at 48 hrs	563/748	0.753	0.720, 0.783	732/748	0.979	0.965, 0.988
CP at 72 hrs / CP last	583/748	0.779	0.748, 0.809	738/748	0.987	0.976, 0.994

Abbreviations: CI: confidence interval; CP: correction phase; sK: serum potassium.
Footnote: One subject had a post-dose value that was more than 1 day after last dose. Therefore, the subject was eligible for the correction phase ITT population; however, the time point was excluded from the analysis.
Source: Adapted from Lokelma SmPC (2026).[1]

Normokalaemia was maintained while patients remained on drug and the mean sK increased following discontinuation compared to baseline.[1, 6] Among those patients using RAASi at baseline, 89% did not discontinue RAASi therapy,74% were able to maintain the same dose during the maintenance phase and, among those not on RAASi at baseline, 14% were able to initiate this therapy.[6] During maintenance phase, 75.6% of subjects maintained normokalaemia, despite use of RAASi.[1]

Figure 2 illustrates the mean sK level over the correction and maintenance phases of the study.

Figure 2: Correction and maintenance phases in 12-month open-label study (Study-ZS005) – mean sK over time with 95% CI.[6]



Abbreviations: CI: confidence interval; sK : serum potassium.
Footnotes: Off-drug values collected 7 (±1) days after the last administration of Lokelma. The extended maintenance group contained a small proportion (11.7%) of patients who were treated with 15 g once daily. This dose is not approved for use in non-haemodialysis patients in the UK.
Source: Adapted from Spinowitz et al. (2019).[6]

7. Tolerability and monitoring

7.1. Summary of the tolerability profile

Summary of the Safety Profile[1]

In clinical trials, the most commonly reported adverse reactions for Lokelma were hypokalaemia (4.1%) and oedema related events (5.7%).

In 2 clinical studies with open-label exposure of Lokelma up to one year in 874 subjects, the following events were reported as related by investigators: Gastrointestinal events [constipation (2.9%), diarrhoea (0.9%), abdominal pain/distension (0.5%), nausea (1.6%) and vomiting (0.5%)]; and hypersensitivity reactions [rash (0.3%) and pruritus (0.1%)]. These events were mild to moderate in nature, none were reported as serious and were generally resolved while the patient continued treatment. Due to the open-label study design, a causal relationship between these events and Lokelma cannot be definitively established.

In clinical studies conducted in countries with a predominantly Asian population, constipation with an estimated frequency of 8.9% occurred in non-dialysis patients receiving Lokelma; and was resolved with dose adjustment or treatment discontinuation.

In a pooled analysis of three placebo-controlled clinical studies of Lokelma in non-dialysis patients, some patients with pre-existing HF experienced worsening of HF, which occurred at a frequency of 13.6% (30/220) on Lokelma and 5.7% (12/209) on placebo. Most cases resolved with appropriate clinical management without withdrawing Lokelma.

Tabulated list of adverse reactions[1]

The safety profile of Lokelma was evaluated in clinical trials involving 1760 patients with 507 patients exposed for one year. The adverse reactions identified from controlled trials and post-marketing reports are shown in Table 3.[3]

The following convention was used for frequency of adverse reactions: Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very rare (<1/10,000), Not known (cannot be estimated from the available data).

Table 3: List of adverse reactions in clinical trials and post-marketing reports.[1]

System organ class	Very common	Common
Metabolism and nutrition disorders		Hypokalaemia
Gastrointestinal disorders		Constipation
General disorders and administration site conditions		Oedema-related events
Cardiac disorders	Worsening of pre-existing heart failure	

Source: Adapted from Lokelma SmPC (2026).[1]

Description of selected adverse reactions[1]

Hypokalaemia
In clinical trials, 4.1% of patients taking Lokelma developed hypokalaemia with an sK value less than 3.5 mmol/L, which was resolved with dose adjustment or discontinuation of Lokelma.

