1.3.1.1. PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

ELTROXIN NEW FORMULATION 25 µg

50 µg/75 µg/88 µg/100 µg/112 µg/125 µg/137 µg/150 µg/175 µg/200 µg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of ELTROXIN NEW FORMULATION contains 25 µg, 50 µg, 75 µg, 88 µg, 100 µg, 112 µg, 125 µg, 137 µg, 150 µg, 175 µg, or 200 µg of levothyroxine sodium.

Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

ELTROXIN NEW FORMULATION 25 µg tablets are round, white to off-white tablets debossed with ‘25’ on the one side and a breakline on the other side.

For ELTROXIN NEW FORMULATION 25 µg tablets the break line facilitates breaking to ensure uniform 12,5 µg dosing.

ELTROXIN NEW FORMULATION 50 µg tablets are round, white to off-white flat, bevelled tablets debossed with ‘50’ on the one side and ‘L01’ on the other side.

ELTROXIN NEW FORMULATION 75 µg tablets are round, white to off-white flat, bevelled tablets debossed with ‘75’ on the one side and ‘L02’ on the other side.

ELTROXIN NEW FORMULATION 88 µg tablets are round, white to off-white flat, bevelled tablets debossed with ‘88’ on the one side and ‘L07’ on the other side.

ELTROXIN NEW FORMULATION 100 µg tablets are round, white to off-white, flat, bevelled tablets debossed with ‘100’ on the one side and ‘L10’ on the other side.

ELTROXIN NEW FORMULATION 112 µg tablets are round, white to off-white, flat, bevelled tablets debossed with ‘112’ on the one side and ‘L11’ on the other side.

ELTROXIN NEW FORMULATION 125 µg tablets are round, white to off-white, flat, bevelled tablets debossed with ‘125’ on the one side and ‘L12’ on the other side.

ELTROXIN NEW FORMULATION 137 µg tablets are round, white to off-white, flat, bevelled tablets debossed with ‘137’ on the one side and ‘L15’ on the other side.

ELTROXIN NEW FORMULATION 150 µg tablets are round, white to off-white flat, bevelled tablets debossed with ‘150’ on the one side and ‘L17’ on the other side.

ELTROXIN NEW FORMULATION 175 µg tablets are round, white to off-white, flat, bevelled tablets debossed with ‘175’ on the one side and ‘L20’ on the other side.

ELTROXIN NEW FORMULATION 200 µg tablets are round, white to off-white, flat, bevelled tablets debossed with ‘200’ on the one side and ‘L21’ on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ELTROXIN NEW FORMULATION is indicated in adults, adolescents and children for untreated hypothyroidism.

4.2 Posology and method of administration

Posology

If the dose of ELTROXIN NEW FORMULATION is increased too rapidly, symptoms such as diarrhoea, nervousness, rapid pulse, insomnia, tremors and sometimes anginal pain where there is latent myocardial ischaemia may occur and the dosage must be reduced or withheld for a day or two, then restarted at a lower level.

Levothyroxine tablets should preferably be taken on an empty stomach in the morning at least half an hour before breakfast. The tablets are swallowed whole, without chewing, with some liquid.

For ELTROXIN NEW FORMULATION 25 µg tablets the break line facilitates breaking to ensure uniform 12,5 µg dosing (see section 3).

Missed dosage

If a scheduled daily dose is missed, the dose should be taken as soon as the patient remembers, unless it is almost time for the patient's next dose. Two doses should not be taken together.

Interactions

In patients whose medications include levothyroxine as in ELTROXIN NEW FORMULATION, and known interfering medicines, administration should be separated by at least 4 hours (see section 4.5).

The dose of ELTROXIN NEW FORMULATION for the treatment of any thyroid disorder

should be individualized on the basis of clinical response and biochemical tests and should be monitored regularly.

Adults

Initially 50 micrograms to 100 micrograms daily, preferably taken at least half an hour before breakfast or the first meal of the day. Adjust at four to six week intervals by 50 micrograms until normal metabolism is steadily maintained. The final daily dose may be up to 100 micrograms to 200 micrograms.

Special populations

Elderly population

Patients over 50 years

For patients over 50 years, initially, it is not advisable to exceed 50 micrograms daily. In this condition, the daily dose may be increased by 50 micrograms at intervals of every 3 to 4 weeks, until stable levothyroxine levels are attained. The final daily dose may be up to 50 micrograms to 200 micrograms.

