ARMOUR® THYROID MANUFACTURED BY FOREST PHARMACEUTICALS, INC. CONTAINS:

Thyroid Powder, USP (active ingredient)
Dextrose, Anhydrous (inactive ingredient)
Microcrystalline Cellulose, NF (inactive ingredient)
Sodium Starch Glycolate, NF (inactive ingredient)
Calcium Stearate, NF (inactive ingredient)
Opadry White (titanium dioxide used as a whitening agent - inactive ingredient)

THYROID USP GUIDELINES

Thyroid USP is the cleaned, dried, and powdered thyroid gland previously deprived of connective tissue & fat. Description: Yellowish to buff-colored, amorphous powder, having a slight, characteristic, meat like odor. It is obtained by domesticated animals that are used for food by humans. It meets the USP microbial requirements for the tests {USP "61"} of absence of *Salmonella* & *Escherichia coli*. Thyroid USP must meet loss on drying tests {USP "731"} with loss of not more than 6% of its weight. Thyroid USP must meet inorganic iodide testing with a limit of 0.01%. Thyroid USP desiccated powder must yield not less than 90% and not more than 110% of the labeled amounts of levothyroxine and liothyronine.

Thyroid Tablets USP contain the labeled amounts of levothyroxine and liothyronine, within +/- 10%, the labeled amounts being 38 mcg levothyroxine and 9 mcg of liothyronine for each 65 mg (1 grain) of the labeled content of thyroid. They must meet the microbial requirements {USP "61"} for absence of *Salmonella & Escherichia coli*. They must meet disintegration testing (15 minutes), uniformity of dosage unit testing, and limit of organic iodide testing (not more than 0.08%). Store in a tight container as defined by the USP.

Note: All information obtained from *1995 USP 23 NF 18*, pp. 2684-2685 & *1997 USPDI-Volume III- 17th Edition.*, p. IV/518. Please see these references for more detail.

ACTIVE INGREDIENTS IN ARMOUR THYROID AND THYROLAR

ARMOUR® THYROID[1]:

	T3	**T4**
1/4 Grain (15mg)	2.25 mcg	9.5 mcg
1/2 Grain (30mg)	4.50 mcg	19.0 mcg
1 Grain (60mg)	9.00 mcg	38.0 mcg
1 & 1/2 Grains (90mg)	13.50 mcg	57.0 mcg
2 Grains (120mg)	18.0 mcg	76.0 mcg
3 Grains (180mg)	27.0 mcg	114.0 mcg
4 Grains (240mg)	36.0 mcg	152.0 mcg
5 Grains (300mg)	45.0 mcg	190.0 mcg

THYROLAR®:

1/4	3.10 mcg	12.5 mcg
1/2	6.25 mcg	25.0 mcg
1	12.50 mcg	50.0 mcg
2	25.00 mcg	100.0 mcg
3	37.50 mcg	150.0 mcg

[1] T3 = Liothyronine, T4 = Levothyroxine
Note: T3 has approximately 4 times the biological potency of T4.

FULL STRENGTH THYROID PROCESSING PROCEDURE

1. **The raw Pork Thyroid is collected at slaughterhouses, which operate under U.S.D.A. inspection to assure that the animals slaughtered are suitable for edible purposes. Also, the proper ante and post mortem inspections have been performed on the animals producing these raw materials.**

2. **The porcine Thyroid glands are held in a frozen state until delivered to the processing laboratory, and processing is begun.**

3. **The slightly tempered, cold thyroid glands are minced using a 3/8" (inch) diameter grinder plate.**

4. **The minced thyroid product is spread uniformly on stainless steel pans, which are placed then on heated shelves in a vacuum dryer.**

5. **The product is dried under vacuum at a shelf temperature of 71 degrees Centigrade.**

6. **The dried Thyroid product is defatted with hexane (C_6H_{14}) so the residual fat content is less than 5%.**

7. **The defatted Thyroid product is poured through a magnetic separator positioned in the hopper of a Fitz-mill, and milled to a coarse powder.**

8. **The Fitz-milled product is milled to a fine powder, using a ball mill containing porcelain balls.**

9. **Routinely, several batches of approximately 200 pounds each are combined by blending in a V-blender to create a lot of Full Strength Thyroid powder.**

10. **The blended Full Strength Thyroid powder is packaged in 50 kilo quantities, and usually a balance quantity in poly-lined drums, then statistically sampled using the relationship $S=\sqrt{N} + 1$, where S = number of samples and N = number of drums of product.**

11. **Full Strength Thyroid samples are tested for chemical and microbiological characteristics.**

12. **The Full Strength Thyroid is then released for sale, provided the test results indicate the product satisfactorily meets established specifications.**

APPROXIMATE EQUIVALENT STRENGTHS OF VARIOUS THYROID PREPARATIONS, BASED ON CLINICAL RESPONSES AS TAKEN FROM THE USP-DI.