Oedema-related events
Oedema-related events, including fluid retention, generalised oedema, hypervolaemia, localised oedema, oedema, oedema peripheral and peripheral swelling, were reported by 5.7% of patients taking Lokelma. The events were observed in the maintenance phase only and were more commonly seen in patients treated with 15 g (15 g is not licensed for use in patients who are not on haemodialysis). Up to 53% were managed by initiating a diuretic or adjusting a diuretic dose; the remainder did not require treatment.

Contraindications[1]

Hypersensitivity to the active substance.

Special warnings and precautions for use[1]

sK levels
sK should be monitored when clinically indicated, including after changes are made to medicinal products that affect the sK concentration (e.g., RAASi or diuretics) and after the Lokelma dose is titrated.
Monitoring frequency will depend upon a variety of factors including other medicinal products, progression of CKD and dietary potassium intake.

Hypokalaemia
Hypokalaemia may be observed. Dose titration as described under maintenance posology may be required in such cases to prevent moderate to severe hypokalaemia. In patients with severe hypokalaemia, Lokelma should be discontinued and the patient re-evaluated.

Worsening of pre-existing HF
Patients with pre-existing HF, particularly those in whom an increased sodium intake may lead to fluid overload and decompensation, should be monitored for manifestations of worsening HF. These may include increased dyspnoea, oedema and rapid weight gain, and should be managed as per standard clinical practice.

QT prolongation
During correction of hyperkalaemia, a lengthening of the QT interval can be observed as the physiologic result of a decline in sK concentration.

The risk of interaction with X-rays
Lokelma may be opaque to X-rays. If the patient is having abdominal X-rays, radiographers should keep this in mind.

Intestinal perforation
The risk for intestinal perforation with the use of Lokelma is currently unknown. No events of intestinal perforation have been reported with Lokelma. Since intestinal perforation has been reported with polymers that act in the gastro-intestinal (GI) tract, specific attention should be paid to signs and symptoms related to intestinal perforation.

Sodium content
This medicinal product contains approximately 400 mg sodium per 5 g dose, equivalent to 20% of the World Health Organisation recommended maximum daily intake for sodium. Lokelma is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

Interactions[1]

Effect of other medicinal products on Lokelma
As Lokelma is not absorbed or metabolised by the body, there are no expected effects of other medicinal products on the pharmacologic action of Lokelma.

Effect of Lokelma on other medicinal products
As Lokelma is not absorbed or metabolised by the body, and does not meaningfully bind other medicinal products, there are limited effects on other medicinal products.

Lokelma can transiently increase gastric pH by absorbing hydrogen ions and can lead to changes in solubility and absorption kinetics for co-administered medicinal products with pH-dependent bioavailability. Lokelma should be administered at least 2 hours before or 2 hours after oral medications with clinically meaningful gastric pH dependent bioavailability. Examples of medicinal products that should be administered 2 hours before or after Lokelma to avoid possible raised gastric pH drug interaction are azole antifungals (ketoconazole, itraconazole and posaconazole), anti-HIV drugs (atazanavir, nelfinavir, indinavir, ritonavir, saquinavir, raltegravir, ledipasvir and rilpivirine), tyrosine kinase inhibitors (erlotinib, dasatinib and nilotinib) and immunosuppressants (tacrolimus). Lokelma can be co-administered without spacing of dosing times with oral medications that do not exhibit pH-dependent bioavailability.

Pregnancy and breast feeding[1]

Pregnancy
There are no data from the use of Lokelma in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Lokelma during pregnancy.

Breast-feeding
Lokelma is not systemically absorbed and is not expected to be excreted in breast milk. No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to Lokelma is negligible. Lokelma can be used during breast-feeding.

Fertility
No human data on the effect of sodium zirconium cyclosilicate on fertility are available.

7.2. Monitoring requirements

Monitoring should be based on clinical judgement and follow standard care principles for patients with CKD and HF, which will include routine assessment of sK, renal function and fluid status.

Please refer to '*sK'* and '*Worsening of Pre-existing Heart Failure*' under '*Special warnings and precautions for use*' for monitoring considerations.

