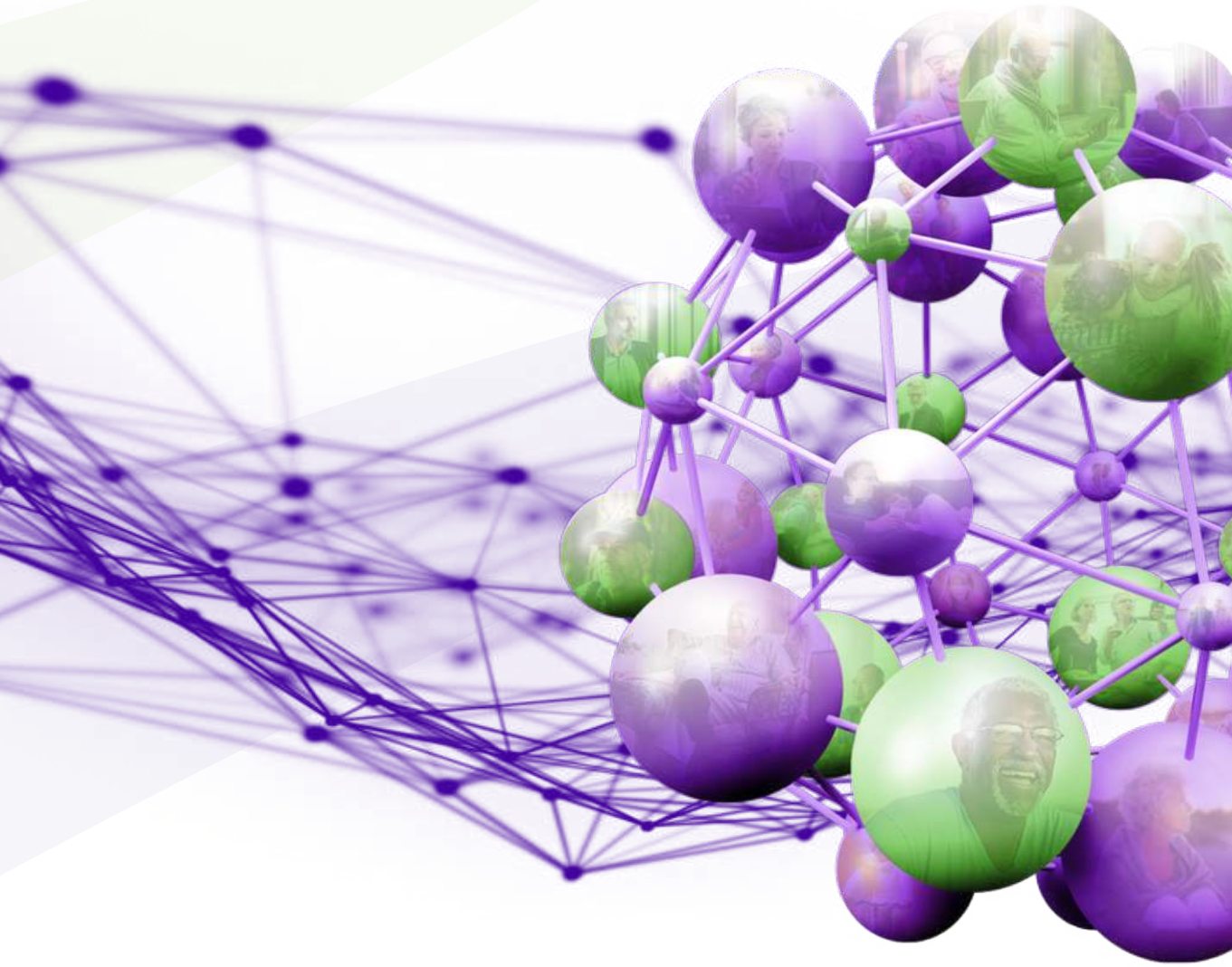
Veltassa®
(patiromer) for oral suspension

