Levothyroxine (Thyroxine) – Intravenous

Newborn use only

2019

Alert	No registered intravenous product is available in Australia. L-Thyroxine-Serb© and L-Thyroxine Henning can be sourced as SAS products.[1] IV replacement – should be commenced at 50–80% of oral dose.[4] Intravenous levothyroxine is to be prescribed only after consultation with Endocrinologist and/or clinician experienced in its use.
Indication	Intravenous replacement therapy for hypothyroidism in whom oral levothyroxine is not possible, e.g. bowel resection or necrotising enterocolitis. Oral absorption of thyroxine occurs in jejuno-ileal area.[2,3]
Action	Levothyroxine (thyroxine) exerts effects on most organ systems and is particularly important in the development of the central nervous system. It increases the metabolic rate of body tissues and is also involved in the regulation of cell growth and differentiation.
Drug Type	Principal hormone of thyroid gland.
Trade Name	L-Thyroxine-Serb©, L-Thyroxine Henning©
Presentation	L-Thyroxine-Serb© 0.2 mg/mL Injection. Contains L-thyroxine sodium. L-Thyroxine Henning© 500 microgram Injection (pack of 1). Each pack includes a 5 mL vial of solvent for reconstitution.
Dosage/Interval	**IV**: 8 (6–12) microgram/kg/dose DAILY. **NOTE:** IV dosing should be commenced at 50–80% of oral dose.[4] Adjusted as per TSH and free T4 concentrations.
Route	IV
Maximum Daily Dose	
Preparation/Dilution	L-Thyroxine-Serb© 0.2 mg/mL Injection: Draw up 1 mL (0.2 mg) of levothyroxine (thyroxine) and add to 9 mL of sodium chloride 0.9% to make a volume of 10 mL with a concentration of 20 microgram/mL. Once prepared, use immediately. L-Thyroxine Henning© 500 microgram Injection: Add 5 mL of water for injection provided to the 500 microgram vial to make a 100 microgram/mL solution. Draw up 1 mL (100 microgram) of levothyroxine (thyroxine) solution and add 4 mL of sodium chloride 0.9% to make a final volume of 5 mL with a final concentration of 20 microgram/mL. Once prepared, use immediately.
Administration	Slow IV bolus over 2–3 minutes.
Monitoring	Close monitoring of TSH and free T4 as per the Endocrine team. Refer to ORAL thyroxine formulary for guidance on initiation and subsequent monitoring.
Contraindications	Known hypersensitivity to levothyroxine (thyroxine). Untreated hyperthyroidism Decompensated heart disease
Precautions	In pre-existing cardiac insufficiency or arrhythmias, may introduce levothyroxine (thyroxine) at 50% of the target replacement dose and increase after 2 weeks based on T4 levels.
Drug Interactions	Concurrent use of levothyroxine (thyroxine) and proton pump inhibitors (omeprazole, pantoprazole) may result in decreased levothyroxine (thyroxine) effectiveness.[3]
Adverse Reactions	Uncommon. Too high replacement therapy can cause manifestations of thyrotoxicosis.
Compatibility	Fluid: Sodium chloride 0.9%[1,3,7] Y-site: No information.
Incompatibility	No information.
Stability	L-Thyroxine-Serb© 0.2 mg/mL Injection: No stability data.[1] L-Thyroxine Henning injection: Diluted solution is stable for 2 hours at room temperature[7]
Storage	L-Thyroxine-Serb© 0.2 mg/mL Injection: No special storage requirements applicable.[1] L-Thyroxine 500 microgram injection: Store in a refrigerator (2–8°C). Protect from light.
Special Comments	
Evidence summary	**Efficacy** 2014 European Society for Paediatric Endocrinology Consensus Guidelines on Screening, Diagnosis, and Management of Congenital Hypothyroidism: Absorption of oral levothyroxine mainly occurs in the jejunoileal area. Bioavailability of oral dose is 50–80%. Intravenous levothyroxine is considered at a dose no more than 50–80% of oral dose.[4]

	Intravenous thyroxine preparations were not used in clinical trials using thyroxine in newborn infants with congenital hypothyroidism. See oral thyroxine ANMF entry for additional information on thyroxine. The following RCTs used higher doses so cannot be used to inform dosing in newborns. **Prophylactic intravenous thyroxine in preterm infants:** A single RCT[5] in 40 newborns with gestational age <31 weeks compared infants given a daily dose of 20 microgram/kg L-T4 for 2 weeks versus control (saline). L-T4 administration induced a marked increase in serum T4 without apparent change in T3 levels. During L-T4 treatment, serum T4 levels rose to 131.3 (96.5–184.0) versus 56.6 (48.9–99.1) nmol/L in controls on day 7 (p <0.001), and to 140.3 (124.8–166.0) versus 75.3 (59.2–95.2) nmol/L, respectively, on day 14 (p <0.001). No clinical effects of L-T4 administration were detected. **Intravenous thyroxine in preterm infants with respiratory distress syndrome:** A single RCT[6] in 36 infants <34 weeks of gestation with respiratory distress syndrome (IRDS) compared intravenous thyroxine 2 x 50 microgram intravenous injections versus control. After treatment, serum T4 levels were similar to those of healthy term infants. No statistically significant effect on mortality rate, duration of mechanical ventilation, need of high oxygen environment and bronchopulmonary dysplasia was observed. **Stability after dilution**: A stability study[8] was conducted by diluting levothyroxine sodium 500 microgram vials to 0.4 microgram/mL and 2 microgram/mL using sodium chloride 0.9% and stored at room temperature. For the 0.4 microgram/mL concentration, the solutions were stable for 16.9 hours when exposed to light and 18 hours when stored in the dark. The 2 microgram/mL solution was stable for 6.5 hours and 12 hours respectively. L-Thyroxin Henning ® Injection Product Information states that the diluted solution is stable for 2 hours at room temperature[7].
References	1. L-Thyroxine-Serb© 0.2 mg/mL Injection product information obtained from Medsurge. Accessed on 14/06/2018 2. Liwanpo L, Hershman JM. Conditions and drugs interfering with thyroxine absorption. Best Practice and Research: Clinical Endocrinology and Metabolism 2009;23:781–792. 3. Micromedex. Levothyroxine. Accessed on 2 February 2019. 4. Léger J, Olivieri A, Donaldson M, et al. European Society for Paediatric Endocrinology consensus guidelines on screening, diagnosis, and management of congenital hypothyroidism. Hormone research in paediatrics. 2014;81(2):80-103. 5. Vanhole C, Aerssens P, Naulaers G, et al. L-thyroxine treatment of preterm newborns: clinical and endocrine effects. Pediatr Res. 1997;42:87-92. 6. Amato M, Pasquier S, Carasso A, et al. Postnatal thyroxine administration for idiopathic respiratory distress syndrome in preterm infants. Horm Res. 1988;29:27-30. 7. L-Thyroxin Henning ® Injection – Product Information obtained from Medsurge. Accessed on 14/06/2018 8. Strong DK. Stability of Levothyroxine in Sodium Chloride for IV Administration. Can J Hosp Pharm. 2010 Nov-Dec; 63(6): 437–443.

Original version Date: 28/03/2019	**Author: Australasian Neonatal Medicines Formulary Group**
Current Version number: 1.0	**Version Date: 28/03/2019**
Risk Rating: Medium	**Due for Review: 28/03/2022**
Approval by:	**Approval Date:**

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