8. Proposed formulary update

8.1. Current potassium management strategies

Prior to the TA1148 expansion, the available treatment options for managing chronic hyperkalaemia have not demonstrated predictable or reliable sustained potassium control. Existing potassium lowering strategies for patients with CKD or HF and persistent hyperkalaemia with sK of ≥5.5–<6.0 mmol/L commonly lead to down-titration/ discontinuation of RAASi therapy.[12]

Other existing and utilised potassium management strategies and treatment options in this patient phenotype, include [12]:

- Low K+ diet, which is now considered not to be clinically effective, associated with decreased patient quality of life, and an unintended shift to a lower dietary quality through reduced intake of other beneficial nutrients;
- Potassium wasting diuretics, the potassium lowering effects rely on preserved kidney function and the degree of response isn't entirely predictable;
- Sodium bicarbonate, few studies have shown a benefit of sodium bicarbonate in the treatment of chronic hyperkalaemia, and other cation exchange resins (e.g. Calcium Polystyrene Sulfonate (CPS), Calcium Resonium) despite these resins being used in clinical practice for decades, tolerability and the risk of severe GI adverse effects limit their long-term use. In addition a Cochrane review (2020) evaluated CPS and SPS (sodium polystyrene sulphonate) in chronic hyperkalaemia and concluded there is insufficient high-quality evidence to recommend their use for chronic hyperkalaemia in patients with CKD, use of these traditional binders has generally been superseded by the novel potassium binders in recent years.

8.2. Proposed place in therapy

Lokelma is indicated for the treatment of hyperkalaemia in adult patients.[1] NICE TA1148 now recommends Lokelma as an option for treating persistent hyperkalaemia at a sK level of ≥5.5 mmol/L, which aligns to the KDIGO 2024 guidance for K^+ binders.[3, 4]

The intended place in clinical practice for Lokelma is as a first-line sustainable treatment option to facilitate maintenance and optimisation of RAASi therapy, reflective of the products' licensing principles, and the treatment and management principles of persistent hyperkalaemia outlined in the 2026 NICE recommendation (TA1148) and the current Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for CKD.[1, 3, 4]

8.3. Treatment setting

Lokelma can be initiated and managed across both primary and secondary care.

TA1148 no longer restricts access to a specialist setting, enabling primary care initiation and expanding the role of primary care beyond the current continuation and long-term management of patients.[3] In TA1148, the committee discussion highlighted several potential system-level benefits associated with enabling initiation of Lokelma within primary care.

- The NICE committee concluded that access to Lokelma may simplify the care pathway, "including reducing the complexity of monitoring persistent hyperkalaemia, [which] may support management in primary care"
- Clinical experts explained that unstable potassium levels can contribute to increased monitoring burden and repeat healthcare interactions. Access to Lokelma in primary care would allow for stabilisation of potassium levels and support RAASi optimisation, therefore reducing the need for repeated monitoring, and increase clinician confidence to maintain ongoing therapy.[41]

According to PES data, between February 2025 and January 2026, a potassium binder was prescribed to 12,930 patients in a primary care setting across NHS England.[35] This demonstrates the existing familiarity of utilising potassium binders in primary care.

8.4. Proposed formulary classification

The proposed formulary classification for Lokelma is green with initiation in primary or secondary care. It is recognised that the meaning of a green classification will vary locally, so the proposed classification should reflect local circumstance and formulary guidance.

8.5. Implementation Considerations

Local guideline updates are needed in line with the updated NICE TA1148 and revised formulary access.

8.6. Formulary impact

The local formulary needs to be updated to include a new therapeutic option for patients with persistent hyperkalaemia and sK level of ≥5.5 mmol/L, and for the Red, Amber, Green (RAG) status of Lokelma to be updated to allow initiation and continued prescribing in primary and secondary care.

9. Cost and resource impact

9.1. Pack size

Lokelma is available in pack sizes of 3 or 30 sachets, each sachet contains either 5 g or 10 g of sodium zirconium cyclosilicate.[1]

9.2. Price

The list price of Lokelma is £156.00 for 5 g x 30 sachet pack, £31.20 for 10 g x 3 sachet pack, and £312.00 for 10 g x 30 sachet pack.[42]

9.3. Duration of treatment

For persistent hyperkalaemia, Lokelma treatment is chronic and life-long, as long as RAASi therapy is indicated.