Patients over 50 years with cardiac disease

Where there is cardiac disease, 25 micrograms daily or 50 micrograms on alternate days is more suitable. In this conditions, the daily dose may be increased by 25 micrograms at intervals of every 4 weeks, until stable levothyroxine levels are attained. The final daily dose may be up to 50 micrograms to 200 micrograms.

For patients aged over 50 years, with or without cardiac disease, clinical response is probably a more acceptable criteria of dosage rather that serum levels.

Paediatric population

Congenital hypothyroidism in children

In congenital hypothyroidism and juvenile myxoedema, the largest dose consistent with freedom from toxic effects should be given. The dosage is guided by clinical response, growth assessment and appropriate thyroid function tests - clinically normal pulse rate and absence of diarrhoea or constipation are the most useful indicators. Thyrotrophin levels may remain elevated during the first year of life in children with neonatal hypothyroidism due to resetting of the hypothalamic-pituitary axis.

The maintenance dose is generally 100 micrograms to 150 micrograms per m² body surface area. The dose for children depends on their age, weight and the condition being treated. Regular monitoring is required to make sure he/she gets the right dose. Infants should be given the total daily dose at least half an hour before the first meal of the day.

Congenital hypothyroidism in infants

For neonates and infants with congenital hypothyroidism a suitable starting dose is 10 to 15 micrograms levothyroxine sodium per kg body weight daily for the first three months. Thereafter the dose should be adjusted individually according to the clinical findings and thyroid hormone and TSH values. The calculated daily dose equivalent should be rounded to the nearest 25 micrograms to determine the actual prescribed dose.

Acquired hypothyroidism in children

For children with acquired hypothyroidism, the initial recommended dosage is 12,5 micrograms to 50 micrograms per day. The dose should be increased gradually every 2 to 4 weeks according to the clinical findings and thyroid hormone and TSH values until the full replacement dose is reached.

Juvenile myxoedema in children

The initial recommended dosage is 25 micrograms daily. In such conditions, the daily dose

may be increased by 25 micrograms at intervals of every 2 to 4 weeks, until mild symptoms of hyperthyroidism is seen. The dose will then be reduced slightly. The starting dose for children older than one year may be 2,5 to 5 micrograms/kg/day. The calculated daily dose equivalent should be rounded to the nearest 25 micrograms to determine the actual prescribed dose.

When applicable

Tablets are to be disintegrated in some water (10 ml to 15 ml) and the resultant suspension, which must be prepared freshly as required, is to be administered with some more liquid (5 ml to 10 ml).

Method of administration

For oral administration.

4.3 Contraindications

ELTROXIN NEW FORMULATION is contraindicated in:

- Patients with hypersensitivity to levothyroxine sodium or to any of the excipients in ELTROXIN NEW FORMULATION (see section 6.1).
- Patients with untreated hyperthyroidism.
- Thyrotoxicosis.
- Untreated adrenal insufficiency.
- Untreated pituitary insufficiency.
- Acute myocardial infarction, acute myocarditis, and acute pancarditis.

4.4 Special warnings and precautions for use

At the beginning of treatment, ordinary therapeutic doses may cause anginal pain, palpitations and cramps in the skeletal muscle.

Before starting therapy with ELTROXIN NEW FORMULATION the following diseases should be excluded or treated: coronary insufficiency, angina pectoris, arteriosclerosis, hypertension, pituitary insufficiency, adrenal insufficiency, thyroid autonomy.

Even slight medicine-induced hyperthyroidism must be avoided in patients with coronary failure, cardiac insufficiency or tachycardiac dysrhythmias.

Hence frequent checks of thyroid hormone parameters must be made in these cases.

In the case of secondary hypothyroidism the cause must be determined before replacement therapy is given and if necessary replacement treatment of a compensated adrenal insufficiency must be commenced.

Where thyroid autonomy is suspected, a TRH test should be carried out or a suppression scintigram obtained before treatment. In postmenopausal women with hypothyroidism and an increased risk of osteoporosis, supraphysiological serum levels of ELTROXIN NEW FORMULATION should be avoided, and, therefore, thyroid function should be checked regularly.

Thyroid storm (or thyrotoxic crisis) is a medical emergency and has been occasionally reported after massive or chronic intoxication. Convulsions, cardiac dysrhythmias, heart failure, coma and death have occurred (see section 4.9).

