

11.04 HIGH FAT FORMULA WITH VITAMINS, MINERALS AND TRACE ELEMENTS AND LOW IN PROTEIN AND CARBOHYDRATE

Oral liquid 250 mL, 30 (KetoVie 3:1)

KetoVie® 3:1

Oral liquid 250 mL, 30 (KetoVie 4:1)

KetoVie® 4:1

Oral liquid 250 mL, 30 (KetoVie Peptide 4:1)

KetoVie® Peptide 4:1

Cortex Health Pty Ltd

1 Purpose of Submission

- 1.1 The Committee Secretariat submission requested that new formulations of high fat formula with vitamins, minerals and trace elements and low in protein and carbohydrate (KetoVie® 3:1, KetoVie® 4:1, KetoVie® Peptide 4:1) continue to be listed on the Pharmaceutical Benefits Scheme (PBS) under the existing conditions of the current formulations.

2 Background

- 2.1 KetoVie® 3:1, KetoVie® 4:1, KetoVie® Peptide 4:1 were recommended by the PBAC at its November 2020 meeting and are currently listed on the PBS as a restricted benefit listing for ketogenic diet.
- 2.2 The submission claimed the new formulations of KetoVie 3:1, KetoVie 4:1 and KetoVie Peptide 4:1 continue to meet the requirements for foods that have special medical purposes as set out under *The Australia New Zealand Food Standards Code – Standard 2.9.5: Food for Special Medical Purposes*.
- 2.3 As these products are marketed as nutritional products and not therapeutic goods, they are not registered in the Australian Register of Therapeutic Goods.

3 Requested listing

- 3.1 The submission requested no changes to the existing listings of KetoVie 3:1, KetoVie 4:1 and KetoVie Peptide 4:1.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer comments

4.2 The PBAC noted that no consumer comments were received for this item.

Nutritional profile

4.3 A comparison of the new and previous formulation of KetoVie 3:1 is provided at Table 1.

4.4 For KetoVie 3:1, the submission stated that the following changes have been made:

- The amount of Vitamin A has been lowered to match the levels in KetoVie 4:1 as previous clinician feedback reported some patients on higher calorie volumes approached upper limits of Vitamin A.
- The amounts for folate and folic acid have been lowered to better meet the dietary requirements and to match the levels in KetoVie 4:1.
- The change in zinc content unifies the micronutrient blend used across the KetoVie line of formulas for the purpose of easier administration.
- The primary fat source in KetoVie flavours was changed from cocoa butter to high oleic sunflower oil as a means of reducing saturated fat content and improving the levels of mono and polyunsaturated fats.

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Table 1: KetoVie 3:1 reformulation

Nutrient	Product nutritional content (per 250 mL carton)		
	KetoVie 3:1 new formulation	KetoVie 3:1 current formulation	New formula/current formula nutritional content
Energy (kilojoule)	1106	1088	102%
Protein (g)	7	7	100%
Carbohydrate (g)	1.3	1.3	100%
Fibre (g)	1	1	100%
Fat (g)	25	25	100%
DHA (mg)	93	93	100%
Vitamin A (mcg retinol equivalents)	167	188	89%
Vitamin D (mcg of cholecalciferol)	6.3	6	105%
Vitamin E (mg a-tocopherol equivalents)	2.8	2.8	100%
Vitamin K (mcg)	20	20	100%
Vitamin K1 (mcg)	10	20	50%
Vitamin K2 (MK-7) (mcg)	10	0	#DIV/0!
Thiamin / B1 (mg)	0.3	0.3	100%
Riboflavin / B2 (mg)	0.5	0.5	100%
Vitamin B6 (mg)	0.3	0.3	100%
Folic acid (mcg)	35	50	70%
Folate, DFE (mcg)	60	83	72%
Pantothenic acid / B5 (mg)	2.1	2.1	100%
Biotin (mcg)	5	5	100%
Vitamin C (mg)	30	30	100%
Choline (mg)	108	108	100%
Inositol (mg)	20	20	100%
Calcium (mg)	314	313	100%
Phosphorous (mg)	217	213	102%
Magnesium (mg)	40	38	105%
Iron (mg)	3.3	3.3	100%
Zinc (mg)	1.7	2	85%
Manganese (mg)	0.29	0.3	97%
Copper (mg)	0.2	0.2	100%
Iodine (mcg)	60	59	102%
Molybdenum (mcg)	11	10	110%
Chromium (mcg)	8	8	100%
Selenium (mcg)	16	15	107%
Sodium (mg)	152	150	101%
Potassium (mg)	418	400	105%
Chloride (mg)	328	376	87%
L-Carnitine (mg)	34	33	103%
Fat content			
Saturated fat, g	8.1	9.3	87%
Trans. fat, g	0	0	-
Mono. fat, g	12	10.7	112%
Poly. fat, g	4.7	4.2	112%