Drug →	Thyroid tablets, USP (Armour® Thyroid)	Liotrix tablets, USP (Thyrolar®)	Liothyronine tablets, USP (Cytomel®)	Levothyroxine tablets, USP (Levothroid®, Synthroid®, ...)	Thyroglobulin tablets, USP (not commercially available in the US)
Approx. Dose Equivalent	1/4 grain (15 mg)	¼	6.25 mcg	25 mcg (.025 mg)	15 mg
Approx. Dose Equivalent	1/2 grain (30 mg)	½	12.5 mcg	50 mcg (.05 mg)	30 mg
Approx. Dose Equivalent	1 grain (60 mg)	1	25 mcg	100 mcg (.1 mg)	60 mg
Approx. Dose Equivalent	1 & 1/2 grains (90mg)	1 & 1/2	37.5 mcg	150 mcg (.15 mg)	90 mg
Approx. Dose Equivalent	2 grain (120 mg)	2	50 mcg	200 mcg (.2 mg)	120 mg
Approx. Dose Equivalent	3 grain (180 mg)	3	75 mcg	300 mcg (.3 mg)	180 mg

Note: These estimated daily doses are based on clinical evaluations. Please keep in mind that a dose adjustment may be required. Thyroid dosing is ***highly patient specific and must always be individualized to achieve maximum benefit and optimal patient health.***

[1] United States Pharmacopoeia – Drug Information 1997, 17th Edition, Drug Information for the Health Care Professional; Vol. 1, pp. 2860-2867. Rand McNally, Taunton, MA 02780

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RESEARCH FOUNDATION, INC.
P.O. BOX 98 • TRUMBULL, CT 06611 USA
(203) 261-2101 PHONE • (203) 261-3017 FAX

September 27, 1991

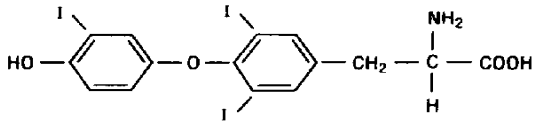
Armour® Thyroid
(thyroid tablets, USP)

Forest Pharmaceuticals, Inc.
A Subsidiary of Forest Laboratories, Inc.
St. Louis, MO 63045

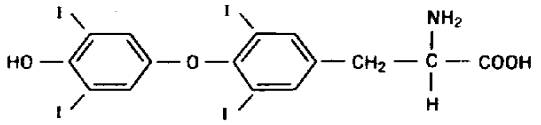
DESCRIPTION

Armour® Thyroid tablets (thyroid tablets, USP) for oral use are natural preparations derived from porcine thyroid glands. (T_3 liothyronine is approximately four times as potent as T_4 levothyroxine on a microgram for microgram basis.) They provide 38 mcg levothyroxine (T_4) and 9 mcg liothyronine (T_3) per grain of thyroid. The inactive ingredients are calcium stearate, dextrose, microcrystalline cellulose, sodium starch glycolate and opadry white.

STRUCTURAL FORMULAS
liothyronine (T_3)



levothyroxine (T_4)



CLINICAL PHARMACOLOGY

The steps in the synthesis of the thyroid hormones are controlled by thyrotropin (Thyroid Stimulating Hormone, TSH) secreted by the anterior pituitary. This hormone's secretion is in turn controlled by a feedback mechanism effected by the thyroid hormones themselves and by thyrotropin releasing hormone (TRH), a tripeptide of hypothalamic origin. Endogenous thyroid hormone secretion is suppressed when exogenous thyroid hormones are administered to euthyroid individuals in excess of the normal gland's secretion.

The mechanisms by which thyroid hormones exert their physiologic action are not well understood. These hormones enhance oxygen consumption by most tissues of the body, increase the basal metabolic rate, and the metabolism of carbohydrates, lipids, and proteins. Thus, they exert a profound influence on every organ system in the body and are of particular importance in the development of the central nervous system.

