NOW IN YOUR HANDS.

New, highly-selective LOKELMA™ (sodium zirconium cyclosilicate) is indicated for the treatment of hyperkalaemia in adult patients\(^1\)

Prescribing Information and Adverse Event Reporting information can be found on the back cover
SWIFT* REDUCTION OF SERUM K+ LEVELS.  

In the 48 hour open label phase of the study:

One dose (10g) of LOKELMA significantly reduced the mean serum K+ level after 1 hour.  
(-0.2 mmol/L compared to baseline.  95% CI: -0.3 to -0.2)  

88% OF PATIENTS ACHIEVED NORMOKALAEMIA AT 48 HOURS.  

*In an emergency situation, standard of care should be used in line with national or local guidelines.

HARMONIZE (ZS004), a Phase III, multicentre, multiphase, placebo-controlled study in 258 patients with hyperkalaemia. Open-label phase: LOKELMA 10 g three times daily, administered for 48 hours, at which time patients (n=237) with normokalaemia (3.5–5.0 mmol/L) were randomised to LOKELMA or placebo once daily, 5 g, 10 g, or 15 g, for 28 days. Primary endpoint: mean serum K+ level with LOKELMA vs placebo on days 8–29. Eligible patients then continued treatment with LOKELMA 10 g once daily, which could be titrated to 5 g or 15 g, in an 11-month, open-label extension study (ZS004E). Please note that LOKELMA 15 g is not approved for use.
SUSTAINED SERUM K+ CONTROL FOR UP TO ONE YEAR WHEN USED AS MAINTENANCE THERAPY.\(^1\)

Once-daily maintenance dosing of LOKELMA sustains normokalaemia (3.5 - 5.0 mmol/L) for up to one year.\(^1\)
(Clinical trials with LOKELMA have not included exposure longer than one year).\(^1\)
88% of patients in the Extension Phase who were receiving LOKELMA maintained an average serum K+ of <5.1 mmol/L over 11 months.\(^1\)
No dietary restrictions were imposed; patients were instructed to continue their usual diet without any specified alterations.\(^1\)

Mean serum K+ levels across correction, maintenance, and extension phases\(^{11}\)

![Graph showing mean serum K+ levels across correction, maintenance, and extension phases](chart.png)

Adapted from LOKELMA SMPC.

\(^{1}\)Please note that the recommended starting dose for maintenance therapy with LOKELMA is 5 g once daily, which may be titrated to 10 g once daily as needed. No more than 10 g once daily should be used for maintenance therapy. The 5 g once daily dose can be down titrated to 5 g every other day.\(^2\)

\(^{2}\)The extended maintenance group contained a small proportion (11%) of patients who were maintained throughout with LOKELMA 15 g once daily.\(^3\)

LOKELMA 15 g is not approved for use.\(^1\)
CONSISTENT SERUM K⁺ REDUCTION IN ALL STUDIED PATIENT GROUPS²

► LOKELMA consistently reduced serum K⁺, regardless of comorbidities†, use of RAASi therapy, or baseline K⁺ level²

► Patients with higher baseline K⁺ levels experienced greater reductions in serum K⁺.²

Mean serum K⁺ levels at 0 and 48 hours across baseline K⁺ levels.²

Adapted from Kosiborod M, et al., 2014.²

1 CKD history, CKD eGFR, heart failure, diabetes mellitus, taking RAASi.
ONCE-DAILY MAINTENANCE DOSING

- LOKELMA is a daily treatment option for hyperkalaemia.
- Recommended dosing of LOKELMA to achieve and sustain normokalaemia:

**CORRECTION PHASE**

<table>
<thead>
<tr>
<th>Morning</th>
<th>Midday</th>
<th>Evening</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 g</td>
<td>10 g</td>
<td>10 g</td>
</tr>
</tbody>
</table>

Recommended starting dose of 10g three times daily for up to 48 hours until normokalaemia is achieved.

**MAINTENANCE PHASE**

1X /day

5 g for up to one year

- To establish minimum effective dose, LOKELMA may be titrated
  - Up to 10 g once daily or
  - Down to 5 g once every other day

- No more than 10 g once daily should be used for maintenance therapy

---

*If normokalaemia is not achieved within 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.

† Patients who miss a dose should be instructed to take the next usual dose at their normal time.

