

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Kauliv 20 micrograms/80 microliters solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 80 microliters contains 20 micrograms of teriparatide*.
Each cartridge of 3 mL of solution contains 750 micrograms of teriparatide (corresponding to 250 micrograms per mL).

*Teriparatide, rhPTH (1-34), produced in E. coli, using recombinant DNA technology, is identical to the 34-N-terminal amino acid sequence of endogenous human parathyroid hormone.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Colourless, clear solution for injection.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Kauliv is indicated in adults.

Treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture (see section 5.1). In postmenopausal women, a significant reduction in the incidence of vertebral and non-vertebral fractures but not hip fractures has been demonstrated.

Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk for fracture (see section 5.1).

4.2. Posology and method of administration

Posology

The recommended dose of Kauliv is 20 micrograms administered once daily.

Patients should receive supplemental calcium and vitamin D supplements if dietary intake is inadequate.

The maximum total duration of treatment with teriparatide should be 24 months (see section 4.4). The 24-month course of teriparatide should not be repeated over a patient's lifetime.

Following cessation of teriparatide therapy, patients may be continued on other osteoporosis therapies.

Special populations

Elderly

Dose adjustment based on age is not required (see section 5.2).

Renal impairment

Teriparatide must not be used in patients with severe renal impairment (see section 4.3). In patients with moderate renal impairment, teriparatide should be used with caution. No special caution is required for patients with mild renal impairment.

Hepatic impairment

No data are available in patients with impaired hepatic function (see section 5.3). Therefore, teriparatide should be used with caution.

Paediatric population and young adults with open epiphyses

The safety and efficacy of teriparatide in children and adolescents less than 18 years have not been established. Teriparatide should not be used in paediatric patients (less than 18 years), or young adults with open epiphyses.

Method of administration

Kauliv should be administered once daily by subcutaneous injection in the thigh or abdomen.

Patients must be trained to use the proper injection techniques (see section 6.6). For instructions of the medicinal product before administration (see section 6.6). Instructions for use which is included in the carton of the pen are also available to instruct patients on the correct use of the pen.

4.3. Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Pregnancy and breast-feeding (see sections 4.4 and 4.6).
- Pre-existing hypercalcaemia.
- Severe renal impairment.
- Metabolic bone diseases (including hyperparathyroidism and Paget's disease of the bone) other than primary osteoporosis or glucocorticoid-induced osteoporosis.
- Unexplained elevations of alkaline phosphatase.
- Prior external beam or implant radiation therapy to the skeleton.
- Patients with skeletal malignancies or bone metastases should be excluded from treatment with teriparatide.

4.4. Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered medicinal product should be clearly recorded.

Serum and urine calcium

In normocalcaemic patients, slight and transient elevations of serum calcium concentrations have been observed following teriparatide injection. Serum calcium concentrations reach a maximum between 4 and 6 hours and return to baseline by 16 to 24 hours after each dose of teriparatide. Therefore, if blood samples for serum calcium measurements are taken, this should be done at least 16 hours after the most recent teriparatide injection. Routine calcium monitoring during therapy is not required.

Teriparatide may cause small increases in urinary calcium excretion, but the incidence of hypercalciuria did not differ from that in the placebo-treated patients in clinical trials.

Urolithiasis

Teriparatide has not been studied in patients with active urolithiasis. Teriparatide should be used with caution in patients with active or recent urolithiasis because of the potential to exacerbate this condition.

Orthostatic hypotension

In short-term clinical

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free”.

4.5. Interaction with other medicinal products and other forms of interaction

In a study of 15 healthy subjects administered digoxin daily to steady state, a single teriparatide dose did not alter the cardiac effect of digoxin. However, sporadic case reports have suggested that hypercalcaemia may predispose patients to digitalis toxicity. Because teriparatide transiently increases serum calcium, teriparatide should be used with caution in patients taking digitalis.

Teriparatide has been evaluated in pharmacodynamic interaction studies with hydrochlorothiazide. No clinically significant interactions were noted.

Co-administration of raloxifene or hormone replacement therapy with teriparatide did not alter the effects of teriparatide on serum or urine calcium or on clinical adverse events.

4.6. Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in females

Women of childbearing potential should use effective methods of contraception during use of teriparatide. If pregnancy occurs, Kauliv should be discontinued.

Pregnancy

Kauliv is contraindicated for use during pregnancy (see section 4.3).

Breast-feeding

Kauliv is contraindicated for use during breast-feeding. It is not known whether teriparatide is excreted in human milk.

Fertility

Studies in rabbits have shown reproductive toxicity (see section 5.3). The effect of teriparatide on human foetal development has not been studied. The potential risk for humans is unknown.

4.7. Effects on ability to drive and use machines

Kauliv has no or negligible influence on the ability to drive and use machines. Transient, orthostatic hypotension or dizziness was observed in some patients. These patients should refrain from driving or the use of machines until symptoms have subsided.

4.8. Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions in patients treated with teriparatide are nausea, pain in limbs, headache and dizziness.

Tabulated list of adverse reactions

Of patients in the teriparatide trials, 82.8% of the teriparatide patients and 84.5% of the placebo patients reported at least 1 adverse event.

The adverse reactions associated with the use of teriparatide in osteoporosis clinical trials and post-marketing exposure are summarised in the table below.

The following convention has been used for the classification of the adverse reactions: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1\ 000$ to $< 1/100$), and rare ($\geq 1/10\ 000$ to $< 1/1\ 000$).

Table 1. Adverse reactions

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Common	Anaemia
Immune system disorders	Rare	Anaphylaxis
Metabolism and nutrition disorders	Common	Hypercholesterolaemia
	Uncommon	Hypercalcaemia greater than 2.76 mmol/L, hyperuricaemia
	Rare	Hypercalcaemia greater than 3.25 mmol/L
Psychiatric disorders	Common	Depression
Nervous system disorders	Common	Dizziness, headache, sciatica, syncope
Ear and labyrinth disorders	Common	Vertigo
Cardiac disorders	Common	Palpitations
	Uncommon	Tachycardia
Vascular disorders	Common	Hypotension
Respiratory, thoracic and mediastinal disorders	Common	Dyspnoea
	Uncommon	Emphysema
Gastrointestinal disorders	Common	Nausea, vomiting, hiatus hernia, gastro-oesophageal reflux disease
	Uncommon	Haemorrhoids
Skin and subcutaneous tissue disorders	Common	Sweating increased
Musculoskeletal and connective tissue disorders	Very common	Pain in limb
	Common	Muscle cramps
	Uncommon	Myalgia, arthralgia, back cramp/pain*

Renal and urinary disorders	Uncommon	Urinary incontinence, polyuria, micturition urgency, nephrolithiasis
	Rare	Renal failure/impairment
General disorders and administration site condition	Common	Fatigue, chest pain, asthenia, mild and transient injection site events, including pain, swelling, erythema, localised bruising, pruritus and minor bleeding at injection site
	Uncommon	Injection site erythema, injection site reaction
	Rare	Possible allergic events soon after injection: acute dyspnoea, oro/facial oedema, generalised urticaria, chest pain, oedema (mainly peripheral)
Investigations	Uncommon	Weight increased, cardiac murmur, alkaline phosphatase increased

*Serious cases of back cramp or pain have been reported within minutes of the injection.