The normal thyroid gland contains approximately 200 mcg of levothyroxine (T_4) per gram of gland, and 15 mcg of liothyronine (T_3) per gram. The ratio of these two hormones in the circulation does not represent the ratio in the thyroid gland, since about 80 percent of peripheral liothyronine (T_3) comes from monodeiodination of levothyroxine (T_4). Peripheral monodeiodination of levothyroxine (T_4) at the 5 position (inner ring) also results in the formation of reverse liothyronine (T_3), which is calorigenically inactive.

Liothyronine (T_3) levels are low in the fetus and newborn, in old age, in chronic caloric deprivation, hepatic cirrhosis, renal failure, surgical stress, and chronic illnesses representing what has been called the "T_3 thyronine syndrome."

Pharmacokinetics - Animal studies have shown that levothyroxine (T_4) is only partially absorbed from the gastrointestinal tract. The degree of absorption is dependent on the vehicle used for its administration and by the character of the intestinal contents, the intestinal flora, including plasma protein, and soluble dietary factors, all of which bind thyroid and thereby make it unavailable for diffusion. Only 41 percent is absorbed when given in a gelatin capsule as opposed to a 74 percent absorption when given with an albumin carrier.

Depending on other factors, absorption has varied from 48 to 79 percent of the administered dose. Fasting increases absorption. Malabsorption syndromes, as well as dietary factors, (children's soybean formula, concomitant use of anionic exchange resins such as cholestyramine) cause excessive fecal loss. Liothyronine (T_3) is almost totally absorbed, 95 percent in 4 hours. The hormones contained in the natural preparations are absorbed in a manner similar to the synthetic hormones.

More than 99 percent of circulating hormones are bound to serum proteins, including thyroid-binding globulin (TBg), thyroid-binding prealbumin (TBPA), and albumin (TBa), whose capacities and affinities vary for the hormones. The higher affinity of levothyroxine (T_4) for both TBg and TBPA as compared to liothyronine (T_3) partially explains the higher serum levels and longer half-life of the former hormone. Both protein-bound hormones exist in reverse equilibrium with minute amounts of free hormone, the latter accounting for the metabolic activity.

Deiodination of levothyroxine (T_4) occurs at a number of sites, including liver, kidney, and other tissues. The conjugated hormone, in the form of glucuronide or sulfate, is found in the bile and gut where it may complete an enterohepatic circulation. Eighty-five percent of levothyroxine (T_4) metabolized daily is deiodinated.

INDICATIONS AND USAGE

Armour Thyroid tablets are indicated:

1. As replacement or supplemental therapy in patients with hypothyroidism of any etiology, except transient hypothyroidism during the recovery phase of subacute thyroiditis. This category includes cretinism, myxedema, and ordinary hypothyroidism in patients of any age (children, adults, the elderly), or state (including pregnancy); primary hypothyroidism resulting from functional deficiency, primary atrophy, partial or total absence of thyroid gland, or the effects of surgery, radiation, or drugs, with or without the presence of goiter; and secondary (pituitary), or tertiary (hypothalamic) hypothyroidism (See WARNINGS).
2. As pituitary TSH suppressants, in the treatment or prevention of various types of euthyroid goiters, including thyroid nodules, subacute or chronic lymphocytic thyroiditis (Hashimoto's), multinodular goiter, and in the management of thyroid cancer.
3. As diagnostic agents in suppression tests to differentiate suspected mild hyperthyroidism or thyroid gland autonomy.

CONTRAINDICATIONS

Thyroid hormone preparations are generally contraindicated in patients with diagnosed but as yet uncorrected adrenal cortical insufficiency, untreated thyrotoxicosis, and apparent hypersensitivity to any of their active or extraneous constituents. There is no well-documented evidence from the literature, however, of true allergic or idiosyncratic reactions to thyroid hormone.

WARNINGS

Drugs with thyroid hormone activity, alone or together with other therapeutic agents, have been used for the treatment of obesity. In euthyroid patients, doses within the range of daily hormonal requirements are ineffective for weight reduction. Larger doses may produce serious or even life-threatening manifestations of toxicity, particularly when given in association with sympathomimetic amines such as those used for their anorectic effects.

The use of thyroid hormones in the therapy of obesity, alone or combined with other drugs, is unjustified and has been shown to be ineffective. Neither is their use justified for the treatment of male or female infertility unless this condition is accompanied by hypothyroidism.

