*Revised: January 2023 (2nd version)
Revised: April 2022 (1st version)
Storage: Store at room temperature.
Shelf Life: 12 months in sealed can

Standard Commodity Classification No. of Japan:	873259

Approval No.	20600AMY00426000
Date of Initial Marketing in Japan	October 1995

Enteral nutrient (for oral/enteral supplementation)

ENSURE® H

®Registered trademark (owner: Abbott Laboratories)

2. CONTRAINDICATIONS

(This drug is contraindicated to the following patients.)

2.1 Patients with known hypersensitivity to the ingredients of ENSURE H

2.2 Patients with milk protein allergy [A milk casein contained in ENSURE H may cause shock or anaphylaxis.]

2.3 Patients with acute nephritis, nephrosis, or end-stage renal failure that requires strict dietary restrictions regarding protein and electrolyte intake. [See 9.2.1.]

2.4 Patients with cardiac failure accompanied by nausea, vomiting, or diarrhoea. [The disease may be aggravated.] [See 9.1.1.]

2.5 Administration of ≥ 5,000 IU/day of vitamin A to pregnant women during the first trimester or women who desire to become pregnant. [See 9.5.1.]

3. COMPOSITION AND PRODUCT DESCRIPTION

3.1 Composition

For ENSURE H, there are seven products available with different flavors (vanilla, coffee, banana, brown sugar, melon, strawberry, and matcha flavors).

Ingredient Composition

Excipients	Carrageenan (suspending agent), Potassium hydroxide (pH adjuster), and Citric acid hydrate (pH adjuster)	
	Flavors Vanilla and coffee flavors: Vanillin, Ethylvanillin, and Propylene glycol Banana and brown sugar flavors: Vanillin Melon and strawberry flavors: Propylene glycol Matcha flavor: Vanillin and Propylene glycol	
Calories	Each 250-mL can of ENSURE H contains 375 kcal.	
Active ingredients in each 250-mL can (375 kcal)	Sodium Caseinate	8.9 g
	Sodium Calcium Caseinate	4.1 g
	Soy Protein Isolate	2.0 g
	Corn Oil	12.5 g
	Soybean Lecithin, S.B. Phosphatide	0.6 g
	Dextrin	41.7 g
	Sucrose	9.8 g
	Retinol Palmitate	516 µg (938 IU)
	Cholecalciferol	1.88 µg (75 IU)
	Tocopherol Acetate	12.35 mg
	Phytonadione	26.3 µg
	Ascorbic Acid	57 mg
	Thiamine Chloride Hydrochloride	0.64 mg
	Riboflavin	0.65 mg
	Pyridoxine Hydrochloride	0.91 mg
	Cyanocobalamin	2.3 µg
	Choline Chloride	0.23 g
	Folic Acid	75 µg
	Nicotinamide	7.5 mg
	Calcium Pantothenate	2.04 mg
	Biotin	57 µg
	Sodium Bicarbonate	114.8 µg
	Magnesium Chloride	0.62 g
	Potassium Citrate	0.69 g
	Tribasic Calcium Phosphate	0.45 g
	Potassium Chloride	0.45 g
	Sodium Citrate Hydrate	0.59 g
	Zinc Sulfate Hydrate	24.74 mg
	Ferrous Sulfate Hydrate	16.80 mg
	Manganese (II) Chloride Tetrahydrate	2.70 mg
	Copper Sulfate	1.47 mg

Nutritional Composition

Nutrients in each 250-mL can (375 kcal)	Protein	13.2 g
	Fat	13.2 g
	Carbohydrate	51.5 g
	Vitamin A	938 IU
	Vitamin D	75 IU
	Vitamin E	11.3 mg
	Vitamin K	26.3 µg
	Vitamin C	57 mg
	Vitamin B_1	0.57 mg
	Vitamin B_2	0.65 mg
	Vitamin B_6	0.75 mg
	Vitamin B_{12}	2.3 µg
	Choline	0.20 g
	Folic Acid	75 µg
	Niacin	7.5 mg
	Pantothenic Acid	1.88 mg
	Biotin	57 µg
	Sodium	0.30 g
	Potassium	0.56 g
	Chloride	0.51 g
	Calcium	0.20 g
	Phosphorus	0.20 g
	Magnesium	75 mg
	Manganese	0.75 mg
	Copper	0.38 mg
	Zinc	5.63 mg
	Iron	3.38 mg

Note: The sodium chloride equivalent per can (250 mL) of ENSURE H is 0.76 g.

