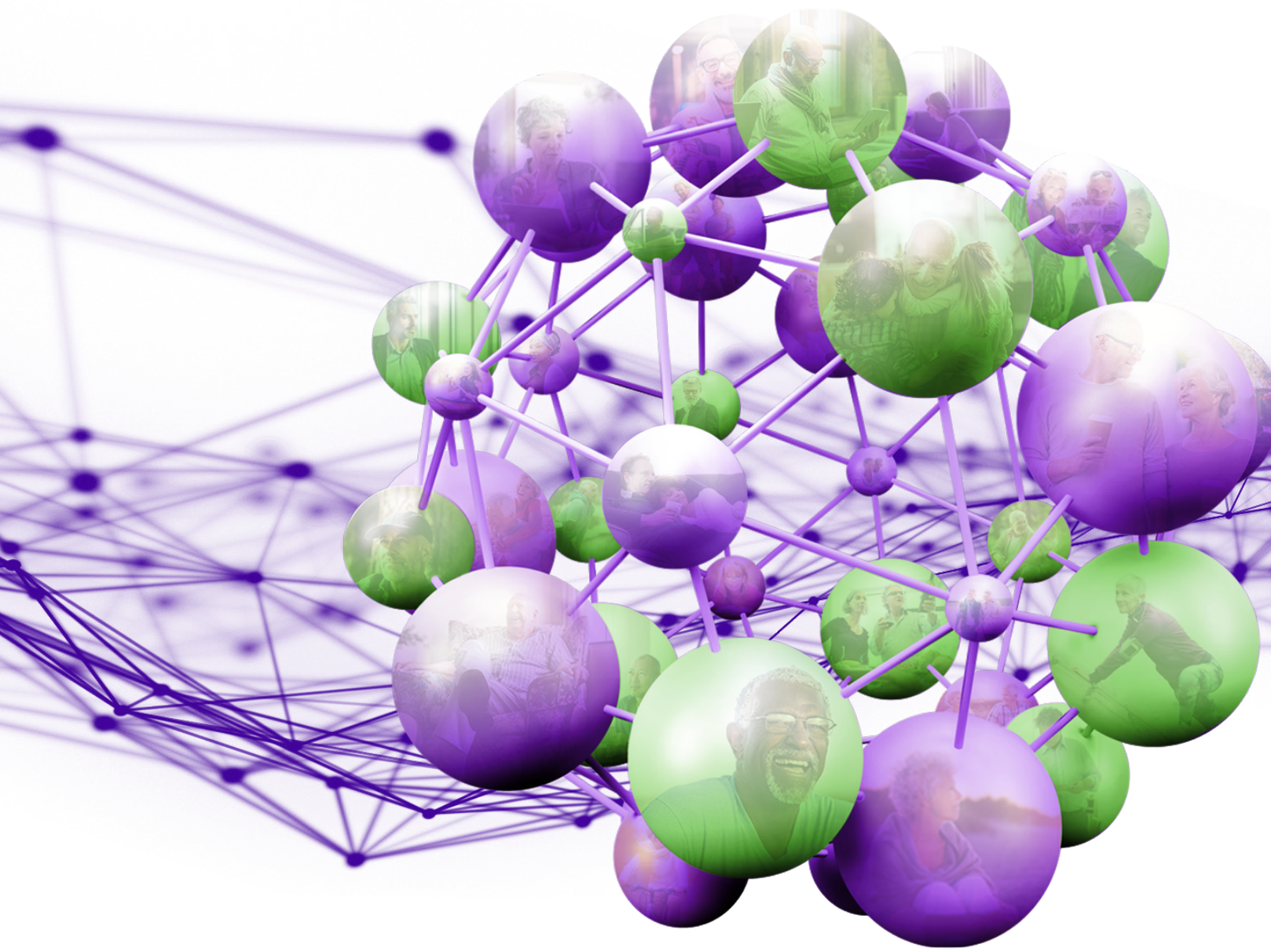
Veltassa® (patiromer) for oral suspension

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[11]

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® SmPC 2022. 11. KDIGO 2021 Clin Pract Guideline for the management of Blood Pressure in CKD. KI Suppl. 2021;99.S1-S87

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 mmoL/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 >0.58 mmoL/L.[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 >0.4 mmoL/L[10]
- 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.** Ayuk J, Gittoes NJ. How should hypomagnesaemia be investigated and treated? Clin Endocrinol (Oxf). 2011 Dec;75(6):743-6. doi: 10.1111/j.1365 **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® SmPC 2022. **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 the mean 24-hour urine ion excretion of calcium increased with 73 mg after a maximal recommended daily dose (25,2g) of Veltassa®; such amounts are 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.