PRECAUTIONS

General—Thyroid hormones should be used with great caution in a number of circumstances where the integrity of the cardiovascular system, particularly the coronary arteries, is suspected. These include patients with angina pectoris or the elderly, in whom there is a greater likelihood of occult cardiac disease. In these patients therapy should be initiated with low doses, i.e., 15-30 mg Armour Thyroid. When, in such

patients, a euthyroid state can only be reached at the expense of an aggravation of the cardiovascular disease, thyroid hormone dosage should be reduced.

Thyroid hormone therapy in patients with concomitant diabetes mellitus or diabetes insipidus or adrenal cortical insufficiency aggravates the intensity of their symptoms. Appropriate adjustments of the various therapeutic measures directed at these concomitant endocrine diseases are required. The therapy of myxedema coma requires simultaneous administration of glucocorticoids (See DOSAGE AND ADMINISTRATION).

Hypothyroidism decreases and hyperthyroidism increases the sensitivity to oral anticoagulants. Prothrombin time should be closely monitored in thyroid-treated patients on oral anticoagulants and dosage of the latter agents adjusted on the basis of frequent prothrombin time determinations. In infants, excessive doses of thyroid hormone preparations may produce craniosynostosis.

Information for the Patient—Patients on thyroid hormone preparations and parents of children on thyroid therapy should be informed that:

1. Replacement therapy is to be taken essentially for life, with the exception of cases of transient hypothyroidism, usually associated with thyroiditis, and in those patients receiving a therapeutic trial of the drug.
2. They should immediately report during the course of therapy any signs or symptoms of thyroid hormone toxicity, e.g., chest pain, increased pulse rate, palpitations, excessive sweating, heat intolerance, nervousness, or any other unusual event.
3. In case of concomitant diabetes mellitus, the daily dosage of antidiabetic medication may need readjustment as thyroid hormone replacement is achieved. If thyroid medication is stopped, a downward readjustment of the dosage of insulin or oral hypoglycemic agent may be necessary to avoid hypoglycemia. At all times, close monitoring of urinary glucose levels is mandatory in such patients.
4. In case of concomitant oral anticoagulant therapy, the prothrombin time should be measured frequently to determine if the dosage of oral anticoagulants is to be readjusted.
5. Partial loss of hair may be experienced by children in the first few months of thyroid therapy, but this is usually a transient phenomenon and later recovery is usually the rule.

Laboratory Tests—Treatment of patients with thyroid hormones requires the periodic assessment of thyroid status by means of appropriate laboratory tests besides the full clinical evaluation. The TSH suppression test can be used to test the effectiveness of any thyroid preparation bearing in mind the relative insensitivity of the infant pituitary to the negative feedback effect of thyroid hormones. Serum T_4 levels can be used to test the effectiveness of all thyroid medications except T_3. When the total serum T_4 is low but TSH is normal, a test specific to assess unbound (free) T_4 levels is warranted. Specific measurements of T_4 and T_3 by competitive protein binding or radioimmunoassay are not influenced by blood levels of organic or inorganic iodine.

Drug Interactions—Oral Anticoagulants—Thyroid hormones appear to increase catabolism of vitamin K-dependent clotting factors. If oral anticoagulants are also being given, compensatory increases in clotting factor synthesis are impaired. Patients stabilized on oral anticoagulants who are found to require thyroid replacement therapy should be watched very closely when thyroid is started. If a patient is truly hypothyroid, it is likely that a reduction in anticoagulant dosage will be required. No special precautions appear to be necessary when oral anticoagulant therapy is begun in a patient already stabilized on maintenance thyroid replacement therapy.

Insulin or Oral Hypoglycemics—Initiating thyroid replacement therapy may cause increases in insulin or oral hypoglycemic requirements. The effects seen are poorly understood and depend upon a variety of factors such as dose and type of thyroid preparations and endocrine status of the patient. Patients receiving insulin or oral hypoglycemics should be closely watched during initiation of thyroid replacement therapy.

Cholestyramine or Colestipol—Cholestyramine or colestipol binds both levothyroxine (T_4) and liothyronine (T_3) in the intestine, thus impairing absorption of these thyroid hormones. *In vitro* studies indicate that the binding is not easily removed. Therefore four to five hours should elapse between administration of cholestyramine or colestipol and thyroid hormones.