The NICE committee in TA1148 concluded that a lifelong treatment duration (subject to an annual stopping rate) is appropriate for decision making, particularly as the underlying cause of hyperkalaemia in CKD and HF patients is unlikely to be reversible.[3]

9.4. Cost-effectiveness evidence

NICE TA1148 has determined that Lokelma is a cost-effective use of NHS resources (please refer to Section 5.2) for persistent hyperkalaemia from sK level ≥5.5 mmol/L.[3]

In TA1148, the committee noted that with its preferred assumptions to modelling, the cost-effectiveness estimate was £33,725 per quality adjusted life year (QALY) gained. The committee stated that there were several benefits of Lokelma that were not captured in the economic model, including the benefit to patients with concomitant CKD and HF, the potential to reduce secondary-care costs through improved management of CKD and HF, and the ability for treatment enabled RAASi use to improve cardiac function. Because of these factors, the committee concluded that an acceptable incremental cost-effectiveness ratio (ICER) would be towards the higher end of the range NICE considers a cost-effective use of NHS resources (£25,000 to £35,000 per QALY gained). The committee recommended Lokelma for use in patients with CKD stage 3b to 5 or HF and a sK level of at least 5.5 mmol/litre.[3]

9.5. Local financial impact

Estimated patients eligible for Lokelma with a sK level between 5.5 to 6 mmol/L

To calculate a local estimate of patient numbers likely to be treated and cost impact, please refer to the NICE resource impact template where users can amend the 'population and treatment', and 'unit costs' worksheets in the template to reflect local data and assumptions. The template is also accompanied by a NICE Resource impact summary report.

Potential capacity savings from Lokelma use in patients with a sK level between 5.5 to 6 mmol/L

Clinical trial evidence suggests that people having Lokelma are less likely to reduce their RAASi dosage than people making dietary changes alone. The evidence also suggests that Lokelma may lower the chance of adverse outcomes, such as hospitalisation, MACE and death which may lead to capacity savings.[43] The data used to demonstrate this in TA1148 that was accepted by NICE is commercial in confidence, so users need to include estimated rates included in the NICE resource impact template to reflect local assumptions. Users can also update the number of appointments and tests in the resource impact template to reflect local practice.

Number of patients likely to be treated in primary versus secondary care

TA1148 no longer restricts access to specialist care allowing primary care initiation.[3] Based on sK level, local

assumptions should be made to reflect what proportion of patients would be initiated in primary care versus secondary care.

9.6. Wider resource impact

The wider resource impact of initiating Lokelma in primary care has been estimated based on a few key assumptions:

1. All scenarios compare pathway for a like for like patient based on sK 5.5-5.9 mmol/L and an assumption that the patient is otherwise stable
2. Hyperkalaemia is identified during routine testing in primary care
3. Only initiation resource use costs have been accounted for. Drug costs have not been included
4. The pathway for continuation of care (maintenance therapy) is not impacted and remains the responsibility of primary care across all scenarios

Where relevant, costs were inflated to the current cost year using the NHS Cost and Inflation Index (NHSCII) and PSS Pay and Prices index to a 2024 cost year.[44] Please refer to Appendix A: Detailed methodology – calculation of Lokelma initiation costs across settings for an explanation of the methodology used to calculate the cost of Lokelma initiation.

Disclaimer: The below scenarios are based on assumptions and actual cost will vary locally. The scenarios represents a conservative example for illustrative purposes only.

The initiation of Lokelma to manage hyperkalaemia in a primary care setting has been estimated to reduce the cost of initiation by **£296** versus a specialist setting and reduce resource burden on emergency and secondary care services by preventing referrals to access binder therapy (Table 4). This is consistent with the viewpoints captured by the NICE committee in TA1148 who concluded that access to Lokelma may simplify the care pathway, "including reducing the complexity of monitoring persistent hyperkalaemia, [which] may support management in primary care".[3] Initiation in primary care is also aligned with the NHS 10-year Health Plan "Fit for Future" which aims to transform care by shifting services from overstrained hospitals to local communities.