Electrolytes: Relevance and impact

Key information on sodium, magnesium and calcium



Sodium Na^+

Definition

Sodium is the most prevalent electrolyte in the extracellular fluid, playing an essential role in cellular homeostasis[1]

Physiological role

Adequate amounts of sodium (1.5 g/day) are needed in the diet to maintain optimal nerve and muscle function, fluid and electrolyte balance, and blood pressure[1]

Potential risks

- High intakes of sodium from diet and medications are known to increase extracellular fluid volume and blood pressure, which may accelerate disease progression in chronic kidney disease (CKD) and heart failure (HF) patients[2–5]
- Consequently, KDIGO and ESC Guidelines recommend that patients with CKD, HF and hypertension limit their dietary sodium intake (<2 g/day) to minimise the risk of adverse renal and cardiovascular outcomes[5–7]

Implication and Relevance

- **Depending on the dosing regimen, some potassium binders (e.g. sodium polystyrene sulphonate) indicated for the treatment of hyperkalaemia may contain up to three times (6.0 g)* the guideline recommended dose of sodium for patients with CKD, HF and hypertension (<2 g/day)[5–7,8]**

- The sodium content in these potassium binders may compromise the efficacy of RAASi therapy, and worsen symptoms of CKD, HF and hypertension[3]

Relevance to Veltassa®

- Veltassa® binds potassium in exchange for calcium instead of sodium, and is excreted with potassium to lower total body K^+ levels[9,10]
- Ensures suitability for patients who cannot tolerate even a small increase in sodium load, such as your patients with severe heart failure, hypertension or marked oedema[9,10]

*Since the *in vivo* efficiency of sodium-potassium exchange resins is approximately 33%, about one third of the resin's actual sodium content is being delivered to the body.

1. Strazzullo P & Leclercq C. *ASN Adv Nutr* 2014;5(2):188–90. **2.** Visser FW, et al. *Obesity* 2009;17(9):1684–8. **3.** Clegg DJ, et al. *Mayo Clin Proc* 2017;92(8): 1248–60. **4.** George J, et al. *BMJ* 2013;347:1–8. **5.** KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. **6.** McMurray JJV, et al. *Eur Heart J* 2012;33:1787–847. **7.** Williams B, et al. *Eur Heart J* 2018;39:3021–104. **8.** Kayexalate® Prescribing Information (Canada). Sanofi 2014. **9.** Li L, et al. *J Card Pharmacol Ther* 2016;21(5):456–65. **10.** Veltassa® EU SmPC, 2017.

Magnesium Mg^{2+}

Definition

Magnesium is a crucial cofactor which helps to stabilise numerous enzymes across the body, including those that are involved in the generation of adenosine triphosphate[1]

Physiological role

Magnesium plays a part in multiple essential physiological functions, such as the regulation of heart rhythm, vascular tone, platelet-activated thrombosis, neurotransmitter release and bone formation.[1] The European Food Safety Authority (EFSA) recommends that adult (≥18 years) men and women consume 350 mg and 300 mg of magnesium each day, respectively[2]

Potential risks

- Hypomagnesaemia (less than 0.7 mEq/L) is thought to have a prevalence of around 2.5–15% in the general population,[3] but is common in hospitalised patients due to issues such as reduced absorption from impaired GI activity, malnutrition, renal wasting of various drugs and diabetes mellitus[4–6]
- Hypomagnesaemia can lead to irregularities in other mineral levels, such as hypocalcaemia and hypokalaemia[4]
- Permanent/chronic hypomagnesaemia is associated with an increased risk of osteoporosis, atherosclerosis, neuromuscular disorders and cardiovascular disease[4,7]
- Whereas, excessive magnesium levels (hypermagnesaemia) can result in other adverse cardiovascular events, ranging from bradycardia (slower than normal heart rate), atrial fibrillation, asystole (cardiac arrest rhythm with no discernible electrical activity) and complete heart blocks[1]