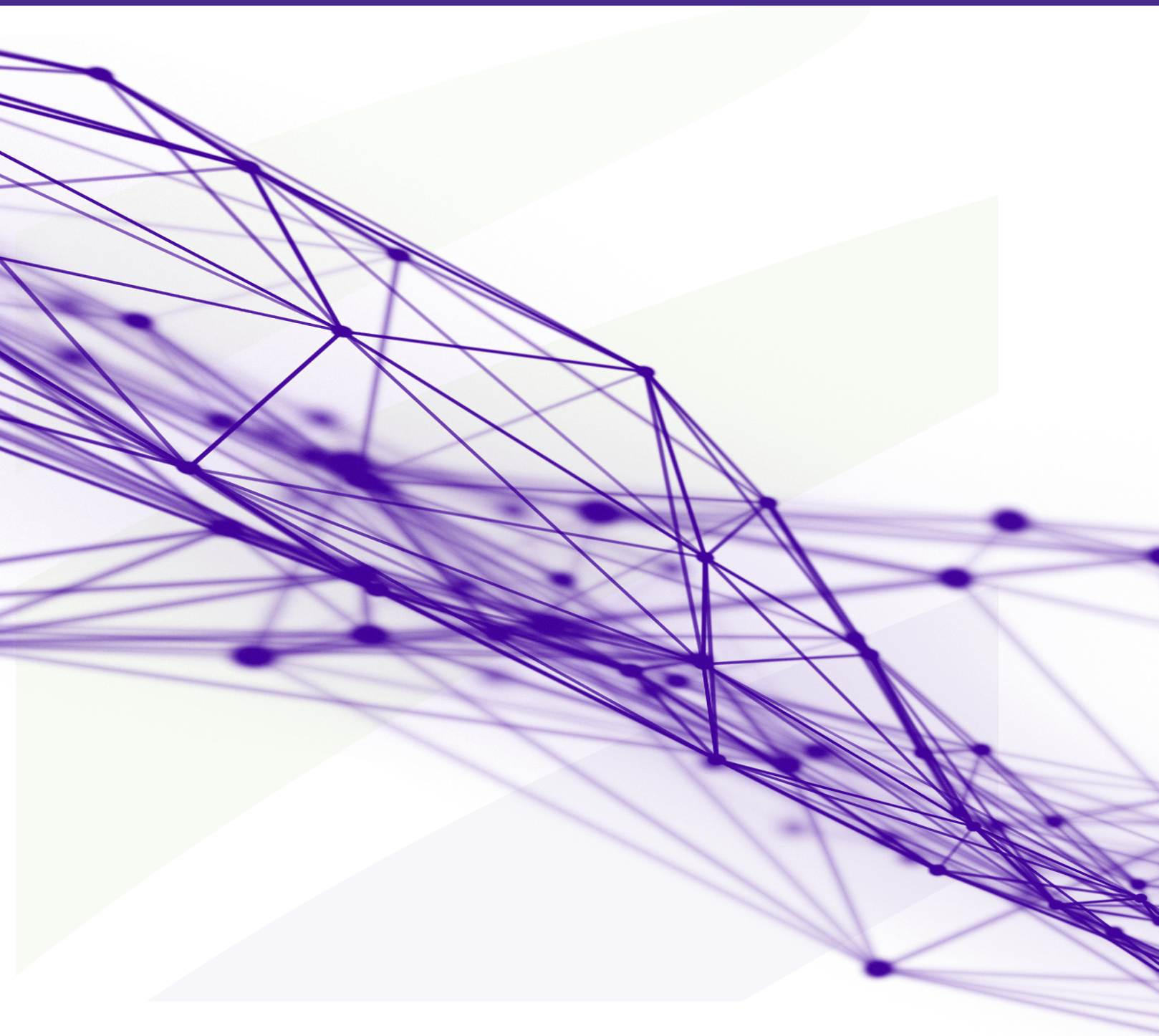
Abbreviated prescribing information Veltassa®

Veltassa (patiromer)

Middel mot hyperkalemi. ATC-nr.: V03AE09. Utleveringsgruppe C. Reseptbelagt legemiddel. Kan forskrives på H-resept.

Pulver til mikstur, suspensjon 8,4 g og 16,8 g.

