**Revised: February 2024 (3rd version)
*Revised: January 2023 (2nd version)
Storage: Store at room temperature.
Shelf Life: 12 months in sealed can

Standard Commodity Classification No. of Japan:	873259

Approval No.	16200AMZ01646000
Date of Initial Marketing in Japan	June 1988

Enteral nutrient (for oral/enteral supplementation)

ENSURE LIQUID®

®Registered trademark (owner: Abbott Laboratories)

ENSURE LIQUID®

2. CONTRAINDICATIONS

(This drug is contraindicated to the following patients.)

2.1 Patients with known hypersensitivity to the ingredients of ENSURE LIQUID®

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

2.3 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

Ingredient Composition

** *	Excipients	Fructo-oligosaccharide (flavoring agent), Carrageenan (suspending agent), Potassium hydroxide (pH adjuster), Citric acid hydrate (pH adjuster), Propylene glycol (flavor)
	Calories	Each 250-mL can of ENSURE LIQUID® contains 250 kcal.
*	Active ingredients in each 250-mL can (250 kcal)	Sodium Caseinate 5.9 g Sodium Calcium Caseinate 2.7 g Soy Protein Isolate 1.3 g Corn Oil 8.3 g Soybean Lecithin, S.B. Phosphatide 0.4 g Dextrin 24.5 g Sucrose 9.8 g Retinol Palmitate 344 μg (625 IU) Cholecalciferol 1.25 μg (50 IU) Tocopherol Acetate 8.23 mg Phytonadione 17.5 μg Ascorbic Acid 38 mg Thiamine Chloride Hydrochloride 0.43 mg Riboflavin 0.43 mg Pyridoxine Hydrochloride 0.61 mg Cyanocobalamin 1.5 μg Choline Chloride 0.15 g Folic Acid 50 μg Nicotinamide 5.0 mg Calcium Pantothenate 1.36 mg Biotin 38 μg Sodium Bicarbonate 76.5 μg Magnesium Chloride 0.41 g Potassium Citrate 0.46 g Tribasic Calcium Phosphate 0.30 g Potassium Chloride 0.30 g Sodium Citrate Hydrate 0.39 g Zinc Sulfate Hydrate 16.49 mg Ferrous Sulfate Hydrate 11.20 mg Manganese (II) Chloride Tetrahydrate 1.80 mg Copper Sulfate 0.98 mg

Nutritional Composition

*	Nutrients in each 250-mL can (250 kcal)	Protein 8.8 g Fat 8.8 g Carbohydrate 34.3 g Vitamin A 625 IU Vitamin D 50 IU Vitamin E 7.5 mg Vitamin K 17.5 μg Vitamin C 38 mg Vitamin B_1 0.38 mg Vitamin B_2 0.43 mg Vitamin B_6 0.50 mg Vitamin B_{12} 1.5 μg Choline 0.13 g Folic Acid 50 μg Niacin 5.0 mg Pantothenic Acid 1.25 mg Biotin 38 μg Sodium 0.20 g Potassium 0.37 g Chloride 0.34 g Calcium 0.13 g Phosphorus 0.13 g Magnesium 50 mg Manganese 0.50 mg Copper 0.25 mg Zinc 3.75 mg Iron 2.25 mg

Note: The sodium chloride equivalent per can (250 mL) of ENSURE LIQUID® is 0.51 g.

3.2 Product Description

Description	A brownish suspension
Odor	A characteristic aroma
Taste	Sweet
pH	ca. 6.6
Osmotic Pressure	ca. 330 mOsm/L
Specific Gravity	ca. 1.1
Viscosity	ca. 9 mPa·s

4. INDICATIONS

Generally, ENSURE LIQUID® is used to maintain the nutritional health of postoperative patients. It can be used for tube feeding, especially in patients who have difficulty in oral intake for a long period of time.

5. PRECAUTIONS CONCERNING INDICATIONS

The recovery of gastrointestinal motility which allows patients to take fluid should be confirmed before administering ENSURE LIQUID® after operation.

6. DOSAGE AND ADMINISTRATION

ENSURE LIQUID® should be administered to adults via a feeding tube or orally at a standard volume of between 1,500 and 2,250 mL (1,500 to 2,250 kcal) per day. One milliliter of ENSURE LIQUID® contains 1 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 LIQUID® should be administered at a rate of 100 to 150 mL/hour continuously or intermittently by dividing the daily dose into several doses. If oral intake is possible, ENSURE LIQUID® may be administered once daily or in multiple divided doses.
Administration of ENSURE LIQUID® should be initiated from a third to a half of the standard volume, and the drug formulation in the early stage of administration should be diluted with approximately the same volume of water (0.5 kcal/mL). Thereafter, gradually increase the concentration and volume according to patient's condition up to the standard volume.

8. IMPORTANT PRECAUTIONS

8.1 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 short-bowel syndrome or other severe functional bowel disorders

Diarrhoea may occur.

9.1.2 Patients with glucose metabolism abnormal

Hyperglycemia may occur.

9.1.3 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.