Laboratory monitoring

ELTROXIN NEW FORMULATION has a narrow therapeutic index. Appropriate ELTROXIN NEW FORMULATION dosage is based upon clinical assessment and laboratory monitoring of thyroid function tests. During the initial titration period, careful dosage titration and

monitoring is necessary to avoid the consequences of under- or over-treatment. The symptoms of excessive ELTROXIN NEW FORMULATION dosage are the same as many features of endogenous thyrotoxicosis.

Parents of children receiving ELTROXIN NEW FORMULATION should be advised that partial loss of hair may occur during the first few months of therapy, but this effect is usually transient and subsequent regrowth may occur.

Special populations

Panhypopituitarism

Treatment with ELTROXIN NEW FORMULATION in patients with panhypopituitarism or other causes predisposing to adrenal insufficiency may cause reactions including dizziness, weakness, malaise, weight loss, hypotension and adrenal crisis. It is advisable to initiate corticosteroid therapy before giving in these cases.

Effect on bone mineral density

Subclinical hyperthyroidism may be associated with bone loss. To minimise the risk of osteoporosis, dosage of ELTROXIN NEW FORMULATION should be titrated to the lowest possible effective level.

In women, long-term levothyroxine therapy has been associated with increased bone resorption, thereby decreasing bone mineral density, especially in post-menopausal women on greater than replacement doses or in women who are receiving suppressive doses of levothyroxine sodium. The increased bone resorption may be associated with increased serum levels and urinary excretion of calcium and phosphorus, elevation in bone alkaline phosphate and suppressed serum parathyroid hormone levels. When administering levothyroxine therapy to postmenopausal women, who are at increased risk of osteoporosis, thyroid function should be monitored more frequently to avoid supraphysiological elderly

blood levels of levothyroxine and the dosage of levothyroxine should be titrated to the lowest possible level necessary to achieve the desired clinical and biochemical response.

Elderly patients

The initial dose and any dose increments (see section 4.2) should be carefully chosen in elderly and in patients with cardiac symptoms, diabetes mellitus or insipidus: too high initial dose or too rapid increase may cause or aggravate symptoms of angina, dysrhythmias, myocardial infarction, cardiac failure or a sudden raise in blood pressure.

Weight loss medicine

Orlistat may decrease ELTROXIN NEW FORMULATION absorption which may result in hypothyroidism. To avoid this orlistat and ELTROXIN NEW FORMULATION should be administered at least 4 hours apart. Regular monitoring for changes in thyroid function is required (see section 4.5).

Myxoedema

Patients with myxoedema have an increased sensitivity for thyroid hormones; in these patients the starting dose should be low with slow dosing increments.

In individuals suspected to have cardiovascular disease or to be at high risk, it is important to perform an ECG prior to commencement of levothyroxine treatment in order to detect changes consistent with ischaemia in which case, levothyroxine should be initiated at a low dose, followed by cautious dose escalation to avoid worsening of ischaemia or precipitation of an infarct.

Malabsorption syndromes

ELTROXIN NEW FORMULATION absorption is decreased in patients with malabsorption syndromes. It is advised to treat the malabsorption condition to ensure effective ELTROXIN

NEW FORMULATION treatment with regular ELTROXIN NEW FORMULATION dose.

Use in Pregnancy (Category A):

If overt hypothyroidism is diagnosed during pregnancy, thyroid function test results should be normalised as rapidly as possible. In newly-diagnosed hypothyroidism in pregnancy, thyroxine dosage should be titrated rapidly, for example 1,5 to 2,0 µg/kg/day may be required for initial replacement. If hypothyroidism has been diagnosed before pregnancy, thyroxine therapy should be optimised before conception and monitored during pregnancy by measurement of serum TSH and thyroxine levels. The thyroxine dose commonly needs incremental adjustments by 4 to 6 weeks of gestation and may require a 25 to 40 % increase in dosage. It is recommended that those levels should be re-evaluated every 3 to 4 weeks during the first and second trimesters, with thyroxine dosage changes as appropriate. The requirement is likely to decrease post-partum.

Monitoring of TSH concentrations can give guidance. TBG (Thyroid-Binding Globulin) increases during pregnancy and therefore total T4 and T3 may appear to be elevated. Measurement of free T4 and T3 may be more appropriate. There is contradictory evidence concerning the passage of T4 and T3 across the placenta but it is unlikely that the foetus is at risk. Clinical experience does not indicate any adverse effects on the foetus when thyroxine is administered during pregnancy (see section 4.6).