3.2 Product Description

Description	A brownish suspension
Odor	A characteristic aroma
Taste	Sweet
pH	ca. 6.5
Osmotic Pressure	ca. 540 mOsm/L
Specific Gravity	ca. 1.1
Viscosity	ca. 17 mPa·s

4. INDICATIONS

Generally, ENSURE H is used to maintain the nutritional health of postoperative patients. It can be used for tube feeding, especially in the following patients who have difficulty in oral intake for a long period of time and require an enteral nutrient with high calories per unit volume (1.5 kcal/mL):

- **Patients requiring restrictions on water intake (e.g., patients with cardiac failure or renal failure)**
- **Patients with increased resting energy expenditure (e.g., patients with burns or infection)**
- **Patients who want to reduce the volume of an enteral nutrient to be administered (e.g., patients who complain of feelings of Abdominal bloating dependent on dosing volume)**
- **Patients in whom it is advisable to shorten the duration of feeding of an enteral nutrient (e.g., postoperative patients after oral surgery or nose and ear surgery)**

6. DOSAGE AND ADMINISTRATION

ENSURE H should be administered to adults via a feeding tube or orally at a standard volume of between 1,000 and 1,500 mL (1,500 to 2,250 kcal) per day. One milliliter of ENSURE H contains 1.5 kcal.

The dose should be adjusted according to patient age and the severity and nature of symptoms, as appropriate.

When feeding via a tube, ENSURE H should be administered at a rate of 50 to 100 mL/hour continuously or intermittently by dividing the daily dose into several doses. For patients without digestion or absorption disorders in whom it is advisable to shorten the duration of feeding of the enteral nutrient, the feeding rate of ENSURE H can be increased to a maximum rate of 400 mL/hour. If oral intake is possible, ENSURE H may be administered once daily or in multiple divided doses.

8. IMPORTANT PRECAUTIONS

8.1 ENSURE H is prepared at a concentration of 1.5 kcal/mL. Before administering ENSURE H, another enteral nutrient with a low concentration (≤ 1 kcal/mL) should be administered in order to confirm that no adverse reactions, such as diarrhoea, occur. For patients without digestion or absorption disorders, however, ENSURE H may be administered in the first place.

8.2 Since patients may become deficient in vitamins, electrolytes, and/or trace elements, they should be supplemented with vitamins, etc. as required. It has been reported that selenium deficiency (reduced cardiac function, white discoloration of nails, muscular weakness, etc.) occurred during long-term enteral feeding.

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS

9.1 Patients with Complication or History of Diseases, etc.

9.1.1 Patients with severe cardiac failure (excluding patients with cardiac failure accompanied by nausea, vomiting, and diarrhoea)

If diarrhoea or other adverse reactions are noted, take appropriate measures, such as discontinuing ENSURE H administration. Fat malabsorption is often observed. [See 2.4 and 9.8.]

9.1.2 Patients with short-bowel syndrome or other severe functional bowel disorders

Diarrhoea may occur.

9.1.3 Patients with glucose metabolism abnormal

Hyperglycemia may occur.

9.1.4 The following patients requiring careful monitoring of fluid balance

- Patients with comatose
- Unconscious patients
- Patients who cannot complain of thirst
- Patients with severe fever
- Patients with significant dehydration, such as serious diarrhoea
- Patients with renal disorder

Dehydration may occur or may be aggravated.

9.2 Patients with Renal Impairment

9.2.1 Patients with acute nephritis, nephrosis, or end-stage renal failure that requires strict dietary restrictions regarding protein and electrolyte intake

Do not administer ENSURE H. The disease may be aggravated. [See 2.3 and 9.8.]