Estrogen, Oral Contraceptives—Estrogens tend to increase serum thyroxine-binding globulin (TBg). In a patient with a nonfunctioning thyroid gland who is receiving thyroid replacement therapy, free levothyroxine (T_4) may be decreased when estrogens are started thus increasing thyroid requirements. However, if the patient's thyroid gland has sufficient function, the decreased free levothyroxine (T_4) will result in a compensatory increase in levothyroxine (T_4) output by the thyroid. Therefore patients without a functioning thyroid gland who are on thyroid replacement therapy may need to increase their thyroid dose if estrogens or estrogen-containing oral contraceptives are given.

Drug/Laboratory Test Interactions—The following drugs or moieties are known to interfere with laboratory tests performed in patients on thyroid hormone therapy: androgens, corticosteroids, estrogens, oral contraceptives containing estrogens, iodine-containing preparations, and the numerous preparations containing salicylates.

1. Changes in TBg concentration should be taken into consideration in the interpretation of levothyroxine (T_4) and liothyronine (T_3) values. In such cases, the unbound (free) hormone should be measured. Pregnancy, estrogens, and estrogen-containing oral contraceptives increase TBg concentrations. TBg may also be increased during infectious hepatitis. Decreases in TBg concentrations are observed in nephrosis, acromegaly, and after androgen or corticosteroid therapy. Familial hyper- or hypothyroxine-binding-globulinemias have been described. The incidence of TBg deficiency approximates 1 in 9,000. The binding of levothyroxine by TBPA is inhibited by salicylates.
2. Medicinal or dietary iodine interferes with all *in vivo* tests of radio-iodine uptake, producing low uptakes which may not be relative of a true decrease in hormone synthesis.
3. The persistence of clinical and laboratory evidence of hypothyroidism in spite of adequate dosage replacement indicates either poor patient compliance, poor absorption, excessive fecal loss, or inactivity of the preparation. Intracellular resistance to thyroid hormone is quite rare.

Carcinogenesis, Mutagenesis, and Impairment of Fertility—A reportedly apparent association between prolonged thyroid therapy and breast cancer has not been confirmed and patients on thyroid for established indications should not discontinue therapy. No confirmatory long-term studies in animals have been performed to evaluate carcinogenic potential, mutagenicity, or impairment of fertility in either males or females.

Pregnancy-Category A—Thyroid hormones do not readily cross the placental barrier. The clinical experience to date does not indicate any adverse effect on fetuses when thyroid hormones are administered to pregnant women. On the basis of current knowledge, thyroid replacement therapy to hypothyroid women should not be discontinued during pregnancy.

Nursing Mothers—Minimal amounts of thyroid hormones are excreted in human milk. Thyroid is not associated with serious adverse reactions and does not have a known tumorigenic potential. However, caution should be exercised when thyroid is administered to a nursing woman.

Pediatric Use—Pregnant mothers provide little or no thyroid hormone to the fetus. The incidence of congenital hypothyroidism is relatively high (1:4,000) and the hypothyroid fetus would not derive any benefit from the small amounts of hormone crossing the placental barrier. Routine determinations of serum T_4 and/or TSH is strongly advised in neonates in view of the deleterious effects of thyroid deficiency on growth and development.

Treatment should be initiated immediately upon diagnosis, and maintained for life, unless transient hypothyroidism is suspected; in which case, therapy may be interrupted for 2 to 8 weeks after the age of 3 years to reassess the condition. Cessation of therapy is justified in patients who have maintained a normal TSH during those 2 to 8 weeks.

ADVERSE REACTIONS

Adverse reactions other than those indicative of hyperthyroidism because of therapeutic overdosage, either initially or during the maintenance period, are rare (See OVERDOSAGE).

OVERDOSAGE

Signs and Symptoms—Excessive doses of thyroid result in a hypermetabolic state resembling in every respect the condition of endogenous origin. The condition may be self-induced.

Treatment of Overdosage—Dosage should be reduced or therapy temporarily discontinued if signs and symptoms of overdosage appear.

Treatment may be reinstituted at a lower dosage. In normal individuals, normal hypothalamic-pituitary-thyroid axis function is restored in 6 to 8 weeks after thyroid suppression.