Indikasjoner: Behandling av hyperkalemi hos voksne. **Dosering:** ***Voksne, inkl. eldre:*** Anbefalt startdose er 8,4 g 1 gang daglig. Daglig dose kan justeres i intervaller på ≥1 uke, basert på serumkaliumnivå og ønsket målområde. Daglig dose kan økes eller reduseres med 8,4 g for å nå ønsket målområde. Maks. dose er 25,2 g daglig. Hvis serumkalium faller under ønsket område, bør dosen reduseres eller avbrytes. Virkning inntrer 4-7 timer etter administrering. Skal ikke erstatte akuttbehandling av livstruende hyperkalemi. ***Tilberedning/ Håndtering:*** Se pakningsvedlegg. ***Administrering:*** Se pakningsvedlegg. **Kontraindikasjoner:** Overfølsomhet for innholdsstoffene. **Forsiktighetsregler:** Serummagnesium bør overvåkes i minst 1 måned etter behandlingsstart, og magnesiumtilskudd vurderes ved utvikling av lave serummagnesiumnivåer. Gastrointestinal iskemi, nekrose og/eller intestinal perforasjon er rapportert med andre kaliumbindere. Fordel/risiko bør vurderes nøye hos pasienter med nåværende eller tidligere alvorlige gastrointestinale sykdommer, før og under behandling. Serumkaliumnivåene kan øke ved seponering, særlig hvis behandling med RAAS-hemmere fortsettes. Pasienten skal instrueres om ikke å avbryte behandlingen uten å rådføre seg med lege. Serumkalium skal overvåkes når klinisk indisert, inkl. etter endring av legemidler som påvirker kaliumkonsentrasjonen (f.eks. RAAS-hemmere eller diuretika) og etter at patiromerdosen er titrert. Inneholder ca. 4 g (10,4 kcal) sorbitol pr. 8,4 g patiromer. Pasienter med sjeldne arvelige problemer med fruktoseintoleranse bør ikke ta dette legemidlet. Inneholder kalsium som frigis delvis, og noe av dette kan bli absorbert. Fordel/risiko bør vurderes nøye ved risiko for hyperkalsemi. **Interaksjoner:** For utfyllende informasjon om relevante interaksjoner, bruk interaksjonsanalyse på felleskatalogen.no. Patiromer har potensiale til å binde enkelte orale legemidler som administreres samtidig, noe som kan redusere gastrointestinal absorpsjon. Som en forholdsregel bør administrering av patiromer derfor skje med 3 timers mellomrom til andre orale legemidler. Reduserer biotilgjengelighet av ciprofloksacin, levotyroksin og metformin ved samtidig inntak, men ikke ved inntak med 3 timers mellomrom. Potensiell interaksjon med bisoprolol, karvedilol, mykofenolatmofetil, nebivolol, kinidin og telmisartan. **Graviditet og amming:** *Graviditet:* Unngå bruk under graviditet. *Amming:* Ingen effekt på nyfødte/spedbarn som ammes er forventet ettersom systemisk eksponering er minimal. Det må tas en beslutning om amming skal opphøre eller behandling avstås fra, basert på nytte-/risikovurdering. **Bivirkninger:** *Vanlige (≥1/100 til <1/10):* Gastrointestinale: Abdominalsmerte, diaré, flatulens, forstoppelse. Stoffskifte/ernæring: Hypomagnesemi. **Pakninger, priser og refusjon (pr. 28.08.2022):** *Pakninger:* 8,4 g, 30 doseposer, Varenr 578950, *Pris:* 2785,60 NOK; 8,4 g, multipakninger som består av 3 esker som inneholder 30 doseposer hver Varenr; 16,8 g, 30 doseposer, Varenr 113451. *Pris:* 2785,60 NOK. *Refusjon:* H-resept: V03A E09_2 Patiromerkalsium. Refusjonsberettiget bruk: Der det er utarbeidet nasjonale handlingsprogrammer/nasjonal faglig retningslinje og/eller anbefalinger fra RHF/LIS spesialistgruppe skal rekvirering gjøres i tråd med disse. Vilkår: (216) Refusjon ytes kun etter resept fra sykehuslege eller avtalespesialist. (222) En blå resept kan ekspederes med H-resept som hjemmel hvis resepten er forskrevet før legemiddelet ble overført til H-reseptordningen. Blå resept: nei. Byttbar: ja, se byttegruppe 002419 på felleskatalogen.no **Innehaver av markedsføringstillatelsen:** Vifor Fresenius Medical Care Renal Pharma France, 100-101 Terrasse Boieldieu, Tour Franklin- La Défense 8, 92042 Paris la Défense Cedex, Frankrig. **Representant:** Vifor Pharma Nordiska AB, Gustav III's boulevard 46, 169 73 Solna, Sverige. Basert på SPC godkjent av SLV: 06.10.2022. **Les felleskatalogtekst eller preparatomtalen (SPC) for mer informasjon, se www.felleskatalogen.no.**



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