DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

Ron Steinhauf
Vice President, Regulatory Affairs
Jerome Stevens Pharmaceuticals, Incorporated
60 DaVinci Drive
Bohemia, NY 11716

JUL - 3 2000

RE: THYROX (Levothyroxine Sodium Tablets, USP)
MACMIS ID# 8964

Dear Mr. Steinhauf:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials for THYROX (Levothyroxine Sodium Tablets, USP), a product of Jerome Stevens Pharmaceuticals (Jerome Stevens). These materials include a journal advertisement (item number JS2401-0004) that appeared in the June, 2000 issue of *U.S. Pharmacist*, a "Dear Pharmacist" letter (item number JS2400-0004A), and a sales aid (item number JS2400-0004). We have reviewed these materials and consider them to be in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and its implementing regulations.

Background

None of the currently marketed levothyroxine sodium products is the subject of an approved New Drug Application (NDA). None of these products have been determined to be equivalent to or inequivalent to any other. There is no standard product. Thus, we consider any claims of equivalence, interchangeability, inequivalence, or superiority to be unsupported.

False or Misleading Claims

Jerome Stevens' promotional materials are misleading because they state that THYROX is "the new standard." In support of this claim, the materials state that Jerome Stevens has filed an NDA with the Food and Drug Administration (FDA). This claim is misleading because it suggests that THYROX is the reference standard for levothyroxine sodium products. However, neither THYROX nor any other levothyroxine sodium product is currently recognized by FDA as a standard or reference product for levothyroxine sodium products. The filing of an NDA does not support this claim or implication.

Similarly, the implied superiority claims inherent in these materials are misleading because THYROX has not been demonstrated to be safer or more effective than any other levothyroxine sodium product. Claims such as "Unparalleled track record of quality" and "Greater stability ensures more predictable results- easier and less frequent titration – less frequent TSH monitoring" clearly imply THYROX is superior to other levothyroxine sodium products. These and similar claims would require substantial evidence from head-to-head clinical trials. Likewise, "One of the only levothyroxine formulations to consistently demonstrate reliable potency, stability, and bioavailability" is an unsupported superiority claim.

Finally, statements such as "all manufacturers who wish to continue marketing levothyroxine must have an approved NDA by August 14, 2000" are now false in light of the Federal Register notice of April 26, 2000 extending the compliance date. (65 FR 24488)

Lack of Fair Balance

The materials lack fair balance because they fail to present any risk information. Risk information must be presented in a manner reasonably comparable to information about drug efficacy. Including only the prescribing information or the brief summary does not satisfy this requirement.

Conclusion and Recommendation

Jerome Stevens has promoted THYROX in a manner that creates false or misleading impressions regarding the current status of levothyroxine sodium drug products and with materials that lack fair balance. Accordingly, Jerome Stevens should immediately cease dissemination of the aforementioned materials and any other promotional materials that contain the same or similar violations. We request that Jerome Stevens respond to this letter within ten business days of receipt. Your response should include a statement of your intent to comply with the above, a list of similarly violative materials, and the date on which their dissemination was discontinued.

Direct your response to the undersigned at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 8964.

Sincerely,

/S/

Margaret M. Kober, R.Ph.
Regulatory Review Officer,
Division of Drug Marketing,
Advertising, and Communications

/S/

/S/

The ability to perform?

Recognizing the limitations of most levothyroxine

- **St*ability***—More than 100 million tablets have been recalled since 1991 due to potency or stability problems.[1]
- **Reli*ability***—Because of serious product quality problems, all marketed levothyroxine tablets must have an FDA-approved New Drug Application (NDA) by August 14, 2001.[1,2]
- **Avail*ability***—Any levothyroxine product marketed after August 14, 2001 without an approved NDA may be removed from the market by the FDA.[2]

Putting stability into our levothyroxine

- **St*ability***—Jerome Stevens Pharmaceuticals, Inc, has produced close to 1 billion levothyroxine tablets without a product recall, batch failure, or product complaint.[3]
- **Reli*ability***—An NDA has been submitted for **THYROX®** tablets demonstrating dependable potency, stability, dissolution, and bioavailability.[3]
- **Avail*ability***—**THYROX®** tablets are one of the only levothyroxine tablet formulations with a submitted NDA.

Put stability into your levothyroxine tablet inventory

Call 1-800-635-3359

THYROX®
(Levothyroxine Sodium Tablets, USP)

Discover the new standard

References:
1. Federal Register Online. Prescription drug products; levothyroxine sodium. August 14, 1997;62(157):43535-43538. Available at: http://www.gpo.ucop.edu/cgi-bin/gpogate. Accessed February 29, 2000.
2. Federal Register Online. Prescription drug products; levothyroxine sodium; extension of compliance date. April 26, 2000;65(81):24488-24489. Available at: http://www.gpo.ucop.edu/cgi-bin/gpogate. Accessed via GPO Access [wais.access.gpo.gov] [DOCID: fr26ap00-69] May 1, 2000.
3. Data on file, Jerome Stevens Pharmaceuticals, Inc.

JSP Jerome Stevens Pharmaceuticals

Please see accompanying brief summary of prescribing information.

JS2401-0004

Because levothyroxine reliability is in question...

Dear Pharmacist:

The reliability of many levothyroxine tablet formulations has been criticized for years. Numerous product recalls, lot-to-lot potency variations, and stability problems have prompted the FDA to require all manufacturers of levothyroxine tablets to submit a New Drug Application (NDA).[1] Currently, there are no levothyroxine tablets on the market with an approved NDA.[1]

The ability to demonstrate reliable results

Manufacturers who wish to continue marketing levothyroxine tablets were given a three-year period to develop, submit, and receive FDA approval for an NDA. Jerome Stevens Pharmaceuticals, Inc, manufacturer of **THYROX®** (Levothyroxine Sodium Tablets, USP), is one of the only manufacturers to comply with the FDA request. This manufacturer has accepted the responsibility to document consistent potency, stability, dissolution, and bioavailability of its formulation and submit an NDA.