Treatment of acute massive thyroid hormone overdosage is aimed at reducing gastrointestinal absorption of the drugs and counteracting central and peripheral effects, mainly those of increased sympathetic activity. Vomiting may be induced initially if further gastrointestinal absorption can reasonably be prevented and barring contraindications such as coma, convulsions, or loss of the gagging reflex. Treatment is symptomatic and supportive. Oxygen may be administered and ventilation maintained. Cardiac glycosides may be indicated if congestive heart failure develops. Measures to control fever, hypoglycemia, or fluid loss should be instituted if needed. Antiadrenergic agents, particularly propranolol, have been used advantageously in the treatment of increased sympathetic activity. Propranolol may be administered intravenously at a dosage of 1 to 3 mg, over a 10-minute period or orally, 80 to 160 mg/day, initially, especially when no contraindications exist for its use.

Other adjunctive measures may include administration of cholestyramine to interfere with thyroxine absorption, and glucocorticoids to inhibit conversion of T_4 to T_3.

DOSAGE AND ADMINISTRATION

The dosage of thyroid hormones is determined by the indication and must in every case be individualized according to patient response and laboratory findings.

Thyroid hormones are given orally. In acute, emergency conditions, injectable levothyroxine sodium (T_4) may be given intravenously when oral administration is not feasible or desirable, as in the treatment of myxedema coma, or during total parenteral nutrition. Intramuscular administration is not advisable because of reported poor absorption.

Hypothyroidism—Therapy is usually instituted using low doses, with increments which depend on the cardiovascular status of the patient. The usual starting dose is 30 mg Armour Thyroid, with increments of 15 mg every 2 to 3 weeks. A lower starting dosage, 15 mg/day, is recommended in patients with long-standing myxedema, particularly if cardiovascular impairment is suspected, in which case extreme caution is recommended. The appearance of angina is an indication for a reduction in dosage. Most patients require 60 to 120 mg/day. Failure to respond to doses of 180 mg suggests lack of compliance or malabsorption. Maintenance dosages 60 to 120 mg/day usually result in normal serum T_4 and T_3 levels. Adequate therapy usually results in normal TSH and T_4 levels after 2 to 3 weeks of therapy.

Readjustment of thyroid hormone dosage should be made within the first four weeks of therapy, after proper clinical and laboratory evaluations, including serum levels of T_4, bound and free, and TSH.

Liothyronine (T_3) may be used in preference to levothyroxine (T_4) during radio-isotope scanning procedures, since induction of hypothyroidism in those cases is more abrupt and can be of shorter duration. It may also be preferred when impairment of peripheral conversion of levothyroxine (T_4) and liothyronine (T_3) is suspected.

Myxedema Coma—Myxedema coma is usually precipitated in the hypothyroid patient of long-standing by intercurrent illness or drugs such as sedatives and anesthetics and should be considered a medical emergency. Therapy should be directed at the correction of electrolyte disturbances and possible infection besides the administration of thyroid hormones. Corticosteroids should be administered routinely. Levothyroxine (T_4) and liothyronine (T_3) may be administered via a nasogastric tube but the preferred route of administration of both hormones is intravenous. Levothyroxine sodium (T_4) is given at a starting dose of 400 mcg (100 mcg/mL) given rapidly, and is usually well tolerated, even in the elderly. This initial dose is followed by daily supplements of 100 to 200 mcg given IV. Normal T_4 levels are achieved in 24 hours followed in 3 days by threefold elevation of T_3. Oral therapy with thyroid hormone would be resumed as soon as the clinical situation has been stabilized and the patient is able to take oral medication.

Thyroid Cancer—Exogenous thyroid hormone may produce regression of metastases from follicular and papillary carcinoma of the thyroid and is used as ancillary therapy of these conditions with radioactive iodine. TSH should be suppressed to low or undetectable levels. Therefore, larger amounts of thyroid hormone than those used for replacement therapy are required. Medullary carcinoma of the thyroid is usually unresponsive to this therapy.

Thyroid Suppression Therapy—Administration of thyroid hormone in doses higher than those produced physiologically by the gland results in suppression of the production of endogenous hormone. This is the basis for the thyroid suppression test and is used as an aid in the diagnosis of patients with signs of mild hyperthyroidism in whom base line laboratory tests appear normal, or to demonstrate thyroid gland autonomy in patients with Grave's ophthalmopathy. ^{131}I uptake is determined before and after the administration of the exogenous hormone. A 50 percent or greater suppression of uptake indicates a normal thyroid-pituitary axis and thus rules out thyroid gland autonomy.

For adults, the usual suppressive dose of levothyroxine (T_4) is 1.56 mg/kg of body weight per day given for 7 to 10 days. These doses usually yield normal serum T_4 and T_3 levels and lack of response to TSH.