Description of selected adverse reactions

In clinical trials the following reactions were reported at a $\geq 1\%$ difference in frequency from placebo: vertigo, nausea, pain in limb, dizziness, depression, dyspnoea.

Teriparatide increases serum uric acid concentrations. In clinical trials, 2.8% of teriparatide patients had serum uric acid concentrations above the upper limit of normal compared with 0.7% of placebo patients. However, the hyperuricaemia did not result in an increase in gout, arthralgia, or urolithiasis.

Anti-drug antibodies if any are likely to be observed in line with other teriparatide containing medicinal products. There was no evidence of hypersensitivity reactions, allergic reactions, effects on serum calcium, or effects on Bone Mineral Density (BMD) response.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

4.9. Overdose

Signs and symptoms

Teriparatide has been administered in single doses of up to 100 micrograms and in repeated doses of up to 60 micrograms/day for 6 weeks.

The effects of overdose that might be expected include delayed hypercalcaemia and risk of orthostatic hypotension. Nausea, vomiting, dizziness, and headache can also occur.

Overdose experience based on post-marketing spontaneous reports

In post-marketing spontaneous reports, there have been cases of medication error where the entire contents (up to 750 micrograms) of a teriparatide pen have been administered as a single dose. Transient events reported have included nausea, weakness/lethargy and hypotension. In some cases, no adverse events occurred as a result of the overdose. No fatalities associated with overdose have been reported.

Overdose management

There is no specific antidote for teriparatide. Treatment of suspected overdose should include transitory discontinuation of teriparatide, monitoring of serum calcium, and implementation of appropriate supportive measures, such as hydration.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Calcium homeostasis, parathyroid hormones and analogues, ATC code: H05AA02

Kauliv is a biosimilar medicinal product. Detailed information is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

Mechanism of action

Endogenous 84-amino -acid parathyroid hormone (PTH) is the primary regulator of calcium and phosphate metabolism in bone and kidney. Teriparatide (rh PTH (1-34)) is the active fragment (1-34) of endogenous human parathyroid hormone. Physiological actions of PTH include stimulation of bone formation by direct effects on bone forming cells (osteoblasts) indirectly increasing the intestinal absorption of calcium and increasing the tubular re-absorption of calcium and excretion of phosphate by the kidney.

Pharmacodynamic effects

Teriparatide is a bone formation agent to treat osteoporosis. The skeletal effects of teriparatide depend upon the pattern of systemic exposure. Once-daily administration of teriparatide increases apposition of new bone on trabecular and cortical bone surfaces by preferential stimulation of osteoblastic activity over osteoclastic activity.

Clinical efficacy and safety

Risk factors

Independent risk factors, for example, low BMD, age, the existence of previous fracture, family history of hip fractures, high bone turnover and low body mass index should be considered in order to identify women and men at increased risk of osteoporotic fractures who could benefit from treatment.

Premenopausal women with glucocorticoid-induced osteoporosis should be considered at high risk for fracture if they have a prevalent fracture or a combination of risk factors that place them at high risk for fracture (e.g., low bone density [e.g., T-score ≤ -2], sustained high dose glucocorticoid therapy [e.g., ≥ 7.5 mg/day for at least 6 months], high underlying disease activity, low sex steroid levels).

Postmenopausal osteoporosis

The pivotal study included 1 637 postmenopausal women (mean age 69.5 years). At baseline, ninety percent of the patients had one or more vertebral fractures, and on average, vertebral BMD was 0.82 g/cm² (equivalent to a T-score = - 2.6). All patients were offered 1 000 mg calcium per day and at least 400 IU vitamin D per day. Results from up to 24 months (median: 19 months) treatment with

teriparatide demonstrate statistically significant fracture reduction (Table 2). To prevent one or more new vertebral fractures, 11 women had to be treated for a median of 19 months.

Table 2. Fracture incidence in postmenopausal women

	Placebo (N = 544) (%)	Teriparatide (N = 541) (%)	Relative risk (95 % CI) Vs. placebo
New vertebral fracture (≥ 1) ^a	14.3	5.0 ^b	0.35 (0.22, 0.55)
Multiple vertebral fractures (≥ 1) ^a	4.9	1.1 ^b	0.23 (0.09, 0.60)
Non-vertebral fragility fractures ^c	5.5%	2.6% ^b	0.47 (0.25, 0.87)
Major non-vertebral fragility fractures ^c (hip, radius, humerus, ribs and pelvis)	3.9%	1.5% ^b	0.38 (0.17, 0.86)

Abbreviations: N = number of patients randomly assigned to each treatment group; CI = confidence interval.

^a The incidence of vertebral fractures was assessed in 448 placebo and 444 teriparatide patients who had baseline and follow-up spine radiographs.

^b $p \leq 0.001$ compared with placebo.

^c A significant reduction in the incidence of hip fractures has not been demonstrated.
 $p \leq 0.025$ compared with placebo.

After 19 months (median) treatment, BMD had increased in the lumbar spine and total hip, respectively, by 9% and 4% compared with placebo ($p < 0.001$).

Post-treatment management: Following treatment with teriparatide, 1 262 postmenopausal women from the pivotal trial enrolled in a post-treatment follow-up study. The primary objective of the study was to collect safety data of teriparatide. During this observational period, other osteoporosis treatments were allowed, and additional assessment of vertebral fractures was performed.

During a median of 18 months following discontinuation of teriparatide, there was a 41% reduction ($p = 0.004$) compared with placebo in the number of patients with a minimum of one new vertebral fracture.