The ability to market levothyroxine

The Food and Drug Administration NDA approval deadline of August 14, 2000, could significantly impact the levothyroxine tablet market. Because Jerome Stevens Pharmaceuticals, Inc, is one of the only manufacturers to submit an NDA, **THYROX®** could be one of the only, if not the only, levothyroxine tablet formulations allowed to be marketed. Other manufacturers, including the market leader, have filed a citizens petition claiming that levothyroxine tablets are not subject to the same regulations as other prescription pharmaceutical products.

The ability to obtain a reliable formulation

Regardless of how the FDA decides, you can discover the new levothyroxine standard with **THYROX®** ***Accelerated stability*** tests for **THYROX®** tablets have demonstrated that the potency at 6 months is maintained well within the required 90% to 110% guidelines[2] (see enclosed brochure). Furthermore, **THYROX®** tablets have demonstrated reliable bioavailability responses (see enclosed brochure) compared against levothyroxine oral solution and multiples of other **THYROX®** tablet dosage strengths.[2]

The ability to partner with a leader in quality

We put stability in levothyroxine. Since 1991, Jerome Stevens Pharmaceuticals, Inc, has produced close to one billion tablets of levothyroxine.[2] In that time there have been no product recalls, no batch failures, and no product complaints.[2] This level of quality is unheard of in the levothyroxine tablet category. Find out how you can partner with an innovator in levothyroxine tablet quality. Call Jerome Stevens Pharmaceuticals, Inc, at **1-800-635-3359.**

Discover the new standard

THYROX®
(Levothyroxine Sodium Tablets, USP)

References:
1. Federal Register Online. Prescription drug products; levothyroxine sodium. August 14, 1997;62(157):43535-43538. Available at: http://www.gpo.ucop.edu/cgi-bin/gpogate. Accessed February 29, 2000.
2. Data on file, Jerome Stevens Pharmaceuticals, Inc.

JSP Jerome Stevens Pharmaceuticals

Please see enclosed full prescribing information

JS2400-0004A

Printed in USA

The *ability* to perform

Creating a new standard in levothyroxine tablets

When ordering levothyroxine tablets *Question the ability to perform*

Reli*ability*

- Most currently marketed levothyroxine tablets have not been shown to demonstrate consistent potency and stability; therefore they are not recognized as safe and effective by the FDA.[1]
- Currently no levothyroxine sodium formulations have an FDA-approved New Drug Application (NDA).[1]
- All manufacturers who wish to continue marketing levothyroxine must have an approved NDA by August 14, 2000.[1]

St*ability*

- Almost every manufacturer, including the market leader, has issued recalls due to potency or stability problems.[1]
- More than 100 million tablets have been recalled due to potency or stability problems since 1991.[1]
- The customary 2-year shelf life may not be appropriate for these products.[1]

Bioavail*ability*

- 58 adverse drug reactions resulting in hypothyroid or hyperthyroid conditions were reported between 1987 and 1994.[1]
  - —Hypothyroid symptoms include severe depression, fatigue, weight gain, cold intolerance, edema, and difficulty concentrating
  - —Hyperthyroid symptoms include atrial fibrillation, heart palpitations, and difficulty sleeping
  - —Hyperthyroidism increases the risk of osteoporosis
- Up until August 14, 2000, only serious and unexpected adverse reactions are required to be reported.[1]
  - —Therefore, many adverse reactions have probably not been documented
- No claims of bioequivalence can be made between levothyroxine tablet formulations because there is no approved reference formulation.[1]

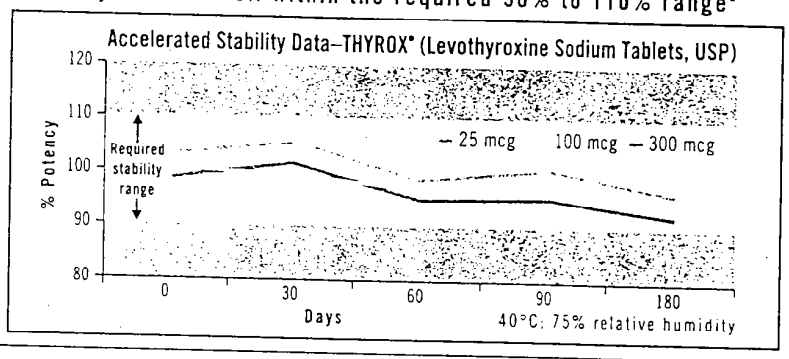
When stocking THYROX®
Discover the ability to perform

Reli*ability*

- Jerome Stevens Pharmaceuticals is one of the only manufacturers to submit a levothyroxine tablet NDA.
- **THYROX®** tablets have demonstrated reliable potency, stability, and bioavailability.[2]

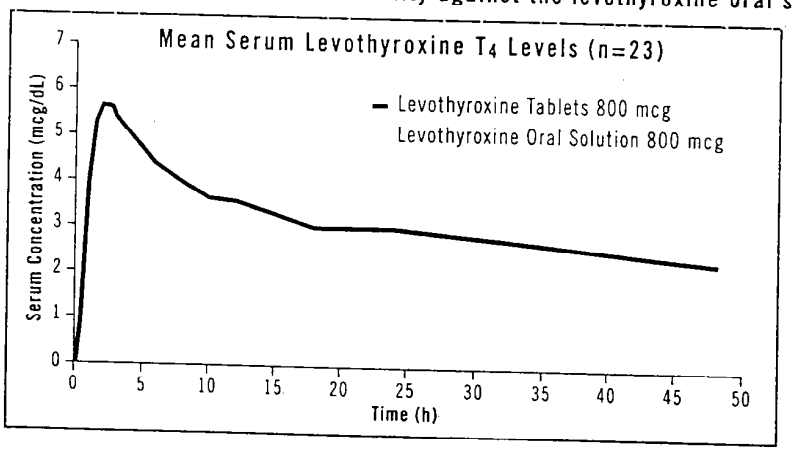
St*ability*

Stability remains well within the required 90% to 110% range[2]