9.4 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 or more of vitamin A per day. When ENSURE LIQUID® is administered, care should be taken regarding the dosage regimen, such as limiting the daily dose of vitamin A derived from ENSURE LIQUID® 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 2.3 and 9.4.]

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

ENSURE LIQUID® 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 LIQUID® aiming to evaluate its efficacy or safety in children has been conducted.

9.8 Geriatric Use

Pay attention to the dosage regimen when administering ENSURE LIQUID®. In general, elderly patients often have reduced physiological function.

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 LIQUID® 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 LIQUID® administration immediately, and treat the patient appropriately.

11.2 Other Adverse Reactions

	≥ 5%	0.1 to < 5%	Unknown incidence
Gastrointestinal	Diarrhoea	Abdominal bloating, Abdominal pain, Nausea, Vomiting, Heartburn	
Liver			Hepatic function abnormal (AST increased, ALT increased, Gamma-GTP increased, ALP increased, etc.)
Metabolism/ Nutrition		BUN increased, Blood potassium increased	
Hypersensitivity			Rash, Redness, Urticaria

14. PRECAUTIONS CONCERNING USE

14.1 Precautions Concerning Administration of the Drug

14.1.1 Use clean apparatus to administer ENSURE LIQUID® 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 LIQUID® 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 LIQUID®.

14.1.4 Do not administer ENSURE LIQUID® intravenously.

14.1.5 Although the standard concentration and standard feeding rate are 1 kcal/mL and 100 to 150 mL/hour, respectively, for tube feeding, feeding should usually be started from a low concentration or a low feeding rate, and the concentration and feeding rate should be increased gradually up to the standard concentration or the standard feeding rate. If any adverse reaction, such as diarrhoea, occurs, the concentration should be decreased to about 0.5 kcal/mL until gastrointestinal tolerance is restored. Once it is restored, make sure to increase the feeding rate again to the standard rate, and then increase the concentration to the standard concentration.

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

14.1.7 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.

14.1.8 Shake the can immediately before opening it to use ENSURE LIQUID®. White floating particles or precipitates

(fat or calcium) that may be observed do not represent the degradation of the product.

14.1.9 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 Clinical studies in Japan

In clinical studies of ENSURE LIQUID® including a comparative study, ENSURE LIQUID® was administered to 213 patients who could not take food orally due to pre- or post-operative condition, consciousness disturbed, trismus, dysphagia, etc. Uneventful or better improvement in nutritional status was observed in 182 subjects (85.4%).[1-5)]

18. PHARMACOLOGY

18.1 Mechanism of Action

ENSURE LIQUID® 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 LIQUID® in a ratio of 86.9:13.1, considering their amino acid complementary effects and the efficient utilization of amino acids, and ENSURE LIQUID® contains 8.8 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 LIQUID® is 0.409. The amino acid score of ENSURE LIQUID® is 100.

18.2.3 In animal studies of protein efficiency ratio, net protein utilization, and nitrogen balance in growing rats, ENSURE LIQUID® showed equivalent or better efficacy results than those of other over-the-counter enteral nutrients and casein as the standard protein.[6)]

18.2.4 Non-protein calorie/nitrogen ratio (NPC/N ratio) of ENSURE LIQUID® is 157.

18.2.5 Since the renal solute load of ENSURE LIQUID® is only 252 mOsm/L in children and 312 mOsm/L in adults, ENSURE LIQUID® can be used in elderly patients, as well.

18.3 Carbohydrate

Dextrin and sucrose are blended as carbohydrate sources of ENSURE LIQUID® in a ratio of 71:29, and ENSURE LIQUID® contains 34.3 g of carbohydrate (energy composition: 54.5%) in a volume of 250 mL. Since ENSURE LIQUID® is lactose-free, it is suitable for patients with lactose intolerance, as well.

18.4 Lipid

The major fat source of ENSURE LIQUID® is corn oil, and ENSURE LIQUID® contains 8.8 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 LIQUID® is not more than 20 mg in the 2,000-kcal drug formulation. ENSURE LIQUID® is a uniform, stable, fine-particle suspension, and is thus readily digestible.

18.5 Water

ENSURE LIQUID® contains 213 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 LIQUID® should be used within 48 hours after opening the can.

20.2 Avoid freezing ENSURE LIQUID®.

22. PACKAGING

24 cans [250 mL (can) × 24]

23. REFERENCES

1) Nagao F, et al. *Japanese Journal of Parenteral and Enteral Nutrition (JJPEN)*, 1985, 6, 737
2) Kanno K, et al. *JJPEN*, 1985, 6, 745
3) Sugahara T, et al. *Japanese Journal of Oral & Maxillofacial Surgery*, 1984, 30, 1634
4) Yamamoto M, et al. *The Clinical Report*, 1986, 20, 7205
5) Sugahara T, et al. *The Clinical Report*, 1986, 20, 6201
6) Abbott Japan LLC (data on file). In-house materials on pharmacology (approved on December 11, 1987)

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

Abbott Japan LLC
3-5-27, Mita, Minato-ku, Tokyo