Relevance of magnesium in Veltassa®

- Veltassa® can also bind to magnesium. The majority of magnesium uptake occurs in the small intestine, therefore any remaining magnesium binding by Veltassa® in the colon is likely to be minor[8,9]
- Approximately 9% of patients in clinical trials developed hypomagnesaemia with a serum Mg^{2+} level of <1.4 mg/dL.[10] Hypomagnesaemia was reported as an adverse reaction in 5.3% of patients treated with patiromer[10]
- Hypomagnesaemia was reported as mild-to-moderate,[1] and no patient developed serum Mg^{2+} levels <1 mg/dL (0.4 mmol/L)[10]
- No patient had cardiac arrhythmias or neuromuscular abnormalities that were associated with hypomagnesaemia (Mg^{2+} <1.2 mg/dL)[11]
- Magnesium supplementation should be considered in patients who develop low serum magnesium levels[10]

1. Jahnen-Dechent W & Ketteler M. *Clin Kidney J* 2012;5(Suppl 1):i3–i14. **2.** Scientific Opinion on Dietary Reference Values for magnesium. *European Food Safety Authority Journal* 2015;13(7):4186. **3.** Harding M. *Patient.* 2014. Available at: https://patient.info/doctor/magnesium-disorders#nav-0. Date accessed: March 2019. **4.** Swaminathan R. *Clin Biochem Rev* 2003;24:47–66. **5.** Hansen B-A & Bruserud Ø. *J Intensive Care* 2018;6:21. **6.** Wang AK, et al. *Indian J Crit Care Med* 2014;18(7):456–60. **7.** Feillet-Coudray, et al. *J Nutr* 2003;133(4):1220–3. **8.** Pitt B & Garza D. *Expert Opinion on Drug Safety* 2018;17(5):525–35. **9.** Beccari BV, et al. *Core Evidence* 2017;12:11–24. **10.** Veltassa® EU SmPC, 2017. **11.** Bakris GL, et al. *JAMA* 2015;314(2):151–61.

Calcium Ca^{2+}

Definition

The majority of calcium in the body (99%) is stored in bones and teeth as a calcium-phosphate crystal lattice called hydroxyapatite[1,2]

Physiological role

Adequate calcium intake is required for normal growth, development and skeletal strength. In addition, small serum calcium levels are necessary for muscle function, nerve transmission, hormonal secretion and vascular contraction.[2] According to the EFSA, all adults aged ≥25 years (including lactating and pregnant women) should consume at least 750 mg of calcium each day[3]

Potential risks

As CKD progresses, and the kidneys stop functioning, calcitriol production ceases and parathyroid hormone levels excessively increase to maintain serum calcium levels. As a result, calcium is extracted from bones in order to maintain adequate levels in the blood, which increases the risk of fractures and osteoporosis. In addition, the excessive production of parathyroid hormone can result in high calcium blood levels (hypercalcaemia), increasing the risk of vascular calcification, atherosclerosis and cardiovascular disease[4]

Relevance of calcium in Veltassa®

- Veltassa® uses calcium as the counter-exchange ion for potassium, with approximately 1.6 g of calcium complexed within an 8.4 g dose of Veltassa®[5]
- Veltassa® is designed to ensure that most of the calcium exchanged for potassium occurs in the colon, where calcium absorption is minimal; with a small calcium fraction being released during transit through the GI system[6,7]
- Studies in healthy individuals have shown that about 73 mg of calcium are absorbed into the body from a maximal recommended daily dose (25.2 g) of Veltassa®; such amounts being unlikely to increase the risk of vascular calcification in CKD patients[6,7]

EFSA, European Food Safety Authority; GI, gastrointestinal.

1. Hill Gallant KM & Spiegel DM. *Curr Osteoporos Rep* 2017;15:214–21. **2.** Flynn A. *Proceedings of the Nutrition Society* 2003;62:851–8. **3.** Scientific Opinion on Dietary Reference Values for calcium. *European Food Safety Authority Journal* 2015;13(5):4101. **4.** Nigwekar SU, et al. *Bonekey Rep* 2014;3:498. **5.** Weir MR, et al. *Am J Med* 2018;131(5):555–64. **6.** Bushinsky DA, et al. *Clin J Am Soc Nephrol* 2016;11(10):1769–76. **7.** Bushinsky DA, et al. *Am J Nephrol* 2016;44:404–10.