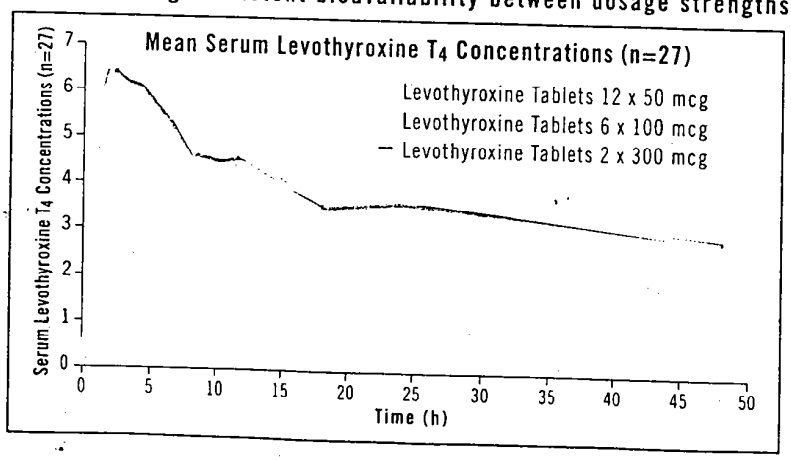


Bioavail*ability*

Demonstrating reliable bioavailability against the levothyroxine oral solution reference standard[2]



Demonstrating consistent bioavailability between dosage strengths[2]



We put stability into levothyroxine therapy

Yesterday's reliability

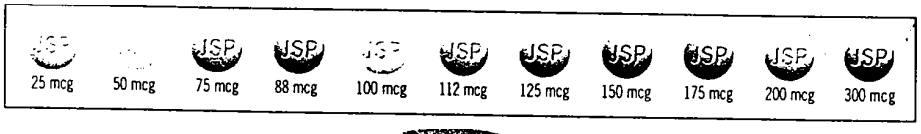
- Almost 10 years of high quality manufacturing experience.
- Close to 1 billion levothyroxine tablets produced.[1]
- Unparalleled track record of quality.[1]
  - —No "spiking"
  - —No recalls
  - —No batch failures
  - —No product complaints

Today's accountability

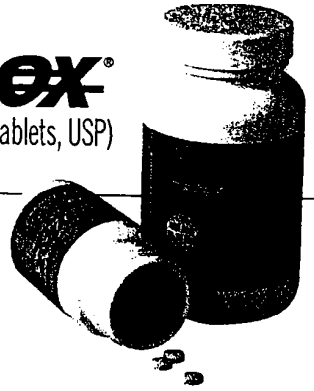
- One of the only manufacturers to submit a levothyroxine tablet NDA.[1]
- One of the only levothyroxine formulations to consistently demonstrate reliable potency, stability, and bioavailability.[1]
- Greater stability ensures more predictable results.
  - —Easier and less frequent titration
  - —Less frequent TSH monitoring

Today's and tomorrow's availability

- Call **1-800-635-3359** for ordering information.



THYROX®
(Levothyroxine Sodium Tablets, USP)



Discover the new standard

Jerome Stevens Pharmaceuticals

References:
1. Federal Register Online. Prescription drug products; levothyroxine sodium. August 14, 1997;62(157):43535-43538. Available at: http://www.gpo.ucop.edu/cgi-bin/gpogate. Accessed February 29, 2000.
2. Data on file, Jerome Stevens Pharmaceuticals, Inc.

Please see enclosed full prescribing information

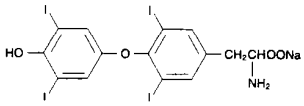
JS2400-0004

Printed in USA

Thyrox® Tablets, USP (Levothyroxine Sodium, USP)

DESCRIPTION: Thyrox® Tablets USP (Levothyroxine Sodium, USP Tablets) contain synthetic crystalline L-3,3',5,5'-tetraiodothyronine sodium salt [levothyroxine (T_4) sodium]. Synthetic T_4 is similar to that produced in the human thyroid gland. T_4 contains four iodine atoms and is formed by the coupling of two molecules of diiodotyrosine (DIT).

Levothyroxine (T_4) Sodium has an empirical formula of $C_{15}H_{10}I_4NNaO_4xH_2O$, molecular weight of 798.86 (anhydrous), and structural formula as shown:



Thyrox® Tablets (Levothyroxine Sodium Tablets) contain the following inactive ingredients: Colloidal silicon dioxide, lactose, magnesium stearate, microcrystalline cellulose and sodium starch glycolate. The following are the color additives per tablet strength:

Strength (mcg)	Color Additive(s)
25	FD&C Yellow Aluminum Lake No. 6
50	None
75	FD&C Red Aluminum Lake No. 40, FD&C Blue Aluminum Lake No. 2
88	D&C Yellow Aluminum Lake No. 10, FD&C Yellow Aluminum Lake No. 6, FD&C Blue Aluminum Lake No. 1
100	D&C Yellow Aluminum Lake No. 10, FD&C Yellow Aluminum Lake No. 6
112	D&C Red Aluminum Lake No. 27
125	FD&C Yellow Aluminum Lake No. 6, FD&C Red Aluminum Lake No. 40, FD&C Blue Aluminum Lake No. 1
150	FD&C Blue Aluminum Lake No. 2
175	FD&C Blue Aluminum Lake No. 1, D&C Red Aluminum Lake No. 27
200	FD&C Red Aluminum Lake No. 40
300	D&C Yellow Aluminum Lake No. 10, FD&C Yellow Aluminum Lake No. 6, FD&C Blue Aluminum Lake No. 1

CLINICAL PHARMACOLOGY: The steps in the synthesis of 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. Thus, when serum concentrations of T_3 and T_4 are increased, secretion of TSH and TRH is increased. 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. T_3 and T_4 are transported into cells by passive and active mechanisms. T_3 in cell cytoplasm and T_3 generated from T_4 within the cell diffuse into the nucleus and bind to thyroid receptor proteins, which appear to be primarily attached to DNA. Receptor binding leads to activation or repression of DNA transcription, thereby altering the amounts of mRNA and resultant proteins. Changes in protein concentrations are responsible for the metabolic changes observed in organs and tissues.