Table 4. Estimated resource use and cost per patient of Lokelma initiation and monitoring during the correction phase following the identification of hyperkalaemia during routine testing in primary or secondary care

Scenarios	Estimated resource use	Estimated cost
Primary care initiation	Approximately 1.6 additional follow-up appointments and blood tests to reach normokalaemia	£84
A&E initiation	Cost of A&E admission (without overnight stay); same requirement for 1.6 additional follow-up appointments and blood tests in primary care to reach normokalaemia	£239
Specialist care initiation	Approximately 1.6 additional follow-up appointments and blood tests to reach normokalaemia	£380
Cost saving from primary care initiation vs A&E	-	**£155**
Cost saving from primary care initiation vs specialist care	-	**£296**

Footnote: Where relevant, costs were inflated to the current cost year using the National Health Service Cost and Inflation Index (NHSCII) and PSS Pay and Prices index to a 2024 cost year.[44] Please refer to Appendix A: Detailed methodology – calculation of Lokelma initiation costs across settings for an explanation of the methodology used to calculate the cost of Lokelma initiation.

Abbreviations: A&E: accident and emergency.

Cost implication of Lokelma use versus no potassium binder

As captured in the NICE resource impact template, patients who are not treated with a potassium binder will require an increased number of specialist appointments, pathology and test resource use compared to a patient being treated with Lokelma. This is in part offset by increased resource use in a primary care setting.[45] The estimated HCRU for a patient with hyperkalaemia treated with Lokelma versus no potassium binder is summarised in Table 5.

Table 5: Estimated annual resource use from NICE resource impact report

Capacity area	Lokelma	No binder
Number of specialist appointments	2	5
Number of GP appointments	3	2
Cardiology tech – ECG	2	3
Pathology – complete blood count	2	5

Abbreviations: ECG: electrocardiogram; GP: general practice; NICE: National Institute of Health and Care Excellence.
Source: [45]

10. Additional considerations

10.1. Environmental Impact

Lokelma does not require any special storage conditions and can be stored at room temperature, whereas Veltassa requires refrigerated storage during transportation and routine storage prior to dispensing and use (2–8 °C).[1, 46] Veltassa also appears more sensitive to environmental degradation, particularly to moisture and temperature fluctuations, as reflected by its requirement for five-layer protective sachets composed of polyethylene, aluminium, polyester, paper, and additional polyethylene layers.[1, 46] Therefore, Lokelma offers a storage advantage, as it does not require refrigerated transport or cold-chain storage. This may provide indirect environmental benefits through reduced energy consumption during transportation and storage, as well as decreased reliance on insulated cold-chain distribution materials. In addition, Lokelma may potentially reduce packaging waste compared with Veltassa, whose multilayer composite sachets are likely to be more difficult to recycle due to their aluminium and mixed-polymer construction.

AstraZeneca has a flagship Ambition Zero Carbon programme and is on track to reduce greenhouse gas emissions from its global operations (scope 1 and 2) by 98% by 2026 (from a 2015 baseline) – by the end of 2024 a 77.5% reduction was achieved. AstraZeneca aims to halve the entire value chain print by 2030 on the way to a 90% reduction and science-based net zero by 2045 (from a 2019 baseline). For more information on the Carbon Reduction Plan, please refer to the AstraZeneca website here: https://www.astrazeneca.co.uk/sustainability.

10.2. Equity and Equality Impact

The expansion of the formulary recommendation for Lokelma will support sustained RAASi therapy in a broader population of patients eligible for Lokelma treatment, enabling an improvement in outcomes for patients with CKD and HF. Please refer to the CVDPrevent explorer tool to evaluate the deprivation quintile by local systems or areas (Data Explorer | CVDPREVENT).