In an open-label study, 503 postmenopausal women with severe osteoporosis and a fragility fracture within the previous 3 years (83% had received previous osteoporosis therapy) were treated with teriparatide for up to 24 months. At 24 months, the mean increase from baseline in lumbar spine, total hip and femoral neck BMD was 10.5%, 2.6 % and 3.9% respectively. The mean increase in BMD from 18 to 24 months was 1.4%, 1.2%, and 1.6% at the lumbar spine, total hip and femoral neck, respectively.

A 24-month, randomised, double-blind, comparator-controlled phase 4 study included 1 360 postmenopausal women with established osteoporosis. 680 subjects were randomised to teriparatide and 680 subjects were randomised to oral risedronate 35 mg/week. At baseline, the women had a mean age of 72.1 years and a median of 2 prevalent vertebral fractures; 57.9% of patients had received previous bisphosphonate therapy and 18.8% took concomitant glucocorticoids during the study. 1 013 (74.5%) patients completed the 24-month follow-up. The mean (median) cumulative dose of glucocorticoid was 474.3 (66.2) mg in the teriparatide arm and 898.0 (100.0) mg in the risedronate arm. The mean (median) vitamin D intake for the teriparatide arm was 1 433 IU/day (1,400 IU/day) and for the risedronate arm was 1 191 IU/day (900 IU/day). For those subjects who had baseline and follow-up spine radiographs, the incidence of new vertebral fractures was 28/516 (5.4%) in teriparatide- and 64/533 (12.0%) in risedronate-treated patients, relative risk (95% CI) = 0.44 (0.29-0.68), $p < 0.0001$. The cumulative incidence of pooled clinical fractures (clinical vertebral and non-vertebral fractures) was 4.8% in teriparatide and 9.8% in risedronate-treated patients, hazard ratio (95% CI) = 0.48 (0.32-0.74), $p = 0.0009$.

Male osteoporosis

437 patients (mean age 58.7 years) were enrolled in a clinical trial for men with hypogonadal (defined as low morning free testosterone or an elevated FSH or LH) or idiopathic osteoporosis. Baseline spinal and femoral neck BMD mean T-scores were -2.2 and -2.1, respectively. At baseline, 35% of patients had a vertebral fracture and 59% had a non-vertebral fracture.

All patients were offered 1 000 mg calcium per day and at least 400 IU vitamin D per day. Lumbar spine BMD significantly increased by 3 months. After 12 months, BMD had increased in the lumbar spine and total hip by 5% and 1%, respectively, compared with placebo. However, no significant effect on fracture rates was demonstrated.

Glucocorticoid-induced osteoporosis

The efficacy of teriparatide in men and women (N=428) receiving sustained systemic glucocorticoid therapy (equivalent to 5 mg or greater of prednisone for at least 3 months) was demonstrated in the 18-month primary phase of a 36-month, randomised, double-blind, comparator -controlled study (alendronate 10 mg/day). Twenty-eight percent of patients had one or more radiographic vertebral fractures at baseline. All patients were offered 1 000 mg calcium per day and 800 IU vitamin D per day.

This study included postmenopausal women (N=277), premenopausal women (N=67), and men (N=83). At baseline, the postmenopausal women had a mean age of 61 years, mean lumbar spine BMD T score of -2.7, median prednisone equivalent dose of 7.5 mg/day, and 34% had one or more radiographic vertebral fractures; premenopausal women had a mean age of 37 years, mean lumbar spine BMD T score of -2.5, median prednisone equivalent dose of 10 mg/day, and 9% had one or more radiographic vertebral fractures; and men had a mean age of 57 years, mean lumbar spine BMD T score of -2.2, median prednisone equivalent dose of 10 mg/day, and 24% had one or more radiographic vertebral fractures.

Sixty-nine percent of patients completed the 18-month primary phase. At the 18 month endpoint, teriparatide significantly increased lumbar spine BMD (7.2%) compared with alendronate (3.4%) ($p<0.001$). Teriparatide increased BMD at the total hip (3.6%) compared with alendronate (2.2%) ($p<0.01$), as well as at the femoral neck (3.7%) compared with alendronate (2.1%) ($p<0.05$). In patients treated with teriparatide, lumbar spine, total hip and femoral neck BMD increased between 18 and 24 months by an additional 1.7%, 0.9%, and 0.4%, respectively.

At 36 months, analysis of spinal X-rays from 169 alendronate patients and 173 teriparatide patients showed that 13 patients in the alendronate group (7.7%) had experienced a new vertebral fracture compared with 3 patients in the teriparatide group (1.7%) ($p=0.01$). In addition, 15 of 214 patients in the alendronate group (7.0%) had experienced a non-vertebral fracture compared with 16 of 214 patients in the teriparatide group (7.5%) ($p=0.84$).

In premenopausal women, the increase in BMD from baseline to 18 month endpoint was significantly greater in the teriparatide group compared with the alendronate group at the lumbar spine (4.2% versus -1.9%; $p<0.001$) and total hip (3.8% versus 0.9%; $p=0.005$). However, no significant effect on fracture rates was demonstrated.

5.2. Pharmacokinetic properties

Distribution

The volume of distribution is approximately 1.7 L/kg. The half-life of teriparatide is approximately 1 hour when administered subcutaneously, which reflects the time required for absorption from the injection site.

Biotransformation

No metabolism or excretion studies have been performed with teriparatide but the peripheral metabolism of parathyroid hormone is believed to occur predominantly in liver and kidney.

Elimination

Teriparatide is eliminated through hepatic and extra-hepatic clearance (approximately 62 L/hr in women and 94 L/hr in men).

Elderly

No differences in teriparatide pharmacokinetics were detected with regard to age (range 31 to 85 years). Dose adjustment based on age is not required.

5.3. Preclinical safety data

Teriparatide was not genotoxic in a standard battery of tests. It produced no teratogenic effects in rats, mice or rabbits. There were no important effects observed in pregnant rats or mice administered teriparatide at daily doses of 30 to 1 000 micrograms/kg. However, foetal resorption and reduced litter size occurred in pregnant rabbits administered daily doses of 3 to 100 micrograms/kg. The embryotoxicity observed in rabbits may be related to their much greater sensitivity to the effects of PTH on blood ionised calcium compared with rodents.

Rats treated with near-life time daily injections had dose-dependent exaggerated bone formation and increased incidence of osteosarcoma most probably due to an epigenetic mechanism. Teriparatide did not increase the incidence of any other type of neoplasia in rats. Due to the differences in bone physiology in rats and humans, the clinical relevance of these findings is probably minor. No bone tumours were observed in ovariectomised monkeys treated for 18 months or during a 3-year follow-up period after treatment cessation. In addition, no osteosarcomas have been observed in clinical trials or during the post treatment follow-up study.