Thyroid hormones enhance oxygen consumption by most tissues of the body and 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. Thyroid hormones also appear to have direct effects of tissues, such as increased myocardial contractility and decreased systemic vascular resistance.

The physiological effects of thyroid hormones are produced primarily by T_3, a large portion of which is derived from the deiodination of T_4 in peripheral tissues. About 70 to 90 percent of peripheral T_3 is produced by monodeiodination of T_4 at the 5' position (outer ring). Peripheral monodeiodination of T_4 at the 5 position (inner ring) results in the formation of reverse triiodothyronine (rT_3), which is calorigenically inactive.

Triiodothyronine (T_3) level is 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 "low triiodothyronine syndrome."

PHARMACOKINETICS: Animal studies have shown that 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, soluble dietary factors, all of which bind thyroid and thereby make it unavailable for diffusion. In animals, the most active sites of absorption appear to be the proximal and mid-jejunum. T_4 is not absorbed from the stomach and little, if any, drug is absorbed from the duodenum. There seems to be no absorption of T_4 from the distal colon in animals. A number of human studies have confirmed the importance of an intact jejunum and ileum for T_4 absorption and have shown some absorption from the duodenum.

Depending on other factors, absorption has varied from 48 to 80 percent of the administered dose. Fasting increased absorption and decreased in malabsorption syndromes, such as sprue. Malabsorption syndromes, as well as dietary factors, (children's soybean formula, concomitant use of anionic exchange resins such as cholestyramine) cause excessive fecal loss. Decreased absorption may result from administration of infant soybean formula, ferrous sulfate, sodium polystyrene sulfonate, aluminum hydroxide sucralfate, or bile acid sequestrants. T_4 absorption following intramuscular administration is variable.

More than 99 percent of circulating hormones are bound to serum proteins, including thyroxine-binding globulin (TBG), thyroxine-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 triiodothyronine (T_3) partially explains the higher serum levels, slower metabolic clearance, and longer half-life of the former hormone. Both protein bound hormones exist in 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.

T_4 is eliminated slowly from the body, with a half-life of 6 to 7 days. T_3 has a half-life of 1 to 2 days. The liver is the major site of degradation for both hormones. T_4 and T_3 are conjugated with glucuronic and sulfuric acids and excreted in the bile. There is an enterohepatic circulation of thyroid hormones, as they are liberated by hydrolisis in the intestine and reabsorbed. A portion of the conjugated material reaches the colon unchanged, is hydrolyzed there, and is eliminated as free compounds in the feces. In man, approximately 20 to 40% of T_4 is eliminated in the stool. About 70 percent of the T_4 secreted daily is deiodinated to yield equal amounts of T_3 and rT_3. Subsequent deiodination of T_3 and rT_3 yields multiple forms of diiodothyronine. A number of other minor T_4 metabolites have also been identified. Although some of these metabolites have biological activity, their overall contribution to the therapeutic effect of T_4 is minimal.

A study (1) demonstrated that the 50, 100 and 300 µg strengths of Jerome Stevens Pharmaceuticals' Levothyroxine Sodium Tablet formulation were bioequivalent in healthy males and females. The product thus exhibits dosage form equivalence or dosage strength proportionality. The female subjects demonstrated significantly greater T_4 AUC and C_{max} than males. This gender difference in bioavailability may be attributed to the significantly smaller total body weight of the female cohort of subjects compared to the males. Gender differences in T_4 absorption or metabolism are unlikely contributing factors to the observed differences in bioavailability between the males and females who participated in this study.

Another study (2) demonstrated that the pharmacokinetics of exogenous levothyroxine following administration of the Levothyroxine Sodium Tablet formulation were similar to those of an oral solution of the drug. The pharmacokinetic profiles of both treatments were almost superimposable, particularly in the post-absorption phase. As evidenced by the arithmetic and geometric T_4 AUC_{0-t} and C_{max} mean ratios and the corresponding 90% confidence intervals, bioavailability of T_4 from the Levothyroxine formulation was equivalent to that of an oral solution of T_4. In conclusion, Jerome Stevens Pharmaceuticals' Levothyroxine Sodium Tablets, 600 µg was found to have a pharmacokinetic profile and T_4 bioavailability similar to an oral solution of the drug.

INDICATIONS AND USAGE:

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, including subclinical hypothyroidism; and secondary (pituitary), or tertiary (hypothalamic) hypothyroidism (see **CONTRAINDICATIONS** and **PRECAUTIONS**).

2. As a pituitary TSH suppressant, 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 conjunction with surgery and radioactive iodine therapy in the management of thyrotropin-dependent well-differentiated papillary or follicular carcinoma of the thyroid.

3. As a diagnostic agent in suppression tests to aid in the diagnosis of 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. Levothyroxine sodium is also contraindicated in the patients with uncorrected adrenal insufficiency, as thyroid hormones increase tissue demands, for adrenocortical hormones and may thereby precipitate acute adrenal crisis (see PRECAUTIONS).

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, who have a greater likelihood of occult cardiac disease. In these patients, therapy should be initiated with low doses, i.e., 25-50 mcg levothyroxine (T_4). 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 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 may require 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.

Seizures have been reported rarely in association with the initiation of levothyroxine sodium therapy, and may be related to the effect of thyroid hormone on seizure threshold.

Lithium blocks the TSH-mediated release of T_4 and T_3. Thyroid function should therefore be carefully monitored during lithium initiation, stabilization, and maintenance. If hypothyroidism occurs during lithium treatment, a higher than usual levothyroxine sodium dose may be required.