The Core20PLUS5 is a national NHS England approach to inform action to reduce healthcare inequalities at both national and system level. The defined target population includes the most deprived 20% of the national population, as identified by the national Index of Multiple Deprivation (IMD).[47]

According to a review funded by Kidney Research UK, there is a higher incidence of CKD in people who are socially deprived, regardless of the measures used to ascertain social disadvantage.[48] The UKKA has also found that people who live in areas of greater deprivation have higher rates of kidney failure and reduced access to home therapies, transplant listing, and early transplantation.[49] People from more deprived areas who have kidney failure are different from people from less deprived areas: they are younger, and a greater proportion of them are female, and from UK minority ethnic groups. Similarly, the British Heart Foundation has reported that people living in socially deprived areas are more likely to develop CV disease (CVD), die prematurely from it, and experience poorer access to healthcare services that could help manage their condition.[50] The most deprived areas of England have been experiencing a rate of early deaths from CVD that is 2.5 times higher than the rate in the least deprived areas.[51]

Lokelma use has the potential to reduce health inequalities by improving outcomes for conditions that disproportionately affect certain groups.[3] RAASi therapy is a core pillar of CKD and HF management.[52-54] Long-term management with RAASi therapy at the maximum tolerated dose has demonstrated to improve health outcomes for both CKD and HF patients; for patients with CKD this includes slowing disease progression, reducing the risk of end-stage kidney failure (ESKF) and need for dialysis, whereas for patients with HF, this includes improving survival and reducing the risk of hospitalisations and symptoms.[52-54]

While international CKD and HF guidelines emphasise the need to prescribe RAASi therapy at the highest licensed and tolerated dose,[4, 17, 32] down-titration or discontinuation of RAASi therapy is common if a patient develops hyperkalaemia.[4, 29] Following discontinuation, patients lose the important cardiorenal protective effect of these therapies in conditions where they have demonstrated additional benefits beyond alternative anti-hypertensives.[55-58]

Protected characteristics

Lokelma is not expected to disadvantage any groups or populations with protected characteristics.

Lokelma is expected to have a positive impact on the protected characteristic, age. Older adults are at greater risk of hyperkalaemia because of declining renal function and increased prevalence of cardiorenal disease.[59] Lokelma may therefore particularly benefit this group by improving potassium control and supporting optimisation of treatment. No specific dose adjustments are required on the basis of age alone.

11. Lokelma Prescribing Information

Prescribing Information

LOKELMA®(sodium zirconium cyclosilicate) 5g & 10g POWDER FOR ORAL SUSPENSION

Consult Summary of Product Characteristics before prescribing.

Indication: Lokelma is indicated for treatment of hyperkalaemia in adults.

Presentation: 5g or 10g powder for oral suspension. Each sachet contains 5g or 10g sodium zirconium cyclosilicate.

Dosage and Administration: **Correction phase:** Recommended starting dose is 10g, administered orally, three times a day as a suspension in water. When normokalaemia is achieved the maintenance regimen should be followed. Typically, normokalaemia is achieved within 24 to 48 hours. If patient is still hyperkalaemic after 48 hours of treatment the same regimen can be continued for an additional 24 hours. If normokalaemia not achieved after 72 hours of treatment, other treatment options should be considered. **Maintenance phase:** Establish the minimal effective dose to prevent recurrence of hyperkalaemia. Recommended starting dose of 5g once daily, with possible titration up to 10g once daily, or down to 5g once every other day, as needed, to maintain normal potassium level. No more than 10g once daily should be used for maintenance therapy. Monitor serum potassium levels regularly during treatment. **Missed dose:** If a dose is missed the patient should take the next usual dose at their normal time. **Renal impairment:** No dosage adjustment required for patients who are not on chronic haemodialysis. For patients on dialysis Lokelma should only be dosed on non-dialysis days. The recommended starting dose is 5g once daily. To establish normokalaemia (4.0-5.0 mmol/L), the dose may be titrated up or down weekly based on the pre-dialysis serum potassium value after the long inter-dialytic interval (LIDI). The dose could be adjusted at intervals of one week in increments of 5g up to 15g once daily on non-dialysis days. It is recommended to monitor serum potassium weekly while the dose is adjusted; once normokalaemia is established, potassium should be monitored regularly (e.g. monthly, or more frequently based on clinical judgement including changes in dietary potassium or medication affecting serum potassium. **Hepatic impairment:** No changes from the normal doses are required for patients with hepatic impairment. **Elderly population:** No special dose and administration guidelines are recommended for this population. **Paediatric population:** Safety and efficacy has not been established in children and adolescents (<18 years). **Method of administration:** The entire contents of the sachet(s) should be emptied in a drinking glass containing approximately 45ml of water and stirred well. The tasteless liquid should be drunk while still cloudy. The powder will not dissolve. If the powder settles, the liquid should be stirred again and taken. If needed, rinse the glass with more water to ensure that all of the content is taken. The suspension can be taken with or without food.