Animal studies have shown that severely reduced hepatic blood flow decreases exposure of PTH to the principal cleavage system (Kupffer cells) and consequently clearance of PTH(1-84).

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Glacial acetic acid
Mannitol
Metacresol
Anhydrous sodium acetate
Diluted hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)
Water for injections

6.2. Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3. Shelf life

24 months

Chemical, physical and microbiological in-use stability has been demonstrated for 28 days at 2 – 8°C.

Once opened, the medicinal product may be stored for a maximum of 28 days within its shelf life at 2°C to 8°C. After insertion of the cartridge into the pen, the combined pen and cartridge should be returned to the refrigerator immediately after use. Do not store the pen with the needle attached. Do not remove the cartridge from the pen after first use. The cartridge within the pen can additionally be placed in the pouch supplied with the pen in order to protect from light.

Other in-use storage times and conditions are the responsibility of the user.

6.4. Special precautions for storage

Store in a refrigerator (2°C – 8°C).

Do not freeze. Keep the cartridge in the outer carton in order to protect from light.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5. Nature and contents of container

3 mL cartridge (USP type-1 glass cartridge), with a plunger stopper (bromobutyl) and disc seal (aluminium and rubber liner seals), packed in a plastic tray sealed with lid foil and supplied in a carton.

Each cartridge contains 3 mL solution for injection corresponding to 28 doses of 20 micrograms (per 80 microliters).

Pack sizes:

Kauliv 1 cartridge or 3 cartridges.

Kauliv cartridge and pen pack:

1 inner carton of Kauliv cartridge (containing 1 cartridge) and 1 inner carton of Kauliv Pen (containing 1 pen).

Not all pack sizes may be marketed.

6.6. Special precautions for disposal and other handling

Handling

Kauliv cartridges should be used exclusively within Kauliv reusable, multidose pen. No needles are supplied with this medicinal product.

Each cartridge and pen should be used by only one patient. The pen can be used with 32 G 4 mm single-use pen needles.

A new, sterile needle must be used for every injection.

The expiry date on the cartridge label must always be checked before inserting the cartridge into Kauliv pen. To avoid medication errors, make sure that the date when starting to use a new cartridge is at least 28 days before its expiry date.

Before using the pen for the first time, the patient should read and understand the instructions on how to use the pen, which are provided with the pen.

After each injection, the pen should be returned to the refrigerator. After the first use, the cartridge should not be removed from the pen during the 28 days of usage. Do not use Kauliv if it is, or has been frozen.

Kauliv must not be transferred to a syringe. Empty cartridges must not be refilled.

Kauliv should not be used if the solution is cloudy, coloured or contains visible particles.

The date of first injection should be written on the outer carton of Kauliv cartridge (see the provided space on the box: “First use“).

The Kauliv reusable pen features a dose selector with audible clicks and visual indicators to ensure correct dose is set for priming (P) and for setting the dose (D).

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Strides Pharma (Cyprus) Ltd.
Themistokli Dervi, 3
Julia House, 1st Floor,
1066, Nicosia,
Cyprus

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1710/001 [1 cartridge]
EU/1/22/1710/002 [3 cartridges]
EU/1/22/1710/003 [cartridge and pen pack]

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

Detailed information on this product is available on the website of the European Medicines Agency
<http://www.ema.europa.eu>

ANNEX II

- A. MANUFACTURER OF THE BIOLOGICAL ACTIVE
SUBSTANCE AND MANUFACTURER(S) RESPONSIBLE
FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY
AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE
MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO
THE SAFE AND EFFECTIVE USE OF THE MEDICINAL
PRODUCT**

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Stelis Biopharma Ltd. (Unit-1)
Plot no.293 Bommasandra Jigani link Road,
Jigani Industrial area,
Anekal Taluk, Bengaluru – 560 105,
India

Name and address of the manufacturer responsible for batch release

Fairmed Healthcare GmbH
Maria-Goeppert-Strasse 3
23562 Luebeck
Germany

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**OUTER CARTON FOR CARTRIDGE****1. NAME OF THE MEDICINAL PRODUCT**

Kauliv 20 micrograms/80 microliters solution for injection
teriparatide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose of 80 microliters contains 20 micrograms of teriparatide.
Each cartridge contains 28 doses of 20 micrograms (per 80 microliters).

3. LIST OF EXCIPIENTS

Glacial acetic acid, anhydrous sodium acetate, mannitol, metacresol, water for injections, diluted hydrochloric acid (for pH adjustment) and sodium hydroxide (for pH adjustment). See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 cartridge
3 cartridges

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use only with Kauliv pen.

8. EXPIRY DATE

EXP

Discard the cartridge 28 days after the first use. Do not remove the cartridge from the pen during the 28 days of use. The cartridge within the pen can additionally be placed in the pouch supplied with the pen in order to protect from light.

First use:/...../.....

Cartridge 1. / /

Cartridge 2. / /

Cartridge 3. / /

{the grey-shaded text refers to the 3x pack size}

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the cartridge in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Strides Pharma (Cyprus) Limited
Themistokli Dervi, 3
Julia House, 1st Floor,
1066, Nicosia,
Cyprus

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1710/001 [1 cartridge]

EU/1/22/1710/002 [3 cartridges]

EU/1/22/1710/003 [cartridge and pen pack]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kauliv

17. UNIQUE IDENTIFIER – 2D BARCODE
--

2D barcode carrying the unique identifier to be included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING**OUTER CARTON FOR CARTRIDGE AND PEN PACK****1. NAME OF THE MEDICINAL PRODUCT**

Kauliv 20 micrograms/80 microliters solution for injection
teriparatide

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each dose of 80 microliters contains 20 micrograms of teriparatide.
Each cartridge contains 28 doses of 20 micrograms (per 80 microliters).

3. LIST OF EXCIPIENTS

Glacial acetic acid, anhydrous sodium acetate, mannitol, metacresol, water for injections, diluted hydrochloric acid (for pH adjustment) and sodium hydroxide (for pH adjustment). See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 Kauliv cartridge
1 Kauliv pen

28 doses

Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

The cartridge and pen pack should be used for treatment initiation.

Read both the package leaflet of Kauliv cartridge and the instructions for use of the Kauliv Pen before use.

Subcutaneous use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

Discard the cartridge 28 days after the first use. Do not remove the cartridge from the pen during the 28 days of use.