TSH monitoring during pregnancy

During pregnancy, serum levothyroxine levels may decrease with a concomitant increase in serum TSH level to values outside the normal range. Patients taking ELTROXIN NEW FORMULATION should have their TSH measured during each trimester. An elevated serum TSH level should be corrected by an increase in the dose of ELTROXIN NEW FORMULATION. Since postpartum TSH serum levels are similar to preconception values, ELTROXIN NEW FORMULATION dosage can be reduced to the pre-pregnancy dose (see section 4.6)

Diabetes

Thyroid replacement therapy may cause an increase in dosage requirements of insulin or other anti-diabetic therapy (such as metformin). Careful monitoring is needed for patients with diabetes mellitus, and diabetes insipidus (see section 4.5).

Paediatric population

It is especially important that children with hypothyroidism have their dosage individualised and treatment monitored.

4.5 Interaction with other medicines and other forms of interaction

Anticoagulants

ELTROXIN NEW FORMULATION can increase the effect of anticoagulants e.g.warfarin. With concomitant treatment, regular monitoring of the INR is therefore required and the dose of anticoagulants must be adjusted as necessary (dose reduction).

Diabetes

Thyroid replacement therapy may cause an increase in dosage requirements of insulin or other anti-diabetic therapy (such as metformin). Careful monitoring is needed for patients with diabetes mellitus, and diabetes insipidus (see section 4.4).

Anti-depressants

Tricyclic anti-depressants (e.g. amitriptyline, imipramine, dosulepin) response may be accelerated because levothyroxine increases sensitivity to catecholamines; thus accelerating the response to tricyclic antidepressants. Concomitant use may precipitate cardiac dysrhythmias. The effects of sympathomimetic medicines (e.g. adrenaline of phenylephrine) are also enhanced.

Phenytoin and carbamazepine

Phenytoin levels may be increased by ELTROXIN NEW FORMULATION. Anticonvulsants such as carbamazepine and phenytoin enhance the metabolism of ELTROXIN NEW FORMULATION and may displace levothyroxine from plasma proteins. Initiation or discontinuation of anticonvulsant therapy may alter levothyroxine sodium dose requirements.

Digoxin

If co-administered with digoxin, adjustment of dosage of may be necessary.

Sympathomimetic medicines (adrenalin/ phenylephrine)

The effects of sympathomimetic medicines are also enhanced. ELTROXIN NEW FORMULATION increases receptor sensitivity to catecholamines thus accelerating the response to tricyclic antidepressants (e.g. amitriptyline, imipramine).

Interactions decreasing thyroxine absorption

Absorption of levothyroxine (thyroxine) is possibly reduced by antacids, proton pump inhibitors, calcium salts, cimetidine, oral iron, sucralfate, polystyrene sulphonate, magnesium, lanthanum, bile acid sequestrants (e.g. colestipol), resin and colestyramine (administration should be separated by 4 to 5 hours).

Oestrogen medicines

Co-administration of oral contraceptives, as well as a number of other medicines, including oestrogen, tamoxifen, clofibrate, methadone, and 5-fluorouracil may increase serum concentration of levothyroxine-binding globulin, and therefore increase ELTROXIN NEW FORMULATION dosage requirements.

Laboratory test interactions

A number of medicines may decrease serum concentration of levothyroxine-binding globulin, and therefore decrease ELTROXIN NEW FORMULATION dosage requirements, including androgens and anabolic steroids.

False low plasma concentrations of T4 and T3 have been observed with concurrent anti-inflammatory treatment such as diclofenac, acetylsalicylic acid and ELTROXIN NEW FORMULATION therapy. Administration of acetylsalicylic acid together with ELTROXIN NEW FORMULATION results in an initial transient increase in serum free T4. Continued administration results in normal free T4 and TSH concentrations, and therefore, patients become clinically euthyroid.

Imatinib and sunitinib

Treatment with imatinib and sunitinib was associated with increased ELTROXIN NEW FORMULATION dosage requirements in hypothyroid patients.

Thyroid function tests

A number of medicines may affect thyroid function tests and this should be borne in mind when monitoring a patient on ELTROXIN NEW FORMULATION therapy.

Antibacterials

Enzyme induction by rifampicin enhances thyroid hormone metabolism resulting in reduced serum concentrations of thyroid hormones. Oral ciprofloxacin can lead to the development of hypothyroidism in stable patients receiving ELTROXIN NEW FORMULATION.