Contraindications: Hypersensitivity to the active substance.

Warnings and Precautions: **Serum potassium levels:** Monitor serum potassium levels 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 Lokelma dose is titrated. Monitoring frequency will depend upon a variety of factors including other medicinal products, progression of chronic kidney disease and dietary potassium intake. **Hypokalaemia:** Hypokalaemia may be observed. To prevent moderate to severe hypokalaemia dose titration (maintenance posology) may be required. Discontinue and re-evaluate treatment in patients with severe hypokalaemia. **Worsening of pre-existing heart failure:** Monitor patients with pre-existing heart failure, particularly those in whom an increased sodium intake may lead to fluid overload and decompensation. Manifestations of worsening heart failure, including increased dyspnoea, oedema and rapid weight gain, should be managed as per standard clinical practice. **QT Prolongation:** During correction phase, a lengthening of QT interval can be observed as the physiologic result of decline in serum potassium concentration. **Risk of interaction with X rays:** Sodium zirconium cyclosilicate may be opaque to X-rays, keep in mind if patient has abdominal X-ray. **Intestinal perforation:** Risk of intestinal perforation unknown. Special attention to be paid as intestinal perforation has been reported with potassium binders including Lokelma. **Sodium content:** Lokelma is considered high in sodium. This should be particularly taken into account for those on a low salt diet.

Drug Interactions: No expected effects of other medicines on sodium zirconium cyclosilicate as it is not absorbed or metabolised by the body. Sodium zirconium cyclosilicate can transiently increase gastric pH and can lead to changes in solubility where co-administered medicinal product has pH-dependent stability and therefore should be administered at least 2 hours before or 2 hours after oral medicinal products with clinically meaningful gastric pH dependent bioavailability (e.g. azole antifungals, a number of anti-HIV agents, and tyrosine kinase inhibitors). Sodium zirconium cyclosilicate can be co-administered without spacing of dosing times with oral medicinal products that do not exhibit pH-dependent bioavailability. Tacrolimus should be taken at least 2 hours before or after Lokelma.

Pregnancy and Lactation: Preferable to avoid use during pregnancy. Can be used during breast-feeding.

Ability to Drive and Use Machines: Lokelma has no or negligible influence on the ability to drive and use machines.

Undesirable Events: **Consult SmPC for full list of side effects.** Very Common: Worsening of pre-existing heart failure (including increased dyspnoea, oedema and rapid weight gain). Common: Hypokalaemia, constipation, oedema related events (including fluid retention, generalised oedema, hypervolaemia, localised oedema, oedema, oedema peripheral, peripheral swelling).

Legal Category: POM.

Marketing Authorisation Numbers: PLGB 17901/0332, PLGB 17901/0331.

Presentation & Basic NHS Cost: 5g x 30 pack: £156; 10g x 3 pack: £31.20; 10g x 30 pack: £312.

Business Responsible for Sale and Supply / Further Information: AstraZeneca UK Ltd., 2 Pancras Square, 8th Floor, London, N1C 4AG, UK.

LOKELMA is a trade mark of the AstraZeneca group of companies.