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Strides Pharma (Cyprus) Limited
Themistokli Dervi, 3
Julia House, 1st Floor,
1066, Nicosia,
Cyprus

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/22/1710/003 [cartridge and pen pack]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

Kauliv cartridge and pen

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier to be included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**LID FOIL****1. NAME OF THE MEDICINAL PRODUCT**

Kauliv 20 micrograms/80 microliters solution for injection
teriparatide

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Strides Pharma (Cyprus) Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Subcutaneous use {1X}
SC use {3X}
Store in refrigerator

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION
--

Kauliv 20 mcg/80 mcL solution for injection
teriparatide
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT
--

3 mL

6. OTHER

Store in refrigerator

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Kauliv 20 micrograms/80 microliters solution for injection teriparatide

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Kauliv is and what it is used for
2. What you need to know before you use Kauliv?
3. How to use Kauliv
4. Possible side effects
5. How to store Kauliv?
6. Contents of the pack and other information

1. What Kauliv is and what it is used for

Kauliv contains the active substance teriparatide that is used to make the bones stronger, and to reduce the risk of fractures by stimulating bone formation.

Kauliv is used to treat osteoporosis in adults. Osteoporosis is a disease that causes your bones to become thin and fragile. This disease is especially common in women after the menopause, but it can also occur in men. Osteoporosis is also common in patients receiving medicines called corticosteroids.

2. What you need to know before you use Kauliv

Do not use Kauliv

- if you are allergic to teriparatide or any of the other ingredients of this medicine (listed in section 6).
- if you have high levels of calcium in your blood (pre-existing hypercalcaemia).
- if you suffer from serious kidney problems.
- if you have ever had bone cancer or if other cancers have spread (metastasised) to your bones.
- if you have certain bone diseases. If you have a bone disease, tell your doctor.
- if you have unexplained high levels of alkaline phosphatase in your blood, which means you might have Paget's disease of bone (disease with abnormal bone changes). If you are not sure, ask your doctor.
- if you have had radiation therapy involving your bones.
- if you are pregnant or breast-feeding.

Warnings and precautions

Kauliv may cause an increase in the amount of calcium in your blood or urine.

Talk to your doctor before or while using Kauliv:

- if you have continuing nausea, vomiting, constipation, low energy, or muscle weakness. These may be signs there is too much calcium in your blood.
- if you suffer from kidney stones or have had kidney stones.
- if you suffer from kidney problems (moderate renal impairment).

Some patients get dizzy or get a fast heartbeat after the first few doses of Kauliv. For the first doses, inject Kauliv in a place where you can sit or lie down right away if you get dizzy.

The recommended treatment time of 24 months should not be exceeded.

Before inserting a cartridge in Kauliv pen write down the batch (Lot) number of the cartridge and its first injection date on a calendar and provide this information when reporting any side effects. The date of first injection should also be recorded on the outer carton of Kauliv cartridge (see the provided space on the box: "First use") (see section 3.).

Kauliv should not be used in growing adults.

Children and adolescents

Kauliv should not be used in children and adolescents (aged less than 18 years).

Other medicines and Kauliv

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. This is important, because some medicines (e.g. digoxin/digitalis, a medicine used to treat heart disease) may interact with teriparatide.

Pregnancy and breast-feeding

Do not use Kauliv if you are pregnant or breast-feeding. If you are a woman of child-bearing potential, you should use effective methods of contraception during use of Kauliv. If you become pregnant while using Kauliv, Kauliv should be discontinued. Ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

Some patients may feel dizzy after injecting Kauliv. If you feel dizzy you should not drive or use machines until you feel better.

Kauliv contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

3. How to use Kauliv

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is 20 micrograms (corresponding to 80 microliters) given once a day by injection under the skin (subcutaneous injection) in the thigh or abdomen.

To help you remember to use your medicine, inject it at about the same time each day. Kauliv can be injected at meal time. Inject Kauliv each day for as long as your doctor prescribes it for you. The total duration of treatment with Kauliv should not exceed 24 months. You should not receive more than one treatment course of 24 months over your lifetime.

Your doctor may advise you to use Kauliv with calcium and vitamin D. Your doctor will tell you how much you should take each day.

Kauliv can be given with or without food.

Kauliv cartridges are designed to be used only with the Kauliv multidose pen and compatible pen needles. The pen and injection needles are not included with Kauliv cartridge.

Before the first use, insert the cartridge into the pen. For the correct use of this medicine it is very important to closely follow the detailed Instructions for Use (IFU) of your pen which are provided with the pen.

Use a new injection needle for each injection to prevent contamination and safely dispose of the needle after use.

Never store your pen with the needle attached.

Never share your pen with others.

Do not use your Kauliv pen to inject any other medicine (e.g. insulin).

The pen is customised for use with Kauliv only.

Do not refill the cartridge.

Do not transfer the medicine into a syringe.

You should inject Kauliv shortly after you take the pen with inserted cartridge out of the refrigerator. Put the pen with inserted cartridge back into the refrigerator immediately after you have used it. Do not remove the cartridge from the pen after each use. The cartridge within the pen can additionally be placed in the pouch supplied with the pen in order to protect from light during the whole 28-day treatment period.

Preparing the pen for use

- To ensure the correct administration of Kauliv always read the IFU of Kauliv pen, which is included in the carton of the pen.
- Wash your hands before handling the cartridge or pen.
- Check the expiry date on the cartridge label before inserting the cartridge into the pen. Make sure that there are at least 28 days remaining before its expiry date. Insert the cartridge into the pen before the first use as detailed in the pen instructions. Write down the batch (Lot) number of each cartridge and its first injection date on a calendar. The date of first injection should also be recorded on the outer carton of Kauliv cartridge (see the provided space on the box: "First use").
- After inserting a new cartridge and before the first injection from this cartridge, prime the pen according to the instructions which are provided with the pen IFU. Please ensure to prime before each dose as per the instructions given in pen IFU.

Injecting Kauliv

- Before you inject Kauliv, clean your skin where you intend to inject (thigh or abdomen) as instructed by your doctor.
- Gently hold a fold of cleansed skin and insert the needle straight into the skin. Press the push button and hold it pressed in until the dose indication has returned to the start position.
- After your injection, leave the needle in the skin for ten seconds to make sure that you receive the whole dose.
- As soon as you have finished the injection, attach the outer needle protective cap on the pen needle and screw the cap anti-clockwise to remove the pen needle.
- Replace the cap on your pen. Leave the cartridge in the pen.

