Levothyroxine (Thyroxine) - ORAL

Newborn use only 2019

Alert	Levothyroxine sodium is the International Nonproprietary Name for thyroxine sodium. Three different brands are available: Eutroxsig, Oroxine and Eltroxin. **Eltroxin is not bioequivalent on a same dose basis with Eutroxsig or Oroxine.** Prescribers should not to interchange Eltroxin and Eutroxsig or Oroxine unless a decision has been made to switch products and there is a plan for monitoring TSH levels and review of dose. The patient should be informed of the same.[1, 2]
Indication	Thyroid hormone deficiency
Action	Levothyroxine exerts effects on most organ systems and is particularly important in the development of the central nervous system. Increases the metabolic rate of body tissues. Also involved in the regulation of cell growth and differentiation.
Drug Type	Levothyroxine sodium previously known as thyroxine sodium, is the monosodium salt of the levo- isomer of thyroxine, the principal secretion of the thyroid gland
Trade Name	Eltroxin tablets, Eutroxsig tablets, Oroxine tablets.
Presentation	Eutroxsig and Oroxine tablets: 50 microgram, 75 microgram, 100 microgram, 200 microgram tablets Eltroxin tablets: 25 microgram, 50 microgram, 75 microgram, 100 microgram, 125 microgram, 200 microgram tablets.
Dosage/Interval	**Starting dose:** 10 to 15 microgram/kg/dose DAILY.[2] **Maintenance dose:** 8 to 10 microgram/kg/dose DAILY. **Severe congenital hypothyroidism** [free T4 <5 pmol/L] –Start with highest initial dose. Round dose to nearest half or whole tablet where possible, particularly for discharge eg 25 microgram or 50 microgram. **Refer to monitoring section for goals of therapy.**
Route	PO
Maximum Daily Dose	
Preparation/Dilution	• Oral compounded suspension is <u>not</u> advised. Tablet freshly dispersed in water immediately prior to administration is recommended. Dose to be rounded to the nearest half/whole tablet where possible and disperse/administer using method 1 or 2 below. Tablets can be difficult to quarter with a tablet cutter. • Tablets can be difficult to halve or quarter accurately with a tablet cutter. Consider keeping the remaining tablet portions for subsequent doses so that the average dose over 2 or 4 days is relatively accurate. • Method 3 is for preparing a 10 microgram/mL dispersion just prior to administration and should only be used for administering small doses where a tablet/tablet portion cannot be used. Method 3 is for inpatient use only. <u>Method 1</u> – round dose to the nearest half or whole tablet: 1. If required, halve tablet using a tablet cutter. 2. Use tablet crusher to crush tablet/tablet portion. 3. Add approximately 1 mL of water (sterile/freshly boiled and cooled) to powder in tablet crusher and mix well. 4. Draw up suspension in oral syringe/dispenser. 5. Rinse tablet cutter with a few drops of water and add to oral syringe/dispenser. Make sure as much as possible of the suspension is transferred to ensure an accurate dose. 6. **Do not allow suspension to settle before administration.** 7. Draw a small amount of air into the oral syringe/dispenser. Administer the contents of the oral syringe/dispenser immediately with the tip pointing down, using the small pocket of air to push all the liquid out of the syringe/oral dispenser.

