BEDFORD LABORATORIES™

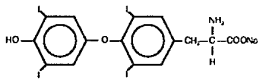
LEVOTHYROXINE SODIUM FOR INJECTION

Rx ONLY.

DESCRIPTION

Levothyroxine Sodium for Injection contains synthetic crystalline levothyroxine sodium (L-thyroxine). L-thyroxine is the principal hormone secreted by the normal thyroid gland.

Levothyroxine sodium is chemically designated as 1-tyrosine, 0-(4-hydroxy-3,5-diiodophenyl)-3,5-diiodo-monosodium salt and has the following structural formula:



$C_{15}H_{10}I_4NNaO_4$ 798.86

Levothyroxine Sodium for Injection is a sterile, lyophilized product and is available in two strengths: 200 or 500 mcg/vial. Each vial also contains mannitol 10 mg and tribasic sodium phosphate anhydrous 0.7 mg. Sodium hydroxide added for pH adjustment.

CLINICAL PHARMACOLOGY

Levothyroxine Sodium for Injection is effective by parenteral route. Following absorption, the synthetic L-thyroxine provided by levothyroxine sodium cannot be distinguished from L-thyroxine that is secreted endogenously. Each is bound to the same serum proteins forming a reservoir of circulating L-thyroxine.

Levothyroxine sodium will provide L-thyroxine (T_4 as a substrate for physiologic deiodination to L-triiodothyronine (T_3). Therefore, patients taking properly adjusted doses of levothyroxine sodium will demonstrate normal blood levels of L-triiodothyronine even when the thyroid gland has been removed surgically or destroyed by radioiodine. Administration of Levothyroxine Sodium for Injection alone will result in complete physiologic thyroid replacement.

INDICATIONS AND USAGE

Levothyroxine Sodium for Injection serves as specific replacement therapy for reduced or absent thyroid function of any etiology. Levothyroxine Sodium for Injection can be used intravenously (IV) whenever a rapid onset of effect is critical, and either IV or intramuscularly (IM) in hypothyroid patients whenever the oral route is precluded for long periods of time.

CONTRAINDICATIONS

There are no absolute contraindications to levothyroxine sodium therapy. Relative contraindications include acute myocardial infarction, uncorrected adrenal insufficiency and thyrotoxicosis (see **WARNINGS**).

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.

Patients with cardiovascular diseases warrant particularly close attention during the restoration of normal thyroid function by any thyroid drug. In such cases, low initial dosage increased slowly by small increments is indicated. Occasionally, the cardiovascular capacity of the patient is so compromised that the metabolic demands of the normal thyroid state cannot be met. Clinical judgement will then dictate a less than complete restoration of thyroid status.

Endocrine disorders such as diabetes mellitus, adrenal insufficiency (Addison's disease), hypopituitarism and diabetes insipidus are characterized by signs and symptoms which may be diminished in severity or obscured by hypothyroidism. Levothyroxine sodium therapy for such patients may aggravate the intensity of previously obscured symptoms and require appropriate adjustment of therapeutic measures directed at these concomitant disorders.

Thyroid replacement may potentiate the effects of anticoagulants. Patients on anticoagulant therapy should have frequent prothrombin determinations when instituting thyroid replacement to gauge the need to reduce anticoagulant dosage.

PRECAUTIONS

Overdosage with any thyroid drug may produce the signs and symptoms of thyrotoxicosis, but resistance to such factitious thyrotoxicosis is the general rule.

Close observation of the patient following the administration of Levothyroxine Sodium for Injection is advised, and appropriate adjustment of repeated dosage is recommended.

ADVERSE REACTIONS

Adverse reactions are due to overdose and induced hyperthyroidism.

DOSAGE AND ADMINISTRATION

Levothyroxine Sodium for Injection by IM or IV routes can be substituted for the oral dosage form when ingestion of tablets is precluded for long periods of time. The initial parenteral dosage should be approximately one half of the previously established oral dosage of levothyroxine sodium tablets. A daily maintenance dose of 50 to 100 mcg parenterally should suffice to maintain the euthyroid state, once established. Close observation of the patient, with individual adjustment of the dosage as needed, is recommended.

In infants and children, there is great urgency to achieve full thyroid replacement because of the critical importance of thyroid hormone in sustaining growth and maturation. Despite the smaller body size, the dosage needed to sustain a full rate of growth, development and general thriving is higher in the child than in the adult.

Optimal maintenance levels should be adjusted individually to obtain normal serum T_3, T_4, free T_4, index and Thyroid Stimulating Hormone (TSH) values after several weeks of therapy for hypothyroidism. The patent's clinical status is most important and some patents may be clinically euthyroid with individual laboratory values that are not within normal range (i.e., elevated total T_4 with normal T_3). An exception may be seen in congenital hypothyroidism where elevated serum TSH values may persist for the first two to three years of life despite normalization of free T_4 measurements. In such cases, it generally is recommended that maintenance of normal serum free T_4 values alone should be considered therapeutically sufficient.

In myxedema coma or stupor, without concomitant severe heart disease, 200 to 500 mcg of Levothyroxine Sodium for Injection may be administered IV as a solution containing 100 mcg/mL. DO NOT ADD TO OTHER IV FLUIDS. Although the patient may show evidence of increased responsivity within six to eight hours, full therapeutic effect may not be evident until the following day. An additional 100 to 300 mcg or more may be given on the second day if evidence of significant and progressive improvements has not occurred. Levothyroxine Sodium for Injection produces a predictable increase in the reservoir level of hormone with a seven day half-life. This usually precludes the need for multiple injections but continued daily administration of lesser amounts parenterally should be maintained until the patient is fully capable of accepting a daily oral dose.

In the presence of concomitant heart disease, the sudden administration of such large doses of L-thyroxine IV is clearly not without its cardiovascular risks. Under such circumstances, IV therapy should not be undertaken without weighing the alternative risks of the myxedema coma and the cardiovascular disease. Clinical judgement in this situation may dictate smaller IV doses of Levothyroxine Sodium for Injection.

The age and general physical condition of the patient and the severity and duration of hypothyroid symptoms determine the starting dosage and the rate of incremental dosage increase leading to a final maintenance dosage. Clearly it is the physician's judgment of the severity of the disease and closer observation of patient response which determine the rate and extent of dosage increase.

Appropriate laboratory tests are beneficial in monitoring thyroid replacement therapy. Although measurements of normal blood levels of thyroxine in patients on oral replacement regimens frequently coincide with clinical impressions of normal thyroid status, higher than normal levels occur occasionally and should not be considered evidence of overdosage per se. In all cases, clinical impressions of the well being of the patient take precedence over laboratory determination of appropriate individual dosage.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED

	NDC Number
Levothyroxine Sodium for Injection 200 mcg/vial in individually-boxed 10 mL flip-top vials.	NDC 55390-880-10
Levothyroxine Sodium for Injection 500 mcg/vial in individually-boxed 10 mL flip-top vials.	NDC 55390-881-10

Store dry product at controlled room temperature 15° to 30°C (59° to 86°F). **Protect from light.**

RECONSTITUTION DIRECTIONS

Reconstitute the lyophilized levothyroxine sodium by aseptically adding 5 mL of 0.9% Sodium Chloride Injection, USP only. Reconstituted concentrations for the 200 mcg and 500 mcg vials are 40 mcg/mL and 100 mcg/mL, respectively. Shake vial to insure complete mixing. **Use immediately** after reconstitution. Do not add to other IV fluids. Discard any unused portion.

Manufactured for Bedford Laboratories™, Bedford, OH 44146

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