Interactions affecting other medicines

Antidepressants

Some medicines such as lithium act directly on the thyroid gland and inhibit the release of thyroid hormones leading to clinical hypothyroidism.

Sertraline

The concurrent use of sertraline can reduce serum levels of ELTROXIN NEW FORMULATION (with concomitant increased TSH levels).

Antivirals

An increased dose of ELTROXIN NEW FORMULATION is necessary with ritonavir whereas a decreased dose is needed with indinavir.

Beta-blockers

Plasma concentrations of propranolol are reduced in hyperthyroidism compared with the euthyroid state, probably due to increased clearance and hypothyroid patients receiving chronic propranolol therapy have a reduction in plasma-propranolol concentrations when given ELTROXIN NEW FORMULATION treatment.

Antimalarials

Increased thyroid-stimulating hormone concentration can occur after the use of chloroquine with proguanil for malaria prophylaxis.

NSAIDs

Falsely low concentrations of levothyroxine (T4) or tri-iodothyronine (T3) can occur during treatment with some anti-inflammatory medicines. Serum TSH measurements are less affected by NSAIDs and therefore TSH would be the optimal screening test in patients receiving an NSAID.

Soya-based infant formula

Soya-based infant formulas may impair absorption of ELTROXIN NEW FORMULATION, and frequent testing may be needed, particularly when there are changes in formula. Soy-containing compounds and high-fibre diets can decrease the intestinal absorption of ELTROXIN NEW FORMULATION. Therefore, a dosage adjustment of thyroxine may be

necessary, in particular at the beginning or after termination of nutrition with soy supplements.

Simvastatin and lovastatin

Increased thyroid stimulating hormone concentrations, requiring increased doses of ELTROXIN NEW FORMULATION, can occur when simvastatin is used. It is unknown if this occurs with all statins. Close monitoring of thyroid function and appropriate ELTROXIN NEW FORMULATION dose adjustments may be necessary when ELTROXIN NEW FORMULATION and statins are co-prescribed.

Furosemide

Furosemide in high doses (250 mg) can displace levothyroxine sodium as contained in ELTROXIN NEW FORMULATION from plasma proteins, resulting in an elevated free-thyroxine (T4) fraction.

Medicines that (partially) inhibit the peripheral transformation of T4 to T3:

Propranolol, amiodarone, lithium, iodide, oral contrast agents, propylthiouracil and glucocorticoids - lower the T3 level and therefore also the therapeutic effect.

General anaesthetics

Isolated reports of marked hypertension and tachycardia have been reported with concurrent ketamine administration.

Cardiac glycosides

If co-administered with cardiac glycosides, adjustment of dosage of cardiac glycoside may be necessary.

Ritonavir

Post-marketing cases have been reported indicating a potential interaction between ritonavir containing medicines and levothyroxine. Thyroid-stimulating hormone (TSH) should be monitored in patients treated with levothyroxine at least the first month after starting and/or ending ritonavir treatment.

Interactions affecting levothyroxine

The metabolism of levothyroxine as in ELTROXIN NEW FORMULATION can be accelerated by enzyme inducing products (e.g.: rifampicin, barbituarates, primidone and oestrogens) (may increase requirements for levothyroxine (thyroxine) in hypothyroidism).

4.6 Fertility, pregnancy and lactation

Pregnancy

ELTROXIN NEW FORMULATION has been taken by pregnant women and women of childbearing age without any form of definite disturbances in the reproductive process having been observed. Thyroid hypo- or hyperactivity in the mother may, however, unfavourably influence the foetal and postnatal development, therefore ELTROXIN NEW FORMULATION dosage may need to be adjusted during pregnancy (see section 4.4).

Lactation

ELTROXIN NEW FORMULATION is excreted in breast milk and this may be sufficient to interfere with neonatal screening for hypothyroidism. It is very important to monitor thyroid function in the mother as well as in the infant regularly.

4.7 Effects on ability to drive and use machines

ELTROXIN NEW FORMULATION has negligible influence on ability to drive and use machines.

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that ELTROXIN NEW FORMULATION do not adversely affect their ability to do so safely (see section 4.4 and/or 4.8).

4.8 Undesirable effects

a) Tabulated list of adverse reactions

The following effects are indicative of excessive dosage, and usually disappear on reduction of dosage or withdrawal of treatment for a few days.

The frequency classification for these adverse reactions is not known due to a lack of robust clinical trial data to accurately determine frequency estimate.