	Method 2 – round dose to the nearest half or whole tablet: 1. Remove plunger from oral syringe/dispenser. 2. If required, halve or quarter tablet using a tablet cutter. 3. Place tablet/tablet portion into the barrel of the oral syringe/dispenser and replace the plunger. 4. Draw up 1–5 mL of water (sterile/freshly boiled and cooled) into the syringe. 5. Cap the oral syringe/dispenser and shake until tablet is fully dispersed. This may take up to 2 minutes. 6. **Do not allow suspension to settle before administration.** 7. Draw a small amount of air into the oral syringe/dispenser. Administer the contents of the oral syringe/dispenser immediately with the tip pointing down, using the small pocket of air to push all the liquid out of the syringe/oral dispenser. Method 3 – For inpatient use only. Reserve this method for small doses which cannot be rounded to a half or whole tablet: 1. Remove the plunger from a 5 mL oral syringe/dispenser. 2. Place one 50 microgram tablet into the barrel of the oral syringe/dispenser and replace the plunger. 3. Draw up exactly 5 mL of water (sterile/freshly boiled and cooled) into the oral syringe/dispenser. 4. Cap the oral syringe/dispenser and shake until tablet is fully dispersed. This may take up to 2 minutes. 5. The resulting suspension concentration is 10 microgram/mL. 6. **Do not allow suspension to settle before discarding the excess**. 7. Immediately discard any excess from the syringe, leaving only dose to be administered in the syringe (eg if 10 microgram is to be delivered, dispose of 4 mL, leaving only 1 mL in the syringe). 8. Administer the medication immediately, just before a feed.
Administration	Can be administered in the morning or evening, preferably before feed. Should be administered in the same way, at the same time every day. Levothyroxine should not be mixed with substances that interfere with gastrointestinal absorption, such as soy protein formula, concentrated iron or calcium [ensure at least a 2-hour interval].
Monitoring	The goal of initial therapy is to raise free T4 concentration to the upper end of the normal range within 2 weeks of starting therapy and decrease the TSH to <20 mU/L within the first month.[1, 2] The goal of maintenance therapy is to normalise the TSH and aim for free T4 in the upper half of the normal range.[2] The baby is re-examined and repeat thyroid tests are performed at two weeks after starting therapy, at 6 weeks, at 3 months and 2–3-monthly for the first year of life. More frequent review may be necessary if problems arise. Thereafter, clinical examination and thyroid function testing occurs three-monthly unless there has been a significant dose change, a change to or from soy-based formula or there is a clinical indication. Reviews can be done at about four-monthly intervals after the age of three years and in older children four- to six-monthly.[1]
Contraindications	Known hypersensitivity to levothyroxine. Untreated hyperthyroidism. Uncorrected primary or secondary adrenal insufficiency. Acute myocardial infarction.
Precautions	In pre-existing cardiac insufficiency, introduce levothyroxine at 50% of the target replacement dose and increase after 2 weeks based on free T4 levels.

Drug Interactions	Ketamine – Concurrent use may result in marked hypertension and tachycardia. Glucocorticoids – can decrease serum thyroglobulin concentration, affect deiodinase activity, decrease TSH secretion. Ferrous sulphate, calcium carbonate, PPIs, H_2 blockers and bile acid sequestrants can affect levothyroxine absorption. Phenytoin, phenobarbital, carbamazepine – can affect thyroid hormone metabolism therefore increasing levothyroxine requirements. Dopamine, dobutamine, growth hormone – can decrease TSH secretion Radioiodine contrast agents and topical iodine application: may lead to transient hypothyroidism associated with low free T4, low free T3 and variable TSH (the Wolff–Chaikoff effect).[3-5]
Adverse Reactions	Uncommon. Too high a replacement dose can cause manifestations of thyrotoxicosis. Overtreatment with levothyroxine may cause craniosynostosis, accelerated growth and maturation, disturbed sleep patterns and effects on temperament. There can also be behavioural problems (social withdrawal, hyperactivity, conduct problems and anxiety) in children treated with initial starting doses of levothyroxine >10 microgram/kg/day. Overtreatment should be avoided by careful monitoring. [2]
Compatibility	Not applicable.
Incompatibility	Not applicable.
Stability	Tablets: discard unused portion.
Storage	Eutroxsig and Oroxine tablets: Store at 2–8°C. Tablets may be stored below 25°C for up to 14 days. Please refer to special comments section for further details. Protect from light. Eltroxin tablets: Store below 25°C. Protect from light.
Special Comments	Milk, calcium, iron, multivitamin supplements – may influence the absorption of levothyroxine. For many years, two levothyroxine preparations have been marketed in Australia, Oroxine and Eutroxsig (both marketed by Aspen Pharmaceuticals), available in 50, 75, 100 and 200 microgram tablets. These preparations are identical, and so it has been immaterial which is dispensed to patients, and brand switching has not been problematic. A new preparation, Eltroxin (also marketed by Aspen) is now available which features a wider range of tablet strengths (25, 50, 75, 100, 125, and 200 microgram) and (unlike Oroxine/Eutroxsig) does not require refrigeration. This may allow more accurate daily dosing for patients and may be more convenient.[6] However, Eltroxin is not bioequivalent on a same dose basis with Eutroxsig/ Oroxine. If a decision is made to switch a patient from Eutroxsig/ Oroxine to Eltroxin, then prescribers should have a plan for monitoring TSH. Prescribers should be aware that dose adjustment may be required. Prescribers should tell their patients not to interchange Eltroxin and Eutroxsig/ Oroxine unless a decision has been made to switch products and there is a plan for monitoring TSH levels and review of dose. [1, 2, 6]
Evidence summary	Refer to full version.
References	Refer to full version.

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