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. Before or at any time while using levothyroxine sodium, you should tell your doctor if you are allergic to any foods or medicines, are pregnant or intend to become pregnant, are breast-feeding, are taking or start taking any other prescription or nonprescription (OTC) medications, or have any other medical problems (especially hardening of the arteries, heart disease, high blood pressure, or history of thyroid, adrenal or pituitary gland problems).
3. Use levothyroxine sodium only as prescribed by your doctor. Do not discontinue levothyroxine sodium or change the amount you take or how often you take it, except as directed by your doctor.
4. Levothyroxine sodium, like all medicines obtained from your doctor, must be used only by you and for the condition determined appropriate by your doctor.
5. It may take a few weeks for levothyroxine sodium to begin working. Until it begins working, you may not notice any change in your symptoms.
6. You should immediately report during the course of therapy any signs or symptoms of thyroid hormone toxicity, e.g., chest pain, shortness of breath, hives, or skin rash, rapid or irregular heartbeat, increased pulse rate, headache, irritability, sleeplessness, diarrhea, changes in appetite, vomiting, weight gain or loss, changes in menstrual periods, fever, hand tremors, leg cramps, palpitations, excessive sweating, heat intolerance, nervousness, or any other unusual event.
7. You should inform your doctor or dentist that you are taking levothyroxine sodium before having any kind of surgery.
8. You should notify your doctor if you become pregnant while taking levothyroxine sodium. Your dose of this medicine will likely have to be increased while you are pregnant.
9. In cases 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 blood or urinary glucose levels is mandatory in such patients.
10. 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.
11. Partial hair loss may occur rarely during the first few months of levothyroxine sodium therapy, but it is usually temporary.
12. Keep levothyroxine sodium out of the reach of children. Store away from heat and moisture.

Laboratory Tests: Treatment of patients with levothyroxine sodium requires periodic assessment of titration by appropriate laboratory tests and clinical evaluation. Selection of appropriate tests for the diagnosis and management of thyroid disorders depends on patient variables such as presenting signs and symptoms, pregnancy, and concomitant medications. A combination of sensitive TSH assay and free T_4 (free T_4, free T_4 index) are recommended to confirm a diagnosis of thyroid disease. Normal ranges for these parameters are age-specific in newborns and younger children. TSH alone or initially may be useful for thyroid disease screening and for monitoring therapy for primary hypothyroidism as a linear inverse correlation exists between serum TSH and free T_4. Measurement of total serum T_4 and T_3, resin T_3 uptake, and free T_3 concentrations may also be useful. Antithyroid microsomal antibodies are an indicator of autoimmune thyroid disease. An elevated serum TSH in the presence of normal T_4 may indicate subclinical hypothyroidism. Intracellular resistance to thyroid hormone is quite rare, and is suggested by clinical signs and symptoms of hypothyroidism in the presence of high serum T_4 levels. Adequacy of levothyroxine sodium therapy for hypothyroidism of pituitary or hypothalamic origin should be assessed by measuring free T_4, which should be maintained in the upper half of the normal range. Measurement of TSH is not a reliable indicator of response to therapy for this condition. Adequacy of levothyroxine sodium therapy for congenital and acquired pediatric hypothyroidism should be assessed by measuring total T_4 or free T_4, which should be maintained in the upper half of the normal range. In congenital hypothyroidism, normalization of serum TSH levels may lag behind normalization of serum T_4 levels by 2 to 3 months or longer. In rare patients serum TSH remains relatively elevated despite clinical euthyroidism and age-specific normal levels of T_4 or free T_4.

Drug Interactions: The magnitude and relative importance of the effects noted below are likely to be patient specific and may vary by such factors as age, gender, race, intercurrent illnesses, dose of either agent, additional concomitant medications, and timing of drug administration. Any agent that alters thyroid hormone synthesis, secretion, distribution, effect on target tissues, metabolism, or elimination may alter the optimal therapeutic dose of levothyroxine sodium.

Levothyroxine Sodium Absorption: The following agents may bind and decrease absorption of levothyroxine sodium from the gastrointestinal tract: aluminum hydroxide, cholestyramine resin, colestipol hydrochloride, ferrous sulfate, sodium polystyrene sulfonate, soybean flour (e.g., infant formula), sucralfate.

Binding to Serum Proteins: The following agents may either inhibit levothyroxine sodium binding to serum proteins or alter the concentrations of serum binding proteins: androgens and related anabolic hormones, asparaginase, clofibrate, estrogens and estrogen-containing compounds, 5-fluorouracil, furosemide, flucocorticoids, meclofenamic acid, mefenamic acid, methadone, perphenazine, phenylbutazone, phenytoin, salicylates, tamoxifen.

Thyroid Physiology: The following agents may alter thyroid hormone or TSH levels, generally by effects on thyroid hormone synthesis, secretion, distribution, metabolism, hormone action, or elimination, or altered TSH secretion: aminoglutethimide, p-aminosalicylic acid, amiodarone, androgens and related anabolic hormones, complex anions (thiocyanate, perchlorate, pertechnetate), antithyroid drugs, β-adrenergic blocking agents, carbamazepine, chloral hydrate, diazepam, dopamine and dopamine agonists, ethionamide, glucocorticoids, heparin, hepatic enzyme inducers, insulin, iodinated cholestographic agents, iodine-containing compounds, levodopa, lovastatin, lithium, 6-mercaptopurine, metoclopramide, mitotane, nitroprusside, phenobarbital, phenytoin, resorcinol, rifampin, somatostatin analogs, sulfonamides, sulfonylureas, thiazide diuretics.

Adrenocorticoids: Metabolic clearance of adrenocorticoids is decreased in hypothyroid patients and increased in hyperthyroid patients, and may therefore change with changing thyroid status.

Amiodarone: Amiodarone therapy alone can cause hypothyroidism or hyperthyroidism.

Anticoagulants (Oral): The hypoprothrombinemic effect of anticoagulants may be potentiated, apparently by increased catabolism of vitamin K-dependent clotting factors.

Antidiabetic Agents (Insulin, Sulfonylureas): Requirements for insulin or oral antidiabetic agents may be reduced in hypothyroid patients with diabetes mellitus and may subsequently increase with the initiation of thyroid hormone replacement therapy.

β-Adrenergic Blocking Agents: Actions of some beta-blocking agents may be impaired when hypothyroid patients become euthyroid.

Cytokines (interferon, interleukin): Cytokines have been reported to induce both hyperthyroidism and hypothyroidism.

