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

**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).

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

**Legal category:** POM

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

**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 on 0800 783 0033.

References:
1. LOKELMA Summary of Product Characteristics. December 2018

GB-15594 March 2019
LOKELMA DOSING

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

**CORRECTION PHASE**

10g 3 times a day for 24 to 48 hours until normokalaemia is achieved.

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, the treatment approaches should be considered.

**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

Serum potassium levels should be monitored regularly during treatment. Monitoring frequency will depend upon a variety of factors including other medications, progression of chronic kidney disease and dietary potassium intake. If severe hypokalaemia should occur, LOKELMA should be discontinued and the patient re-evaluated.

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.

**ORAL ADMINISTRATION**

- Mix LOKELMA with 3 tablespoons (45 mL) of water for oral administration

- Tasteless and odourless
- May be taken with many other medications
- May be taken with or without food
- No special conditions for storage

Drug:drug interactions.

- 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 after oral medications with clinically meaningful gastric pH dependent bioavailability. e.g. azole antifungals (ketoconazole, itraconazole and posaconazole), anti-HIV drugs (atazanavir, nevirapin, indinavir, ritonavir, saquinavir, raltegravir, ledipasvir and rilpivirine) and tyrosine kinase inhibitors (erlotinib, dasatinib and nilotinib).