Date of preparation: 02/2026

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Adverse events should be reported. Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard** or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to AstraZeneca by visiting **https://contactazmedical.astrazeneca.com** or by calling **0800 783 0033.**

AstraZeneca

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13. Appendix A: Detailed methodology – calculation of Lokelma initiation costs across settings

The wider resource impact of initiating Lokelma in primary care has been estimated based on a few key assumptions:

1. All scenarios compare pathway for a like for like patient based on sK 5.5-5.9 mmol/L and an assumption that the patient is otherwise stable
2. Hyperkalaemia is identified during routine testing in primary care
3. Only initiation resource use costs have been accounted for. Drug costs have not been included
4. The pathway for continuation of care (maintenance therapy) is not impacted and remains the responsibility of primary care across all scenarios

Where relevant, costs were inflated to the current cost year using the NHS Cost and Inflation Index (NHSCII) and PSS Pay and Prices index to a 2024 cost year.[44]

Disclaimer: The below scenarios are based on assumptions and actual cost will vary locally. The scenarios represent a conservative example for illustrative purposes only.

Scenario 1: Primary care initiation of Lokelma

- During routine testing in primary care, hyperkalaemia has been identified
- As per the SmPC, the recommended starting dose of Lokelma is 10 g, administered three times a day orally as a suspension in water (typically, normokalaemia is achieved within 24 to 48 hours. If patients are still hyperkalaemic after 48 hours of treatment, the same regimen can be continued for an additional 24 hours. If normokalaemia is not achieved after 72 hours of treatment, other treatment approaches should be considered).[1]
- A blood test would be required in primary care to reassess serum potassium levels to enable the maintenance regimen to be initiated. The average additional touchpoints required to conduct the blood test and determine normokalaemia has been calculated as 1.6 based on Study ZS005 (Table 6)

Table 6. Calculation of average follow-up blood tests required based on time to normokalaemia from Study-ZS005

Step*	Patients needing a test	Contribution
First follow-up test (24 hours)	100%	1.0
Second test (48 hours)	34.0%	0.34
Third test (72 hours)	24.7%	0.247
Total expected tests		1.6

Source: [6]

*Assumes: Every patient gets the first follow-up blood test at 24h; only non-responders get another test at 48h; only remaining non-responders get another at 72h.

On average, the cost implications of 1.6 additional touchpoints and blood tests in primary care equates to £84:

- £72 for the GP visit (£45 per visit multiplied by 1.6)[44]
- £12 for the Urea and Electrolytes (U&E) test (£7.57 multiplied by 1.6)[60]

Scenario 2: A&E administration of Lokelma

- During routine testing in primary care, hyperkalaemia is identified and the patient is referred to A&E
- Lokelma is prescribed in A&E and the follow-up blood tests then occur in primary care (the cost implication of if a patient remains hyperkalaemic and needs to return to A&E is not included in pricing estimate)
- The minimum core additional cost would be for the A&E admission without overnight stay (£155),[61] and the same assumptions above would apply for the additional blood tests and follow-up

appointments (£84). Therefore, the minimum cost implication is estimated to be £239 (please note inflation to the current cost year, as mentioned above).

Scenario 3: Primary care referral to secondary care for initiation of Lokelma

- During routine testing in primary care, hyperkalaemia is identified and the patient is referred to specialist care
- Initiation and monitoring of Lokelma is managed in the specialist setting
- As per the SmPC, the recommended starting dose of Lokelma is 10 g, administered three times a day orally as a suspension in water (typically, normokalaemia is achieved within 24 to 48 hours. If patients are still hyperkalaemic after 48 hours of treatment, the same regimen can be continued for an additional 24 hours. If normokalaemia is not achieved after 72 hours of treatment, other treatment approaches should be considered).
- A blood test would be required in specialist care to reassess sK levels to enable the maintenance regimen to be initiated. The average additional touchpoints required to conduct the blood test and determine normokalaemia has been calculated as 1.6 based on Study ZS005 (Table 6)

On average, the cost implications of 1.6 additional touchpoints and blood tests in a specialist setting equates to £380:

- £368 for the specialist appointment (£230 per visit multiplied by 1.6)[44]
- £12 for the U&E test (£7.57 multiplied by 1.6)[60]