Digitalis Glycosides: Therapeutic effects of digitalis glycosides may be reduced. Serum digitalis levels may be decreased in hyperthyroidism or when a hypothyroid patient becomes euthyroid.

Ketamine: Marked hypertension and tachycardia have been reported in association with concomitant administration of levothyroxine sodium and ketamine.

Maprotiline: Risk of cardiac arrhythmias may increase.

Sodium Iodide (^{123}I and ^{131}I), Sodium Pertechnetate Tc99m: Uptake of radiolabeled ions may be decreased.

Somatrem/Somatropin: Excessive concurrent use of thyroid hormone may accelerate epiphyseal closure. Untreated hypothyroidism may interfere with the growth response to somatrem or somatropin.

Theophylline: Theophylline clearance may decrease in hypothyroid patients and return toward normal when a euthyroid state is achieved.

Tricyclic Antidepressants: Concurrent use may increase the therapeutic and toxic effects of both drugs, possibly due to increased catecholamine sensitivity. Onset of action of tricyclics may be accelerated.

Sympathomimetic Agents: Possible increased risk of coronary insufficiency in patients with coronary artery disease.

Drug/Laboratory Test Interactions: The following drugs or moieties are known to interfere with some 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 T_4 and T_3 values. 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 9000. The binding of thyroxine by TBPA is inhibited by salicylates. In such cases, the unbound (free) hormone should be measured. Alternatively, an indirect measure of free thyroxine, such as the Free Thyroxine Index (FTI) may be used.

2. Medicinal or dietary iodine interferes with all *in vivo* tests of radioiodine uptake, producing low uptakes which may not indicate 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, impaired absorption, inactivity of the preparation, drug interactions, or decreased potency of the preparation due to improper storage. Intracellular resistance to thyroid hormone is quite rare, and is suggested by clinical signs and symptoms of hypothyroidism in the presence of high serum T_4 levels.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: A reported association between prolonged thyroid therapy and breast cancer has not been confirmed and patients on thyroid therapy 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. Synthetic T_4 is identical to that produced by the human thyroid gland.

Pregnancy: Pregnancy category A. Studies in pregnant women have not shown that levothyroxine sodium increases the risk of fetal abnormalities if administered during pregnancy. If levothyroxine sodium is used during pregnancy, the possibility of fetal harm appears remote. Because the studies cannot rule out the possibility of harm, levothyroxine sodium should be used during pregnancy only if clearly needed.

Thyroid hormones cross the placental barrier to some extent. T_4 levels in the cord blood of athyroid fetuses have been shown to be about one-third of maternal levels. Nevertheless, maternal-fetal transfer of T_4 may not prevent in utero hypothyroidism.

Hypothyroidism during pregnancy is associated with a higher rate of complications, including spontaneous abortion and preeclampsia, and has been reported to have an adverse effect on fetal and childhood development. Studies have shown that during pregnancy T_4 concentrations may decrease and TSH concentrations may increase to values outside normal ranges. Postpartum values are similar to preconception values. Elevations in TSH may occur as early as at 4 weeks gestation.

Pregnant women who are maintained on levothyroxine sodium should have their TSH measured periodically. An elevated TSH should be corrected by an increase in levothyroxine sodium dose. After pregnancy, the dose can be decreased to the optimal preconception dose.

Nursing Mothers: Minimal amounts of thyroid hormones are excreted in human milk. Thyroid is not associated with serious adverse reactions and does not have known tumorigenic potential. While caution should be exercised when thyroid is administered to nursing women, adequate replacement doses of levothyroxine are generally needed to maintain normal lactation.

Pediatric Use:

Congenital Hypothyroidism: Rapid restoration of normal serum T_4 concentrations is essential for preventing the deleterious effects of neonatal thyroid hormone deficiency on intelligence, as well as on overall growth and development. Levothyroxine sodium should be initiated immediately upon diagnosis, and is generally continued for life. The goal of therapy is to maintain the serum total T_4 or FT_4 in the upper half of the normal range and serum TSH in the normal range. As initial starting dose of 10 to 15 mcg/kg/day (ages 0-3 months) will generally increase serum T_4 concentrations to the upper half of the normal range in less than 3 weeks. Clinical assessment of growth and development and thyroid status should be monitored frequently. In most cases, the dose of levothyroxine sodium per body weight will decrease gradually as the patient grows through infancy and childhood (see TABLE 1). Prolonged use of large doses in infants may be associated with later behavior problems.

Thyroid function tests (serum total T_4 or FT_4 and TSH) should be monitored closely and used to determine the adequacy of levothyroxine sodium therapy. Normalization of serum T_4 levels is usually followed by a rapid decline of TSH levels. Nevertheless, normalization of TSH may lag behind normalization of T_4 levels by 2 to 3 months or longer. The relative elevation of serum TSH is more marked during the early months of therapy, but can persist to some degree throughout life. In rare patients TSH remains relatively elevated despite clinical euthyroidism and age-specific normal levels of total T_4 or FT_4. Increasing the levothyroxine sodium dosage to suppress TSH into the normal range may result in overtreatment, with an elevated serum T_4 level and clinical features of hyperthyroidism, including irritability, increased appetite with diarrhea, and sleeplessness. Another risk or prolonged overtreatment in infants is premature cranial synostosis.

Assessment of permanence of hypothyroidism may be done when transient hypothyroidism is suspected. Levothyroxine therapy may be interrupted for 30 days after 3 years of age and serum measurement of T_4 and TSH levels obtained. If T_4 is low and the TSH level is elevated, permanent hypothyroidism is confirmed and therapy should be re-instituted. If T_4 and TSH remain in the normal range, a presumptive diagnosis of transient hypothyroidism can be made. In this instance, continued clinical monitoring and periodic reevaluation of thyroid function may be warranted.

Acquired hypothyroidism: The initial dose of levothyroxine sodium varies with age and body weight, and should be adjusted to maintain serum total T_4 or free T_4 levels in the upper half of the normal range. In general, in the absence of overriding clinical concerns, children should be started on a full replacement dose. Children with underlying heart disease should be started at lower doses, with careful upward titration. Children with severe, long-standing hypothyroidism may also be started on a lower initial dose with upward titration in an attempt to avoid premature closure of epiphyses. The recommended dose per body weight decreases with age (see TABLE 1).