** Clinical trials with LOKELMA have not included exposure longer than one year.

In an emergency situation, standard of care should be used in line with national or local guidelines.
GENERALLY WELL TOLERATED K+ CONTROL IN CLINICAL TRIALS.¹

- The safety profile of LOKEMA was evaluated in clinical trials involving 1760 patients with 507 patients exposed for one year.¹

- 5.7% of patients receiving LOKELMA reported oedema-related events*, observed more frequently in patients taking a 15 g dose. Please note the 15 g dose is not a licensed dose.

- No clinically significant changes in urinary sodium excretion, or serum magnesium and calcium levels, were observed with LOKELMA.

- 4.1% of patients receiving LOKELMA developed hypokalaemia (serum K+ level <3.5 mmol/L), which resolved with dosage adjustment or discontinuation of LOKELMA**

*Including fluid overload, fluid retention, generalised oedema, hypervolamia, localised oedema, oedema, oedema peripheral, and peripheral swelling.¹ Studies beyond the first month of therapy were single-armed so comparative placebo rates are not available.

**Clinical trials with LOKELMA have not included exposure longer than one year.
Drug-Drug interactions.\(^1\)

LOKELMA can transiently increase gastric pH by absorbing hydrogen ions.\(^1\)

► As a result, LOKELMA can change the solubility and absorption of co-administered drugs that exhibit pH-dependent bioavailability, potentially altering efficacy or safety of these drugs when taken close to the time LOKELMA is administered.

► 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. In a clinical drug-drug interaction study conducted in healthy subjects, co administration of LOKELMA with amlodipine, clopidogrel, atorvastatin, furosemide, glipizide, warfarin, losartan or levothyroxine did not result in clinically meaningful drug-drug interactions. Consistent with co-administration of dabigatran with other gastric acid modifiers, dabigatran Cmax and AUC values were approximately 40% lower when co-administered with LOKELMA.

► No dose adjustments or separation of time of dosing are required for any of these medicinal products. However, LOKELMA should be administered at least 2 hours before or 2 hours after oral medications with clinically meaningful gastric pH dependent bioavailability.
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 for adults and elderly is 10g, administered orally, three times a day as a suspension in water, with or without food. Empty entire contents of sachet into approximately 45ml of water, stir if powder settles. 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. Monitoring frequency will depend on factors such as other medications, progression of chronic kidney disease and dietary potassium intake. Discontinue and re-evaluate patient if severe hypokalaemia occurs. No clinical data available for treatment beyond one year. Renal/hepatic impairment: No dosage adjustment required. Paediatric population: Safety and efficacy has not been established in children and adolescents (<18 years).

**Contraindications:** Hypersensitivity to the active substance.

**Warnings and precautions:** 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. 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. During correction phase, a lengthening of QT interval can be observed as the physiologic result of decline in serum potassium concentration. Sodium zirconium cyclosilicate may be opaque to X-rays, keep in mind if patient has abdominal X-ray. Risk of intestinal perforation unknown. Special attention to be paid as intestinal perforation has been reported with polymers that act in the gastrointestinal tract. No experience with patients receiving dialysis treatment. Limited experience in patients with serum potassium concentrations greater than 6.5 mmol/L. Preferable to avoid use during pregnancy.

Can be used during breast-feeding.

**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 medications with clinically meaningful gastric pH dependent bioavailability (e.g. azole antifungals, a number of anti-HIV drugs, and tyrosine kinase inhibitors). Sodium zirconium cyclosilicate can be co-administered without spacing of dosing times with oral medications that do not exhibit pH-dependent bioavailability.

**Undesirable events:** Consult SmPC for full list of side effects. **Common:** Hypokalaemia, oedema related events (including fluid overload, fluid retention, generalised oedema, hypervolaemia, localised oedema, oedema, oedema peripheral, peripheral swelling).

**Legal category:** POM.

**Marketing authorisation numbers:** EU/1/17/1173/002-004

**Presentation and Basic NHS cost:** 5g x 30 pack: £213.60; 10g x 3 pack: £42.72; 10g x 30 pack: £427.20.

**Marketing Authorisation Holder:** AstraZeneca AB, SE-151 85 Södertälje, Sweden.

**Further information is available from:** AstraZeneca UK Ltd., 600 Capability Green, Luton, LU1 3LU, UK.

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

Date of preparation: 03/2019

CV 19 0043

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to AstraZeneca by visiting https://aereporting.astrazeneca.com/ or by calling 0800 783 0033.

References:
1. LOKELMA Summary of Product Characteristics. AstraZeneca, 2018