Thyroid hormones should be administered cautiously to patients in whom there is strong suspicion of thyroid gland autonomy, in view of the fact that the exogenous hormone effects will be additive to the endogenous source.

Pediatric Dosage—Pediatric dosage should follow the recommendations summarized in Table 1. In infants with congenital hypothyroidism, therapy with full doses should be instituted as soon as the diagnosis has been made.

Recommended Pediatric Dosage for Congenital Hypothyroidism

	Armour Thyroid Tablets	
Age	Dose per day	Daily dose per kg of body weight
0-6 mos	15-30 mg	4.8-6 mg
6-12 mos	30-45 mg	3.6-4.8 mg
1-5 yrs	45-60 mg	3-3.6 mg
6-12 yrs	60-90 mg	2.4-3 mg
Over 12 yrs	Over 90 mg	1.2-1.8 mg

Table 1

HOW SUPPLIED

Armour Thyroid tablets (thyroid tablets, USP) are supplied as follows: 15 mg (1/4 gr) are available in bottles of 100 (NDC 0456-0457-01). 30 mg (1/2 gr) are available in bottles of 100 (NDC 0456-0458-01), 1000 (NDC 0456-0458-00), containers of 50,000 (NDC 0456-0458-69) and unit dose cartons of 100 (NDC 0456-0458-63). 60 mg (1 gr) are available in bottles of 100 (NDC 0456-0459-01), 1000 (NDC 0456-0459-00), 5000 (NDC 0456-0459-51), containers of 50,000 (0456-0459-69) and unit dose cartons of 100 (NDC 0456-0459-63). 90 mg (1 1/2 gr) are available in bottles of 100 (NDC 0456-0460-01). 120 mg (2 gr) are available in bottles of 100 (NDC 0456-0461-01), 1000 (NDC 0456-0461-00), containers of 50,000 (NDC 0456-0461-69) and unit dose cartons of 100 (NDC 0456-0461-63). 180 mg (3 gr) are available in bottles of 100 (NDC 0456-0462-01) and 1000 (NDC 0456-0462-00). 240 mg (4 gr) are available in bottles of 100 (NDC 0456-0463-01). 300 mg (5 gr) are available in bottles of 100 (NDC 0456-0464-01). The bottles of 100 are special dispensing bottles with child-resistant closures.

Armour Thyroid tablets are evenly colored, light tan, round tablets, with convex surfaces. One side is debossed with a mortar and pestle beneath the letter "A" on the top and strength code letters on the bottom as defined below

Strength	Code	
1/4 grain	TC	
1/2 grain	TD	
1 grain	TE	
1 1/2 grain	TJ	
2 grain	TF	
3 grain	TG	(bisected)
4 grain	TH	
5 grain	TI	(bisected)

Note: (T_3liothyronine is approximately four times as potent as T_4levothyroxine on a microgram for microgram basis.)

Tablets should be stored at controlled room temperature, 59°-86° F (15°-30° C), in capped bottles or unbroken plastic strip packing.

CAUTION: Federal law prohibits dispensing without prescription.

REV 8/95

Dear International Customer,

Regarding your recent difficulty in obtaining Armour Thyroid Tablets, please be advised that an agreement has been made between Rhone-Poulenc Rorer, Forest Pharmaceutical and the Broda O. Barnes, M.D. Research Foundation, Inc., stating that all international orders for Armour Thyroid must now be handled through the Broda O. Barnes, M.D. Research Foundation.

To more efficiently serve your needs we have enclosed Forest Pharmaceuticals current price list for Armour Thyroid products. Prices are in U.S. dollars.

Instructions for placing orders:

1. All orders must be placed through the Barnes Foundation by 24-hour fax, telephone or in writing.

2. All first-time orders must be accompanied by a current medical or pharmaceutical license.

3. All orders will be priced using the current international price list plus freight and collection charges.

4. Forest Pharmaceuticals will not accept orders for less than $250.00 US.

5. Orders will be charged actual freight and collection fees only.

6. Payment terms on all orders shall be payment-in-full, thirty days from invoice date (Net 30). Payment shall be made via bank wire transfer using the following information:

   BANK OF AMERICA
   100 NORTH BROADWAY
   ST. LOUIS, MO 63201
   FOR THE ACCOUNT OF FOREST PHARMACEUTICALS, INC.
   ROUTING NUMBER 081000032
   ACCOUNT NUMBER 350100158576
   SWIFT# BOFAUS3N

If you have any questions please contact the Barnes Foundation by phone at 203-261-2101 or by fax at 203-261-3017.