If you use more Kauliv than you should

If, by mistake, you have used more Kauliv than you should, contact your doctor or pharmacist. The expected effects of overdose include nausea, vomiting, dizziness, and headache.

If you forget to use Kauliv

If you forget an injection or cannot use your medicine at your usual time, inject it as soon as possible on that day. Do not use a double dose to make up for a forgotten dose. Do not take more than one injection in the same day.

If you stop using Kauliv

If you are considering stopping Kauliv treatment, please discuss this with your doctor. Your doctor will advise you and decide how long you should be treated with Kauliv.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

Kauliv is not recommended for use by the blind or visually impaired persons without the assistance from a person trained in the proper use of the pen.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The most common side effects are pain in limb (which may affect more than 1 in 10 people). Other common side effects (affecting up to 1 in 10 people) include feeling sick, headache and dizziness. If you become dizzy (light-headed) after your injection, you should sit or lie down until you feel better. If you do not feel better, you should call a doctor before you continue treatment. Cases of fainting have occurred after teriparatide use.

If you have discomfort around the area of the injection such as redness of the skin, pain, swelling, itching, bruising or minor bleeding (which can occur commonly), this should clear up in a few days or weeks. Otherwise tell your doctor.

Rarely (may affect up to 1 in 1 000 people), patients may suffer allergic reactions consisting of breathlessness, swelling of the face, rash and chest pain. These reactions usually occur soon after injection. In rare cases, serious and potentially life-threatening allergic reactions including anaphylaxis can occur.

Other side effects include:

Common (may affect up to 1 in 10 people)

- increase in blood cholesterol levels
- depression
- nerve pain in the leg
- feeling faint
- spinning sensation
- irregular heartbeats
- breathlessness
- increased sweating
- muscle cramps
- loss of energy
- tiredness
- chest pain
- low blood pressure
- heartburn (painful or burning sensation just below the breast bone)
- being sick (vomiting)
- a hernia of the tube that carries food to your stomach (hiatus hernia)
- low haemoglobin or red blood cell count (anaemia).

Uncommon (may affect up to 1 in 100 people)

- increased heart rate
- abnormal heart sound
- shortness of breath
- piles (haemorrhoids)
- leakage of urine
- increased need to pass water

- weight increase
- kidney stones
- pain in the muscles and pain in the joints. Some patients have had severe back cramps or pain which led to admission into hospital.
- increase in blood calcium level
- increase in blood uric acid level
- increase in an enzyme called alkaline phosphatase.

Rare (may affect up to 1 in 1 000 people)

- reduced kidney function, including renal failure
- swelling, mainly in the hands, feet and legs.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system](#) listed in [Appendix V](#). By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Kauliv

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the cartridge after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C – 8 °C). Do not freeze.

Keep the cartridge in the outer carton in order to protect from light.

You can use Kauliv for up to 28 days after the first injection, as long as the cartridge/pen with the cartridge inserted is stored in a refrigerator (2 °C to 8 °C). The cartridge/pen can additionally be placed in the pouch supplied with the pen in order to protect from light.

Avoid placing the cartridge close to the ice compartment of the refrigerator to prevent freezing. Do not use Kauliv if it is, or has been, frozen.

Each cartridge should be properly disposed of after 28 days of first use, even if it is not completely empty.

Kauliv contains a clear and colourless solution. Do not use Kauliv if solid particles appear or if the solution is cloudy or coloured.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Kauliv contains

- The active substance is teriparatide. Each dose of 80 microliters contains 20 micrograms of teriparatide. Each cartridge of 3 mL contains 750 micrograms of teriparatide (corresponding to 250 micrograms per mL).
- The other ingredients are: anhydrous sodium acetate, glacial acetic acid, mannitol, metacresol, diluted hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment), water for injections. See section 2. “Kauliv contains sodium”.

What Kauliv looks like and contents of the pack

Kauliv is a colourless and clear solution for injection. It is supplied in a cartridge. Each cartridge contains 3 mL of solution, adequate for 28 doses.

Pack sizes:

1 cartridge or 3 cartridges packed in a plastic tray sealed with lid foil and packed in a carton.

Kauliv cartridge and pen pack:

1 inner carton of Kauliv cartridge (containing 1 cartridge) and 1 inner carton of Kauliv Pen (containing 1 pen).

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Strides Pharma (Cyprus) Limited
Themistokli Dervi, 3
Julia House, 1st Floor,
1066, Nicosia, Cyprus

Manufacturer

Fairmed Healthcare GmbH
Maria-Goeppert-Strasse 3
23562 Luebeck
Germany

This leaflet was last revised in

Other sources of information

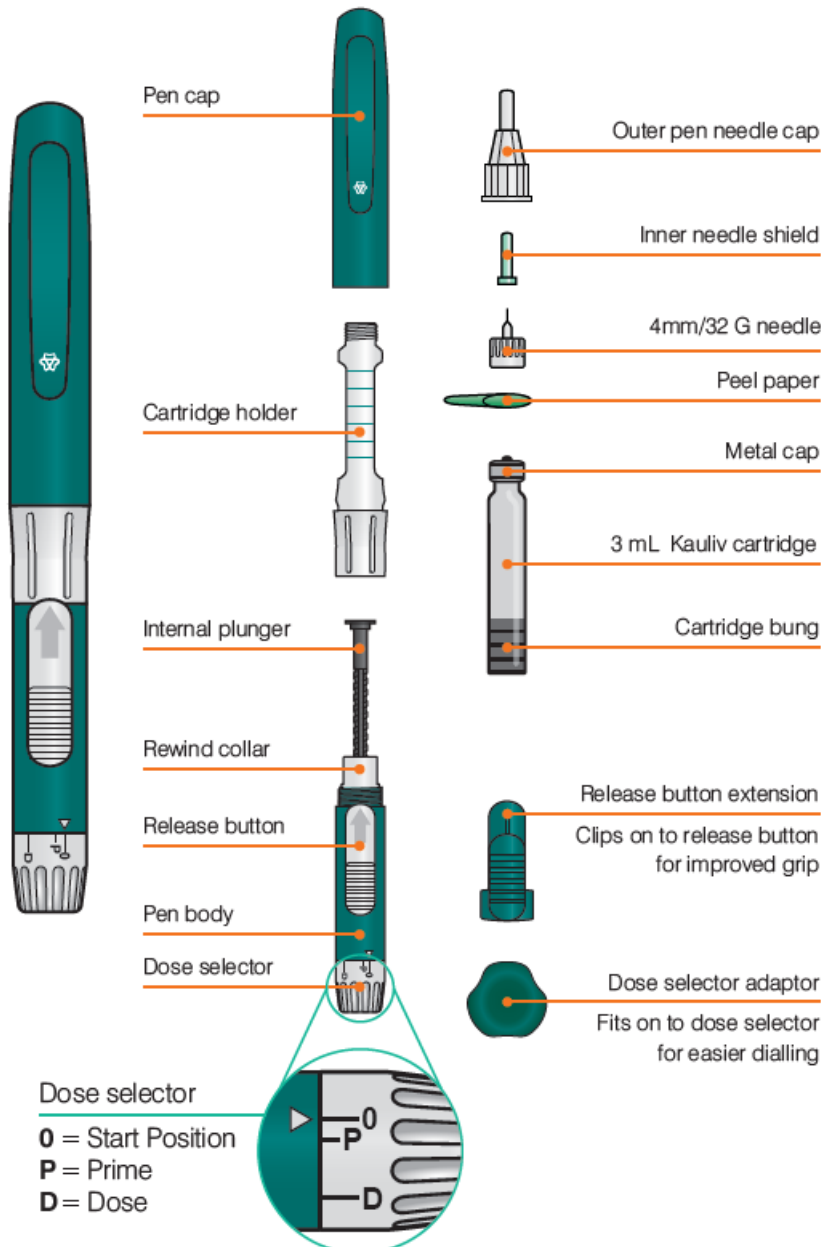
Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu>