Source: submission main body pp5-7

AI: average intake; DFE: dietary folate equivalent; DHA: Docosahexaenoic Acid; NRV: nutrient reference values; Phe: phenylalanine; RDI:

recommended daily intake

4.5 A comparison of the new and previous formulation of KetoVie 4:1 is provided at Table 2.

4.6 For KetoVie 4:1, the submission stated that the following changes have been made:

- The primary fat source in KetoVie 4:1 flavours has been changed from cocoa butter to high oleic sunflower oil as a means of reducing saturated fat content and improving the levels of mono and polyunsaturated fats.
- The amount of Vitamin A has been lowered in the KetoVie 4:1 flavours reformulation to match the levels in KetoVie 4:1 unflavoured as clinician feedback reported some patients on higher calorie volumes approached upper limits of Vitamin A.
- The amounts of vitamin E and calcium have been increased and the amount of folate lowered in the KetoVie 4:1 flavours reformulation to better meet the dietary requirements and to match the levels in KetoVie 4:1 unflavoured.
- The change in zinc content unifies the micronutrient blend used across the KetoVie line of formulas for the purpose of easier administration.
- The amount of potassium has been increased closer to recommended daily intake (RDI).

Table 1: KetoVie 4:1 Vanilla reformulation

Nutrient	Product nutritional content (per 250 mL carton)		
	KetoVie 4:1 vanilla new formulation	KetoVie 4:1 vanilla current formulation	New formula/current formula nutritional content
Energy (kilojoule)	1548	1506	103%
Protein (g)	8.5	8.5	100%
Carbohydrate (g)	0.4	0.4	100%
Fibre (g)	4.4	4.4	100%
Fat (g)	36	35.4	102%
Linoleic acid (g)	3.953	2.25	176%
alpha-linoleic acid (g)	1.158	0.93	125%
DHA (mg)	77	76	101%
Vitamin A (mcg retinol equivalents)	180	225	80%
Vitamin D (mcg of cholecalciferol)	6.3	6.3	100%
Vitamin E (mg a-tocopherol equivalents)	3.8	3.1	123%
Vitamin K (mcg)	31	30	103%
Vitamin K1 (mcg)	16	15	107%
Vitamin K2 (MK-7) (mcg)	15	15	100%
Thiamin / B1 (mg)	0.5	0.5	100%
Riboflavin / B2 (mg)	0.5	0.5	100%
Vitamin B6 (mg)	0.5	0.5	100%
Vitamin B12 (mcg)	0.6	0.6	100%
Niacin (mg niacin equivalents)	6.3	4	158%
Folic acid (mcg)	53	150	35%

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Nutrient	Product nutritional content (per 250 mL carton)		
	KetoVie 4:1 vanilla new formulation	KetoVie 4:1 vanilla current formulation	New formula/current formula nutritional content
Folate, DFE (mcg)	89	255	35%
Pantothenic acid / B5 (mg)	1.8	1.8	100%
Biotin (mcg)	7.5	7.5	100%
Vitamin C (mg)	25	25	100%
Choline (mg)	150	150	100%
Inositol (mg)	30	0	-
Calcium (mg)	300	260	115%
Phosphorous (mg)	244	250	98%
Magnesium (mg)	65	60	108%
Iron (mg)	4.5	4.5	100%
Zinc (mg)	2.4	3	80%
Manganese (mg)	0.64	0.8	80%
Copper (mg)	0.251	0.2	126%
Iodine (mcg)	46	45	102%
Molybdenum (mcg)	17	16	106%
Chromium (mcg)	13	13	100%
Selenium (mcg)	23	22	105%
Sodium (mg)	273	270	101%
Potassium (mg)	306	270	113%
Chloride (mg)	381	200	191%
L-Carnitine (mg)	50	50	100%
Fat content			
Saturated fat, g	14	21	67%
Trans. fat, g	0	0	-
Mono. fat, g	17	10.9	156%
Poly. fat, g	4.2	3.5	120%

Source: submission main body pp8-10. Note: KetoVie 4:1 comes in both chocolate and vanilla and they have slightly different nutrient values. Details of KetoVie 4:1 vanilla only are provided in Table 2 for brevity, due to the only very small nutrient differences between flavours. AI: average intake; DFE: dietary folate equivalent; DHA: Docosahexaenoic Acid; MCT: medium chain triglyceride; NRV: nutrient reference values; Phe: phenylalanine; RDI: recommended daily intake

4.7 A comparison of the new and previous formulation of KetoVie 4:1 Peptide is provided at Table 3.

4.8 For KetoVie 4:1 Peptide, the submission stated that the following changes have been made:

- The primary fat source has been changed from high oleic canola oil to high oleic sunflower oil for unification of fat sources across the KetoVie line of formulas.
- DHA levels were reduced levels reduced to unify levels across all KetoVie 4:1 product line.
- The amount of Vitamin A has been lowered in the KetoVie 4:1 flavours reformulation as clinician feedback reported some patients on higher calorie volumes approached upper limits of Vitamin A.