F O R E S T P H A R M A C E U T I C A L S
INTERNATIONAL PRICE LIST
November 1, 1999

FOREST PRODUCT NUMBER	DESCRIPTION	SIZE	UNIT PRICE
401	Armour Thyroid ¼ grain	100	$ 9.13
402	Armour Thyroid ½ grain	10 x 10	$ 18.81
403	Armour Thyroid ½ grain	100	$ 10.73
405	Armour Thyroid ½ grain	1000	$ 85.57
406	Armour Thyroid 1 grain	10 x 10	$ 20.00
407	Armour Thyroid 1 grain	100	$ 11.90
410	Armour Thyroid 1 grain	1000	$ 115.06
408	Armour Thyroid 1 grain	5000	$ 447.03
411	Armour Thyroid 1.5 grain	100	$ 18.81
412	Armour Thyroid 2 grain	10 x 10	$ 24.95
413	Armour Thyroid 2 grain	100	$ 22.03
415	Armour Thyroid 2 grain	1000	$ 220.28
416	Armour Thyroid 3 grain	100	$ 34.96
417	Armour Thyroid 3 grain	1000	$ 349.90
418	Armour Thyroid 4 grain	100	$ 52.39
419	Armour Thyroid 5 grain	100	$ 64.95

Forest Pharmaceuticals, Inc.

Subsidiary of Forest Laboratories, Inc.
13600 Shoreline Drive Tel. (800)678-1605
St. Louis, MO 63045 Fax (314) 493-7455

ACCOUNT INFORMATION FORM

Corporation __ Proprietorship __ Partnership __ Other _____ Account Rep. Broda Barnes

BILL TO:

Complete Name:

_____

Main Office Address:

_____

_____

Billing Address: (if different)

_____

_____

Telephone: (_____) _____ Federal I.D. #: _____ DEA # _____

If you are a subsidiary, branch, or division of a corporation or other entity, please list the name and address of such corporation or entity.

SHIP TO:

Name:

_____

Address 1:

_____

If more than one ship to, please attach a separate listing. If only one ship to, but additional branches at separate locations, please attach a separate listing of branches.

Buyer: _____Telephone # (_____) _____

Accts. Payable: _____ Telephone # (_____) _____

PRINCIPAL OWNERS AND OFFICERS:

Name Home Address

1. _____

_____

Telephone # (_____) _____

2. _____

_____

Telephone # (_____) _____

CREDIT INFORMATION: YOU ARE REQUIRED TO SEND US A COPY OF YOUR FINANCIAL STATEMENTS FOR YOUR LAST FISCAL YEAR.

Name of Bank: _____

Address: _____

Acct. _____

Bank Officer to Contact: _____ Bank Phone #: (_____)

Years in Business: _____ Years at Present Location: _____

Names, Addresses and Phone Numbers of Principal Suppliers:

1. _____(_____)_____

2 ._____(_____)_____

3. _____(_____)_____

4. _____(_____)_____

I HEREBY CERTIFY THAT THE ABOVE INFORMATION IS TRUE AND ACCURATE AN[) HEREBY ACKNOWLEDGE THAT FOREST PHARMACEUTICALS, INC. IS RELYING ON SUCH INFORMATION IN OPENING THIS ACCOUNT AND EXTENDING CREDIT. SHOULD AN ACCOUNT BE OPENED, I ACKNOWLEDGE THAT ALL RIGHTS, OBLIGATIONS, AND LIABILITIES THEREUNDER SHALL BE GOVERNED BY MISSOURI LAW. I AGREE THAT ANY SUIT, ACTION OR PROCEEDING ARISING OUT OF OR RELATING TO SAID ACTION SHALL BE INSTITUTED IN A STATE OR FEDERAL COURT IN THE STATE OF MISSOURI AND I AGREE TO SUBMIT TO THE JURISDICTION OF ANY SUCH COURT.

RE: COMPANY POLICIES
I have been advised ...

1. That no allowances will be honored, or returns accepted, without prior written authorization.
2. Terms of Sale – Net 30 days – F.O.B. Forest Pharmaceuticals, Inc. Warehouse
3. Payments are due at Forest Pharmaceuticals, Inc., P>O> Box 18821-B, St Louis, MO 63160

Date_____ Title _____

Signature_____