Instructions for Use Kauliv Pen

Please follow these step-by-step instructions carefully before using Kauliv pen.

The Kauliv pen should not be used for any other purpose than that advised by your healthcare professional.

Kauliv pen parts



INDICATIONS FOR USE

Kauliv pen is a reusable injection pen for self-administering subcutaneous injections of teriparatide. For further information, please refer to “What Kauliv is and what it is used for” in the package leaflet for Kauliv. The Kauliv pen must only be used with Kauliv cartridge and 32 G 4 mm single-use pen needles.

Each cartridge contains 28 doses of teriparatide. Inject a single dose (**D**) of 20 micrograms (corresponding to 80 microliters) every day.

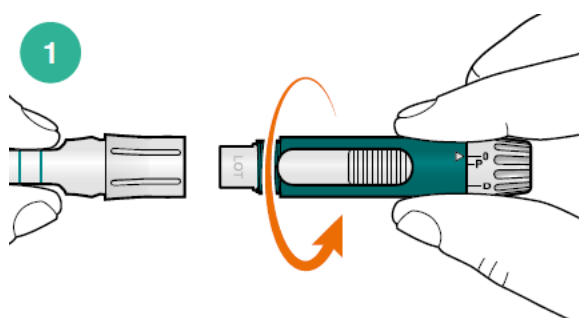
You need to load a new cartridge at the start of each new 28 day period.

Patients and caregivers who administer Kauliv should receive appropriate training and instruction on the proper use of the Kauliv pen from a qualified health professional and read the package leaflet for Kauliv cartridge before the first use. It is important to read, understand, and follow the instructions for using the pen as given in the Instructions for Use for Kauliv pen

PEN PREPARATION: FIRST USE AND CHANGING CARTRIDGES

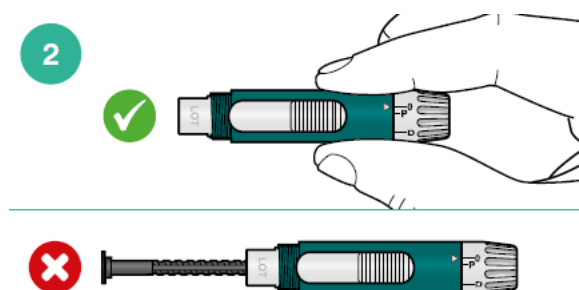
Write down the first injection date of each new cartridge in the space provided on the carton box. This helps you to know when the 28 daily doses per cartridge are used (see section 2 “Warnings and precautions” and section 3 “How to use Kauliv” in the Package leaflet of Kauliv). Follow the instructions every time you insert a new Kauliv cartridge into your Kauliv pen.

LOAD A CARTRIDGE

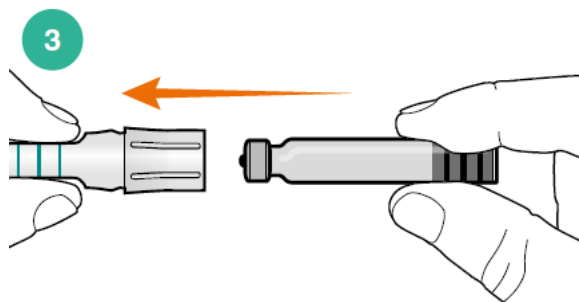


Pull off the pen cap.

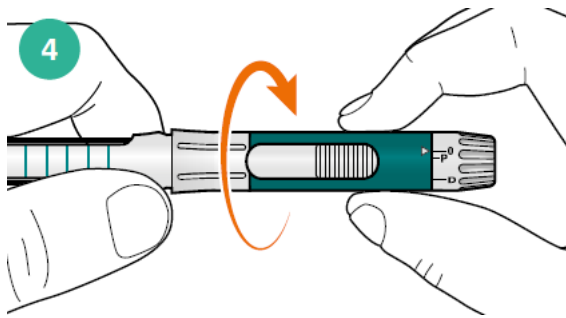
Unscrew by turning the pen body from the cartridge holder (fig. 1).



Check to ensure that the internal plunger is fully retracted (fig. 2). If the internal plunger is extended, please refer to fig. 12 to see how to wind it back in.

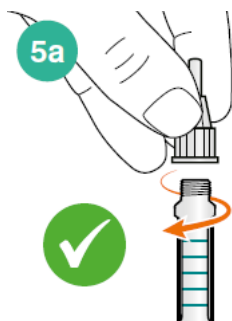


Check the teriparatide cartridge. If the solution appears cloudy, then use a new cartridge. Load the Kauliv cartridge into the cartridge holder, metal cap in first (fig. 3).

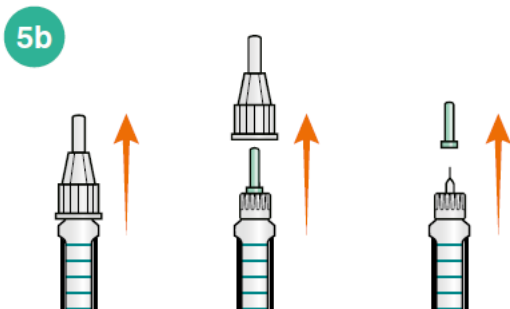


Screw the cartridge holder and pen body firmly together (fig. 4).