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- Micronutrient blends such as zinc content have been unified across the KetoVie line of formulas for easier administration.
- Vitamin E levels have been increased and Vitamin C and Phosphorus levels reduced to unify levels across all KetoVie 4:1 product line.
- Niacin amount has been increased to reach RDI for all categories.
- The amount for folate was lowered in the KetoVie 4:1 reformulation to better meet the dietary requirements.
- The amount of calcium in KetoVie 4:1 Peptide was reduced to meet dietary requirement while not overburdening those patients who may be sensitive to calcium based on clinician feedback. As hypercalcemia has been reported in some patients following a ketogenic diet, this change will allow for unification of calcium levels across the KetoVie line of formulas.

Table 2: KetoVie 4:1 Peptide reformulation

Nutrient	Product nutritional content (per 250 mL carton)		
	KetoVie 4:1 Peptide new formulation	KetoVie 4:1 Peptide current formulation	New formula/current formula nutritional content
Energy (kilojoule)	1580	1561	101%
Protein (g)	8.1	8.1	8.1
Carbohydrate (g)	0.8	0.9	0.8
Salt (g)	0.86	1	0.86
Fibre (g)	2.7	2.6	2.7
Fat (g)	37	37	37
Linoleic acid (g)	5.624	5.85	5.624
alpha-linoleic acid (g)	1.378	0.78	1.378
DHA (mg)	77	140	77
Vitamin A (mcg retinol equivalents)	180	225	80%
Vitamin D (mcg of cholecalciferol)	6.3	6.2	102%
Vitamin E (mg a-tocopherol equivalents)	3.8	1.9	200%
Vitamin K (mcg)	31	30	103%
Vitamin K1 (mcg)	16	15	107%
Vitamin K2 (MK-7) (mcg)	15	15	100%
Thiamin / B1 (mg)	0.5	0.4	125%
Riboflavin / B2 (mg)	0.5	0.5	100%
Vitamin B6 (mg)	0.5	0.5	100%
Vitamin B12 (mcg)	0.6	0.5	120%
Niacin (mg niacin equivalents)	4.2	5.2	81%
Folic acid (mcg)	52	150	35%
Folate, DFE (mcg)	89	90	99%
Pantothenic acid / B5 (mg)	1.8	1.8	100%
Biotin (mcg)	7.5	7.5	100%
Vitamin C (mg)	25	44	57%
Choline (mg)	150	150	100%
Inositol (mg)	32	32	100%
Calcium (mg)	320	454	70%

Nutrient	Product nutritional content (per 250 mL carton)		
	KetoVie 4:1 Peptide new formulation	KetoVie 4:1 Peptide current formulation	New formula/current formula nutritional content
Phosphorous (mg)	272	323	84%
Magnesium (mg)	57	57	100%
Iron (mg)	4.5	4.4	102%
Zinc (mg)	2.4	3.2	75%
Manganese (mg)	0.6	0.8	75%
Copper (mg)	0.3	0.2	150%
Iodine (mcg)	46	46	100%
Molybdenum (mcg)	17	15	113%
Chromium (mcg)	13	13	100%
Selenium (mcg)	23	23	100%
Sodium (mg)	344	382	90%
Potassium (mg)	345	607	57%
Chloride (mg)	392	467	84%
L-Carnitine (mg)	50	50	100%
Fat content			
Saturated Fat, g	12	12.4	97%
Trans Fat, g	0.2	0	-
Monounsaturated Fat, g	20	17.7	113%
Polyunsaturated Fat, g	4.3	6.6	65%

Source: submission main body pp11-12.

AI: average intake; DFE: dietary folate equivalent; DHA: Docosahexaenoic Acid; NRV: nutrient reference values; Phe: phenylalanine; RDI: recommended daily intake

- 4.9 The PBAC advised that the new formulations are expected to provide non-inferior clinical benefits for the management of a ketogenic diet in comparison to the current formulations.

Estimated PBS utilisation and financial implications

- 4.10 The submission did not present economic or financial evaluations. The submission requested no change to the current pricing arrangements.
- 4.11 The submission considered the formulation changes will have nil financial impact to Government as no change in price is requested and it did not estimate any change in utilisation would occur.

For more detail on PBAC's view, see section 6 PBAC outcome.

5 NPWP consideration

- 5.1 The Nutritional Products Working Party (NPWP) advised that the new formulations are expected to provide non-inferior clinical benefit for the management of a ketogenic diet.
- 5.2 The NPWP supported the new formulations of KetoVie 3:1, KetoVie 4:1 and KetoVie Peptide 4:1 continuing to be listed on the PBS under the existing conditions as the existing formulations.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended that new formulations of high fat formula with vitamins, minerals and trace elements and low in protein and carbohydrate (KetoVie® 3:1, KetoVie® 4:1, KetoVie® Peptide 4:1) continue to be listed on the PBS under the existing conditions of the current formulations.
- 6.2 The PBAC noted and supported the NPWP advice that the new formulations are expected to provide a non-inferior clinical benefit for the management of a ketogenic diet.
- 6.3 The PBAC noted there were no changes requested to the circumstances under which the existing listings are available.
- 6.4 The PBAC considered the formulation changes would not be expected to result in a financial impact to Government.
- 6.5 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

- 7.1 No change to the existing listing

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.