Treated children may resume growth at a rate greater than normal (period of transient catch-up growth). In some cases catch-up growth may be adequate to normalize growth; however, in children with severe and prolonged hypothyroidism, adult height may be reduced. Excessive thyroxine replacement may initiate accelerated bone maturation resulting in disproportionate advancement in skeletal age and shortened adult stature.

ADVERSE REACTIONS: Adverse reactions other than those indicative of thyrotoxicosis because of therapeutic overdosage, either initially or during the maintenance periods, are rare (see **OVERDOSAGE**). Inadequate doses of levothyroxine sodium may produce or fail to resolve symptoms of hypothyroidism. Hypersensitivity reactions to the product excipients, such as rash and urticaria, may occur. Partial hair loss may occur during the initial months of therapy, but is generally transient. The incidence of continued hair loss is unknown. Pseudotumor cerebri has been reported in pediatric patients receiving thyroid hormone replacement therapy.

OVERDOSAGE: Signs and Symptoms: Excessive doses of thyroid result in 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 reinstated at a lower dosage. In normal individuals, normal hypothalamic-pituitary-thyroid axis function is restored in 6 to 8 weeks after thyroid suppression.

Signs and Symptoms: Excessive doses of levothyroxine sodium result in a hypermetabolic state indistinguishable from thyrotoxicosis of endogenous origin. Signs and symptoms of thyrotoxicosis include weight loss, increased appetite, palpitations, nervousness, diarrhea, abdominal cramps, sweating, tachycardia, increased pulse and blood pressure, cardiac arrhythmias, tremors, insomnia, heat intolerance, fever, and menstrual irregularities. Symptoms are not always evident or may not appear until several days after ingestion.

Treatment of acute massive thyroid hormone overdosage is aimed at reducing gastrointestinal absorption of the drugs and counteracting central 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. Cholestyramine and activated charcoal have also been used to decrease levothyroxine sodium absorption. 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, 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.

Since T_4 is extensively protein bound, very little drug will be removed by dialysis.

DOSAGE AND ADMINISTRATION: The dosage and rate of administration of Thyrox® Tablets USP (Levothyroxine Sodium, USP) is determined by the indication and must in every case be individualized according to patient response and laboratory findings.

Hypothyroidism: Thyrox® Tablets USP (Levothyroxine Sodium, USP Tablets) are usually instituted using low doses, with increments which depend on the cardiovascular status of the patient. The usual starting dose is 50 mcg, with increments of 25 mcg every 2 to 3 weeks. A lower starting dosage; 25 mcg/day or less, is recommended in patients with long standing hypothyroidism, 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 not more than 200 mcg/day. Failure to respond to doses of 300 mcg suggests lack of compliance or malabsorption. Adequate therapy usually results in normal TSH and T_4 levels after 2 to 3 weeks of the maintenance dose.

Readjustment of dosage should be made within the first four weeks of therapy, after proper clinical laboratory evaluations.

The goal of therapy for primary hypothyroidism is to achieve and maintain a clinical and biochemical euthyroid state with consequent resolution of hypothyroid signs and symptoms. The starting dose of levothyroxine sodium, the frequency of dose titration, and the optimal full replacement dose must be individualized for every patient, and will be influenced by such factors as age, weight, cardiovascular status, presence of other illness, and the severity and duration of hypothyroid symptoms.

The usual full replacement dose of levothyroxine sodium for younger, healthy adults is approximately 1.6 mcg/kg/day administered once daily. In the elderly, the full replacement dose may be altered by decreases in T_4 metabolism and levothyroxine sodium absorption. Older patients may require less than 1 mcg/kg/day. Children generally require higher doses (see Pediatric Dosage). Women who are maintained on levothyroxine sodium during pregnancy may require increased doses (see Pregnancy).

Therapy is usually initiated in younger, healthy adults at the anticipated full replacement dose. Clinical and laboratory evaluations should be performed at 6 to 8 week intervals (2 to 3 weeks in severely hypothyroid patients), and the dosage adjusted by 12.5 to 25 mcg increments until the serum TSH concentration is normalized and signs and symptoms resolve. In older patients or in younger patients with a history of cardiovascular disease, the starting dose should be 12.5 to 50 mcg once daily with adjustments of 12.5 to 25 mcg every 3 to 6 weeks until TSH is normalized. If cardiac symptoms develop or worsen the cardiac disease should be evaluated and the dose of levothyroxine sodium reduced. Rarely, worsening angina or other signs of cardiac ischemia may prevent achieving a TSH in the normal range.

Treatment of subclinical hypothyroidism, when indicated, may require lower than usual replacement doses, (e.g., 1.0 mcg/kg/day). Patients for whom treatment is not initiated should be monitored yearly for changes in clinical status, TSH, and thyroid antibodies.

In patients with hypothyroidism resulting from pituitary or hypothalamic disease, the possibility of secondary adrenal insufficiency should be considered, and if present, treated with glucocorticoids prior to initiation to levothyroxine sodium. The adequacy of levothyroxine sodium therapy should be assessed in these patients by measuring FT_4, which should be maintained in the upper half of the normal range, in addition to clinical assessment. Measurement of TSH is not a reliable indicator of response to therapy for this condition.

Few patients require doses greater than 200 mcg/day. An inadequate response to daily doses of 300 to 400 mcg/day is rare, and may suggest malabsorption, poor patient compliance, and/or drug interactions.

Once optimal replacement is achieved, clinical and laboratory evaluations should be conducted at least annually or whenever warranted by a change in patient status. Levothyroxine sodium products from different manufacturers should not be used interchangeably unless retesting of the patient and retitration of the dosage, as necessary, accompanies the product switch.