System organ class	**Frequency unknown** (cannot be estimated from the available data)
Immune system disorders	Hypersensitivity reactions, rash, pruritus, anaphylactic reactions
Endocrine disorders	Hyperthyroidism
Metabolism and nutrition disorders	Increased appetite, loss of weight
Psychiatric disorders	Excitability, restlessness, insomnia, confusion, agitation, anxiety, affect emotional lability, nervousness
Nervous system disorders	Headache, tremors, seizure, cases of benign intracranial hypertension
Cardiac disorders	Angina pectoris, cardiac dysrhythmias, palpitations, tachycardia, cardiac failure, myocardial infarction
Vascular disorders	Increased blood pressure, flushing

Respiratory, thoracic and mediastinal disorders	Dyspnoea
Gastrointestinal disorders	Abdominal pain, nausea, vomiting, diarrhoea
Skin and subcutaneous tissue disorders	Hyperhidrosis, hair loss, rash, pruritus, angioedema, urticaria
Musculoskeletal and connective tissue disorders	Muscle spasms, muscular weakness, arthralgia
Reproductive system and breast disorders	Irregular menstruation, infertility
Congenital and familial and genetic disorders	Excessive dose may result in craniosynostosis in infants, and epiphyses premature fusion in children with compromised adult height[2]
General disorders and administrative site conditions	Fatigue, temperature intolerance, pyrexia, malaise, oedema
Investigations	Decreased bone mineral density

b) Paediatric population

[2]Heat intolerance, transient hair loss, benign intracranial hypertension, craniostenosis in infants and premature closure of epiphysis in children.

Cases of benign intracranial hypertension have been reported, especially in children.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to:

SAHPRA: https://www.sahpra.org.za/health-products-vigilance/

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088/ +27 (0)11 239-6200

4.9 Overdose

Symptoms

In addition to exaggeration of side effects, the following symptoms may be seen: agitation, confusion, irritability, hyperactivity, headache, sweating, mydriasis, tachycardia, dysrhythmias, tachypnoea, pyrexia, increased bowel movements and convulsions. The appearance of clinical hyperthyroidism may be delayed for up to five days. Thyrotoxic crisis has been occasionally reported following massive or chronic intoxication, leading to cardiac dysrhythmias, heart failure and coma.

In addition to all known side effects, thyroid storm (or thyrotoxic crisis) a medical emergency, may occur and require urgent medical attention as soon as possible. Some of the signs of thyrotoxicosis that have been reported include fever, dysrhythmias, tachycardia, increased blood pressure, confusion, agitation, neurological complications and coma.

The appearance of clinical hyperthyroidism may be delayed for up to five days. Thyrotoxic crisis has been occasionally reported following massive or chronic intoxication, leading to cardiac dysrhythmias, heart failure and coma.

Treatment

The goal of therapy is restoration of clinical and biochemical euthyroid state by omitting or reducing the ELTROXIN NEW FORMULATION dosage and other measures as needed

depending on clinical status.

Treatment is symptomatic and tachycardia has been controlled in an adults by 40 mg doses of propranolol given every six hours and other symptoms by diazepam and/or chlorpromazine as appropriate.

Further management should be as clinically indicated or as recommended by the national poison centre, where available.

Give oral activated charcoal if more than 10 mg has been ingested by an adult or more than 5 mg by a child, within 1 hour. If more than 10 mg has been ingested by an adult or more than 5 mg by a child, take blood 6 to 12 hours after ingestion for measurement of the free thyroxine concentration. Patients with normal free thyroxine concentrations do not require follow up. Those with high concentrations should have outpatient review 3 to 6 days after ingestion to detect delayed onset hyperthyroidism. Features of clinical hyperthyroidism should be controlled with beta-blockers, e.g. propranolol.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 21.3 Thyroid preparations

Pharmacological group: Thyroid hormones

ATC: H03AA01

Mechanism of action

Thyroxine (T4) is a naturally occurring hormone produced by the thyroid gland and converted to the more active hormone tri-iodothyronine (T3) in peripheral tissues. The precise signals controlling the conversion of T4 to T3 within the cell are not known. The thyroid hormones are required for normal growth and development, particularly of the nervous system. They increase the resting or basal metabolic rate of the whole organism and have stimulatory effects on the heart, skeletal muscle, liver and kidney. Thyroid hormones enhance lipolysis and the utilisation of carbohydrate. 100 µg levothyroxine is

equivalent in activity to 20 µg to 30 µg liothyronine/tri-iodothyronine or 60 mg thyroid BP.