Abbreviated prescribing information Veltassa®

For full prescribing information refer to the Summary of Product Characteristics (SmPC).

Presentation and active ingredient: Patiromer (as patiromer sorbitex calcium) powder for oral suspension available in sachets containing either 8.4 g, 16.8 g or 25.2 g.

Indication: Treatment of hyperkalaemia in adults.

Dosage and Administration: The recommended starting dose of Veltassa® is 8.4 g administered orally once-daily with or without food. The daily dose may be adjusted by 8.4 g as needed at one-week intervals or longer to reach desired serum potassium target range, up to a maximum dose of 25.2 g daily. If serum potassium falls below the desired range, the dose should be reduced or discontinued. If a dose is missed, the missed dose should be taken as soon as possible on the same day and should not be taken with the next dose. Veltassa® may affect certain oral medicines taken at the same time, such as ciprofloxacin, levothyroxine, metformin and quinidine and therefore Veltassa® administration should be separated by at least 3 hours from other oral medicinal products. The onset of action of Veltassa® occurs 4–7 hours after administration. Veltassa® should not replace emergency treatment for life-threatening hyperkalaemia. There is limited data on the use of Veltassa® in patients on dialysis; no special dose and administration guidelines were applied to these patients in clinical studies.

Contraindications: Veltassa® is contraindicated in patients with a history of a hypersensitivity reaction to Veltassa® or any of its excipients including xanthan gum.

Special warnings and precautions: Due to potential hypomagnesaemia, serum magnesium should be monitored for at least 1 month after initiating treatment, and magnesium supplementation considered in patients who develop low serum magnesium levels. A risk/benefit evaluation is required in patients with current or a history of severe gastrointestinal disorders, before and during treatment. When discontinuing Veltassa®, serum potassium levels may rise, especially if RAAS inhibitor treatment is continued, so patients should be instructed not to discontinue therapy without consulting their physicians. Increases in serum potassium may occur as early as 2 days after the last Veltassa® dose. Serum potassium should be monitored when clinically indicated, including after changes are made to medicinal products that affect the serum potassium concentration (e.g. RAAS inhibitors or diuretics) and after the Veltassa® dose is titrated. Veltassa® contains sorbitol as part of the counterion complex (4.0 g per 8.4 g of patiromer), therefore patients with hereditary problems of fructose intolerance should not take this medicine. Veltassa® contains calcium as part of the counterion complex; calcium is partially released, some of which may be absorbed therefore a risk/benefit evaluation is required in patients at risk of hypercalcaemia. There are limited clinical data in patients with end-stage renal disease and in patients with serum potassium concentrations greater than 6.5 mEq/L.

Overdosage: Since excessive doses of Veltassa® may result in hypokalaemia, serum potassium levels should be monitored.

Special populations: The use of Veltassa® has not been studied in children under 18 years. Since there are no data from the use of patiromer in pregnant women, it is preferable to avoid the use of Veltassa® during pregnancy. No special dose and administration guidelines are recommended for elderly population.

Undesirable effects: Common (≥1/100 to <1/10): hypomagnesaemia, constipation, diarrhoea, abdominal pain, flatulence. Please consult the SmPC in relation to other undesirable effects.

Prescription Only Medicine. Full prescribing information is available on request. Please read the full SmPC prior to administration. Veltassa® is a registered trademark.

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[TO BE COMPLETED WITH LOCAL REQUIREMENTS (e.g. MA number, contact address, adverse events reporting details, price, date of revision)]

The information and materials for Veltassa contained in this website were prepared based on the EU SmPC. Prescribing information may vary depending on local approval in each country.

Therefore, before prescribing any product, always refer to local materials such as the prescribing information and/or the Summary of Product Characteristics (SPC).

VIFOR PHARMA

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