TSH Suppression in Thyroid Cancer, Nodules, and Euthyroid Goiters: 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 following surgery or radioactive iodine. Medullary and anaplastic carcinoma of the thyroid is usually unresponsive to this therapy. TSH should be suppressed to low or undetectable levels. Therefore, larger amounts of thyroid hormone than those used for replacement therapy are frequently required. This therapy is also used in treating nontoxic solitary nodules and multinodular goiters, and to prevent thyroid enlargement in chronic (Hashimoto's) thyroiditis.

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 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 Graves' ophthalmopathy. ^{131}I uptake is determined before and after the administration of the exogenous hormone. A fifty percent or greater suppression of uptake indicates a normal thyroid-pituitary axis and thus rules out thyroid gland autonomy.

For adults, the average suppressive dose of levothyroxine (T_4) is 2.6 mcg/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.

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

No controlled studies have compared the various degrees of TSH suppression in the treatment of either benign or malignant thyroid nodular disease. Further, the effectiveness of TSH suppression for benign nodular disease is controversial. The dose of levothyroxine sodium used for TSH suppression should therefore be individualized by the nature of the disease, the patient being treated, and the desired clinical response, weighing the potential benefits of therapy against the risks of iatrogenic thyrotoxicosis. In general, levothyroxine sodium should be given in the smallest dose that will achieve the desired clinical response.

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. Thyrox® Tablets USP (Levothyroxine Sodium, USP Tablets) may be given to infants and children who cannot swallow intact tablets by crushing the proper dose tablet and suspending the freshly crushed tablet in a small amount of water or formula. The suspension can be given by spoon or dropper. DO NOT STORE THE SUSPENSION FOR ANY PERIOD OF TIME. The crushed tablet may also be sprinkled over a small amount of food, such as cooked cereal or apple sauce. Foods or formula containing large amounts of soybean fiber or iron should not be used for administering levothyroxine sodium.

Congenital or Acquired Hypothyroidism: The dosage of levothyroxine sodium for pediatric hypothyroidism varies with age and body weight. Levothyroxine sodium should be given at a dose that maintains the serum total T_4 or free T_4 concentrations in the upper half of the normal range and serum TSH in the normal range (see Pediatric Use).

Levothyroxine sodium therapy is usually initiated at the full replacement dose (see TABLE 1). Infants and neonates with very low or undetectable serum T_4 levels (<5 mcg/dl) should start at the higher end of the dosage range (e.g., 50 mcg daily). A lower starting dosage (e.g., 25 mcg daily) should be considered for neonates at risk of cardiac failure, increasing every few days until a full maintenance dose is reached. In children with severe, long-standing hypothyroidism, levothyroxine sodium should be initiated gradually, with an initial dose of 25 mcg for 2 weeks, and then increasing the dose by 25 mcg every 2 to 4 weeks until the desired dose based on serum T_4 and TSH levels is achieved. (see Pediatric Use).

Serum T_4 and TSH measurements should be evaluated at the following intervals, with subsequent dosage adjustments to normalize serum total T_4 or FT_4 and TSH: 2 and 4 weeks after the initiation of levothyroxine sodium treatment; every 1 to 2 months during the first year of life; every 2 to 3 months between 1 and 3 years of age; every 3 to 12 months thereafter until growth is completed. Evaluation at more frequent intervals is indicated when compliance is questioned or abnormal values are obtained.

Table 1

Recommended Pediatric Dosage For Congenital Hypothyroidism*

Age	Thyrox® Tablets, USP (Levothyroxine Sodium Tablets, USP)	
	Dose per day	Daily doses per kg of body weight
0 - 6 mos.	25 - 50 mcg	8 - 10 mcg
6 - 12 mos.	50 - 75 mcg	6 - 8 mcg
1 - 5 yrs.	75 - 100 mcg	5 - 6 mcg
6 - 12 yrs.	100 - 150 mcg	4 - 5 mcg

*To be adjusted on the basis of clinical response and laboratory tests (See **Laboratory Tests**).

PATIENT INFORMATION:
Levothyroxine is a synthetic thyroid hormone used for treatment of hypothyroidism (low thyroid hormone secretion). Inform your physician if you are pregnant or nursing. Take this medication on an empty stomach at approximately the same time each morning. Do not stop taking levothyroxine without talking with your physician. Do not change from one brand of this medication to another without talking with your pharmacist or physician. Notify your physician if headache, nervousness, diarrhea, excessive sweating, chest pain, increased pulse rate, or palpitations occur.

HOW SUPPLIED: Thyrox® Tablets USP (Levothyroxine Sodium, USP Tablets): round, color coded, scored tablet debossed with JSP and ID Number.

25 mcg, Peach
Bottles of 100 NDC 50564-513-01
Bottles of 1000 NDC 50564-513-10

50 mcg, White
Bottles of 100 NDC 50564-514-01
Bottles of 1000 NDC 50564-514-10

75 mcg, Purple
Bottles of 100 NDC 50564-515-01
Bottles of 1000 NDC 50564-515-10

88 mcg, Olive
Bottles of 100 NDC 50564-561-01
Bottles of 1000 NDC 50564-561-10

100 mcg, Yellow
Bottles of 100 NDC 50564-516-01
Bottles of 1000 NDC 50564-516-10

112 mcg, Rose
Bottles of 100 NDC 50564-562-01
Bottles of 1000 NDC 50564-562-10

125 mcg, Tan
Bottles of 100 NDC 50564-519-01
Bottles of 1000 NDC 50564-519-10

150 mcg, Blue
Bottles of 100 NDC 50564-520-01
Bottles of 1000 NDC 50564-520-10

175 mcg, Lilac
Bottles of 100 NDC 50564-563-01
Bottles of 1000 NDC 50564-563-10

200 mcg, Pink
Bottles of 100 NDC 50564-522-01
Bottles of 1000 NDC 50564-522-10

300 mcg, Green
Bottles of 100 NDC 50564-523-01
Bottles of 1000 NDC 50564-523-10

Store at controlled room temperature 15°-30°C (59°-86°F).

Rx Only

Manufactured by:
Jerome Stevens Pharmaceuticals, Inc.
Bohemia, NY 11716

01/00
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