ELTROXIN NEW FORMULATION is a tablet containing the hydrated form of levothyroxine sodium which is used for the treatment of hypothyroidism. The main action of levothyroxine is to increase the rate of cell metabolism. Levothyroxine is deiodinated in peripheral tissues to form Tri-iodothyronine which is thought to be the active tissue form of thyroid hormone. Tri-iodothyronine is certainly more rapid acting and has a shorter duration of action than levothyroxine.

5.2 Pharmacokinetic properties

Absorption

Following oral administration the absorption of levothyroxine is incomplete and variable especially when taken with food. The amount absorbed increases during fasting conditions.

Distribution

Levothyroxine is nearly totally bound to serum protein.

Metabolism

The main pathway for the metabolism of levothyroxine (T4) is its conversion, by de-iodination, to the active metabolite tri-iodothyronine (T3). Further de-iodination of T4 and T3 leads to production of inactive products.

Elimination

Levothyroxine is eliminated slowly from the body with a half-life of approximately seven days in a normal person. This may be reduced in hyperthyroid states or increased in hypothyroid patients.

In man approximately 20 % to 40 % of levothyroxine is eliminated in the faeces and approximately 30 % to 55 % of a dose of levothyroxine is excreted in the urine.

Special populations

Renal impairment

Renal disease does not appear to have any significant effect on the disposition of levothyroxine.

Hepatic impairment

Hepatic disease does not appear to have any significant effect on the disposition of levothyroxine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silica dioxide, magnesium stearate, microcrystalline cellulose, pregelatinised maize starch, talc.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C

Protect from light.

Keep in original packaging until required for use.

Keep container tightly closed.

6.5 Nature and contents of container

The tablets are packed in 40 ml white multilayer HDPE bottles, closed with white polypropylene child-resistant caps with foil heat induction seals, and with a 1 g white polypropylene canister containing oxygen absorber. The tablets are packed in pack sizes of 30's, 50's and 100's.

Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal

No special requirements.

7.HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

ELTROXIN NEW FORMULATION 25 µg:	47/21.3/0614
ELTROXIN NEW FORMULATION 50 µg:	47/21.3/0615
ELTROXIN NEW FORMULATION 75 µg:	47/21.3/0616
ELTROXIN NEW FORMULATION 88 µg:	47/21.3/0617
ELTROXIN NEW FORMULATION 100 µg:	47/21.3/0618
ELTROXIN NEW FORMULATION 112 µg:	47/21.3/0619
ELTROXIN NEW FORMULATION125 µg:	47/21.3/0620
ELTROXIN NEW FORMULATION 137 µg:	47/21.3/0621
ELTROXIN NEW FORMULATION 150 µg:	47/21.3/0622
ELTROXIN NEW FORMULATION 175 µg:	47/21.3/0623
ELTROXIN NEW FORMULATION 200 µg:	47/21.3/0624

9. DATE OF FIRST AUTHORISATION

30 September 2016

10. DATE OF REVISION OF TEXT

30 June 2022

Die Afrikaanse Professionele Inligting is op versoek beskikbaar. Mediese Blitslyn: 0800 118 088.

Namibia: NS2	
ELTROXIN NEW FORMULATION 25 µg:	16/21.3/0096
ELTROXIN NEW FORMULATION 50 µg:	16/21.3/0097
ELTROXIN NEW FORMULATION 75 µg:	16/21.3/0098
ELTROXIN NEW FORMULATION 88 µg:	16/21.3/0099
ELTROXIN NEW FORMULATION 100 µg:	16/21.3/0100
ELTROXIN NEW FORMULATION 112 µg:	16/21.3/0101
ELTROXIN NEW FORMULATION 125 µg:	16/21.3/0102
ELTROXIN NEW FORMULATION 137 µg:	16/21.3/0103
ELTROXIN NEW FORMULATION 150 µg:	16/21.3/0104
ELTROXIN NEW FORMULATION 175 µg:	16/21.3/0105
ELTROXIN NEW FORMULATION 200 µg:	16/21.3/0106

Zimbabwe: P.P.10	
ELTROXIN NEW FORMULATION 50 µg:	2017/17.8.1/5414
ELTROXIN NEW FORMULATION 100 µg:	2017/17.8.1/5413