9.2.2 Patients with renal disorder (excluding patients with acute nephritis, nephrosis, or end-stage renal failure that requires strict dietary restrictions regarding protein and electrolyte intake)

Observe the patient carefully, and if any abnormality is observed, take appropriate measures, such as discontinuing ENSURE H administration. Serum potassium level and/or blood urea nitrogen (BUN) level may be elevated. [See 9.8.]

9.4 Patients with Reproductive Potential

[See 9.5.1.]

9.5 Pregnant Women

9.5.1 Women during the first trimester of pregnancy or who desire to become pregnant

Do not administer ≥ 5,000 IU/day of vitamin A. When ENSURE H is administered, care should be taken regarding the dosage regimen, such as limiting the daily dose of vitamin A derived from ENSURE H to less than 5,000 IU per day. An overseas epidemiological study has suggested an increased incidence of malformations, mainly in the cranial neural crest among neonates born from women who took 10,000 IU or more of vitamin A per day during the three months before pregnancy and the first trimester of pregnancy. [See 2.5 and 9.4.]

9.5.2 Pregnant women (except pregnant women during the first trimester)

ENSURE H should be administered only when the therapeutic benefits are expected to outweigh the risks.

9.6 Breast-feeding Women

Considering the therapeutic and breast-feeding benefits, determine whether breast-feeding should be continued or discontinued.

9.7 Pediatric Use

No clinical study of ENSURE H aiming to evaluate its efficacy or safety in children has been conducted.

9.8 Geriatric Use

Care should be taken when administering ENSURE H to elderly patients. For example, start administering it at a lower feeding rate of 50 mL/hour and observe their condition during administration. In general, elderly patients often have reduced physiological function. [See 9.1.1, 9.2.1, and 9.2.2.]

11. ADVERSE REACTIONS

Since the following adverse reactions may occur, observe the patient carefully, and if any abnormality is noted, take appropriate measures, such as discontinuing ENSURE H administration.

11.1 Clinically Significant Adverse Reactions

11.1.1 Shock, anaphylaxis (unknown incidence for both)

In the event of blood pressure decreased, consciousness disturbed, dyspnoea, cyanosis, nausea, chest distress, facial flushing, itching, sweating, etc., discontinue ENSURE H administration immediately, and treat the patient appropriately.

11.2 Other Adverse Reactions

	≥ 5%	0.1 to < 5%	Unknown incidence
Gastrointestinal	Diarrhoea	Gastric discomfort, Abdominal bloating, Nausea, Vomiting	
Liver			Hepatic function abnormal (AST increased, ALT increased,

	≥ 5%	0.1 to < 5%	Unknown incidence
			Gamma-GTP increased, ALP increased, etc.)
Metabolism/ Nutrition		BUN increased, Blood potassium increased, LDH increased, Amylase increased	
Hypersensitivity			Rash

14. PRECAUTIONS CONCERNING USE

14.1 Precautions Concerning Administration of the Drug

14.1.1 Use clean apparatus to administer ENSURE H for tube feeding.

14.1.2 It is recommended that a feeding tube with an interior diameter of ≥ 2 mm be used when administering ENSURE H for tube feeding.

14.1.3 The use of an enteral feeding set or feeding tube, etc. made of polyvinyl chloride containing di-(2-ethylhexyl) phthalate (DEHP) as a plasticizer will cause elution of DEHP into the drug formulation. Therefore, it is advisable that a DEHP-free feeding set and feeding tube, etc. should be used to administer ENSURE H.

14.1.4 Do not administer ENSURE H intravenously.

14.1.5 Although the standard feeding rate is 50 to 100 mL/hour, feeding should usually be started from a lower rate, and the feeding rate should be increased gradually up to the standard feeding rate. If any adverse reaction, such as diarrhoea, occurs, the feeding rate should be decreased until gastrointestinal tolerance is restored. Once it is restored, make sure to increase the rate again to the standard feeding rate.

14.1.6 Use ENSURE H for administration without diluting it with water.

14.1.7 Check gastric residuals at the start of intermittent feeding or every several hours during continuous feeding.

14.1.8 For tube feeding, flush the feeding tube with a small amount of water at the end of intermittent feeding or every several hours during continuous feeding.

14.1.9 Shake the can immediately before opening it to use ENSURE H. White floating particles or precipitates (fat or calcium) that may be observed do not represent the degradation of the product.

14.1.10 When warming the drug formulation, it is advisable to warm it in the unopened can by immersing in warm water (30 to 40°C). Avoid heating the can over an open flame.

17. CLINICAL STUDIES

17.1 Clinical Studies for Efficacy and Safety

17.1.1 Comparative study in postoperative patients after upper gastrointestinal surgery in Japan

Moderate or better improvement in nutritional status in terms of rapid turnover protein and NI value, etc. was observed in 26 (74.3%) of 35 subjects. ENSURE H was shown to be at least equivalent in efficacy to ENSURE Liquid.[1)]

Adverse reactions were reported in 5 (12.5%) of 40 subjects. They were primarily gastrointestinal symptoms, including diarrhoea in 3 subjects (7.5%) and abdominal bloating in 2 subjects (5.0%). As laboratory abnormalities, amylase increased was noted in 1 subject (2.5%).

17.1.2 Open clinical study in postoperative patients after oral surgery in Japan

Moderate or better nutritional improvement in terms of rapid turnover protein and NI value, etc. was observed in 88 (74.6%) of 118 subjects.[2)]

Adverse reactions were reported in 18 (14.5%) of 124 subjects. They were primarily gastrointestinal symptoms, including diarrhoea in 12 subjects (9.7%) and gastric discomfort in 3 subjects (2.4%). As laboratory abnormalities, BUN increased was noted in 3 subjects (2.4%), and blood potassium increased and LDH increased in 1 subject (0.8%) each.

18. PHARMACOLOGY

18.1 Mechanism of Action

ENSURE H is effective for supplementation of protein, carbohydrate, lipid, electrolytes, energy, vitamins, minerals, and water.

18.2 Protein

18.2.1 Milk protein and soybean protein are blended as protein sources of ENSURE H in a ratio of 86.7:13.3, considering their amino acid complementary effects and the efficient utilization of amino acids, and ENSURE H contains 13.2 g of protein (energy composition: 14.0%) in a volume of 250 mL.

18.2.2 The ratio of essential amino acids to total amino acids in the protein sources of ENSURE H is 0.409. The amino acid score of ENSURE H is 100.

18.2.3 Non-protein calorie/nitrogen ratio of ENSURE H (NPC/N ratio) is 157.

18.3 Carbohydrate

Dextrin and sucrose are blended as carbohydrate sources of ENSURE H in a ratio of 81:19, and ENSURE H contains 51.5 g of carbohydrate (energy composition: 54.5%) in a volume of 250 mL. Because ENSURE H is lactose-free, it is also suitable for patients with lactose intolerance.

18.4 Lipid

The major fat source of ENSURE H is corn oil, and ENSURE H contains 13.2 g of fat (energy composition: 31.5%) in a volume of 250 mL. Corn oil contains two essential fatty acids: linolic acid and linolenic acid. The cholesterol content of ENSURE H is not more than 20 mg in the 2,000-kcal drug formulation. ENSURE H is a uniform, stable, fine-particle suspension.

18.5 Water

ENSURE H contains 194 mL of water in a volume of 250 mL.

20. PRECAUTIONS FOR HANDLING

20.1 After opening the can, the can with unused drug formulation in it should be tightly resealed and kept in a refrigerator. ENSURE H should be used within 48 hours after opening the can.

20.2 Avoid freezing ENSURE H.

22. PACKAGING

24 cans [250 mL (can) × 24]

23. REFERENCES

1) Hiramatsu Y, et al. *The Clinical Report*, 1990, 24, 5533
2) Sugahara T, et al. *Japanese Journal of Oral & Maxillofacial Surgery*, 1990, 36, 2879

24. REFERENCE REQUEST AND CONTACT INFORMATION

Abbott Japan LLC Customer Service
3-5-27, Mita, Minato-ku, Tokyo 108-6305
Toll-free number: 0120-964-930

26. MARKETING AUTHORIZATION HOLDER, etc.

26.1 Marketing Authorization Holder

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