ATTACH A NEW NEEDLE



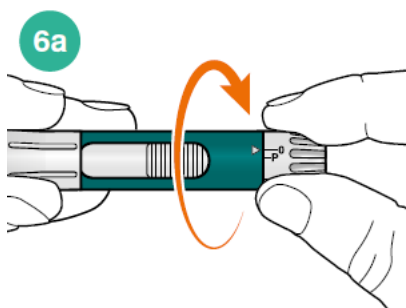
Peel the protective paper from a new pen needle (Size: 32G 4mm).
Screw the pen needle straight onto the cartridge holder (fig. 5a). The pen needle must be changed for every injection.



Pull off the outer needle cap and save it.

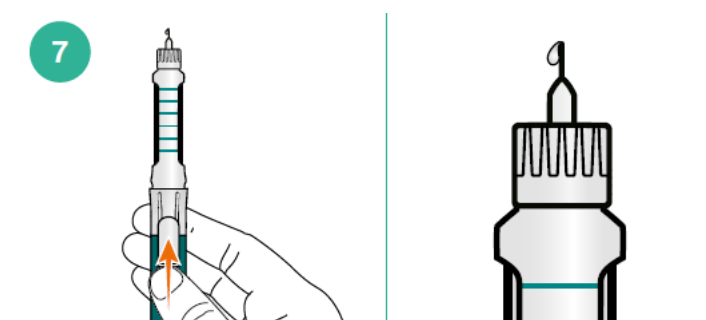
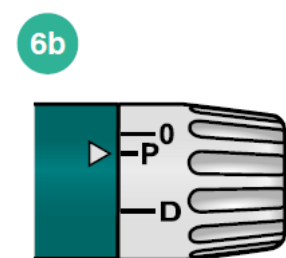
Pull out the inner needle shield and dispose of it (fig. 5b).

PRIME THE PEN



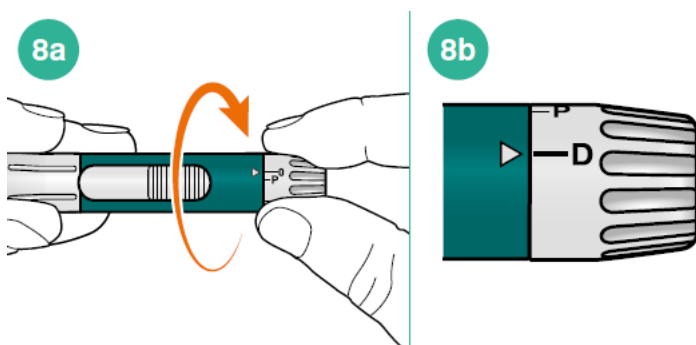
It is important to prime the Kauliv pen before every daily use to remove any air that may be inside the needle and cartridge. (fig. 6a)

Dial the dose selector to P to prime the Kauliv pen (fig. 6b). If you over-dial, proceed to fig. 7.

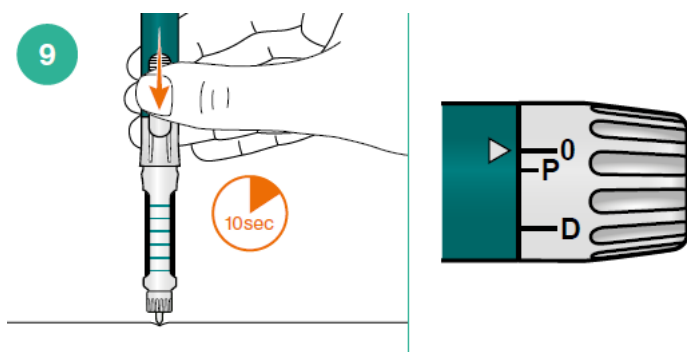


Hold the Kauliv pen with the needle pointing up. Push and hold the release button towards the needle until the arrow on the dose selector points to **0**. Keep dialling to **P** and releasing until a drop of teriparatide appears at the needle tip (fig. 7). The Kauliv pen is now ready for use. (If the arrow does not return to **0** after pushing the release button, refer to the priming advice given above.)

INJECT A DOSE

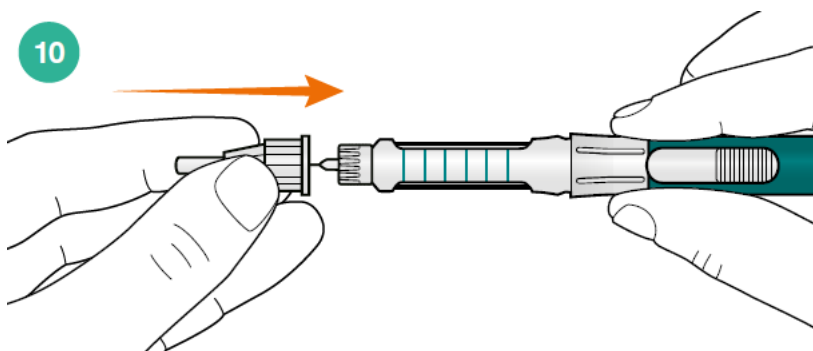


Make sure the arrow points to **0** on the dose selector (fig. 8a). Now dial up to **D** (fig. 8b).



Using the technique recommended by your healthcare professional gently insert the needle of the Kauliv pen into the injection site. Push the release button towards the pen needle and hold it in place until the arrow on the dose selector points to **0** and continue holding the release button down for 10 seconds, then remove the needle from the skin (fig. 9).

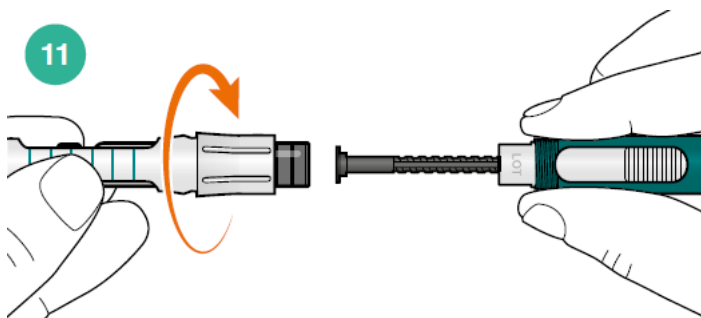
REMOVE THE NEEDLE



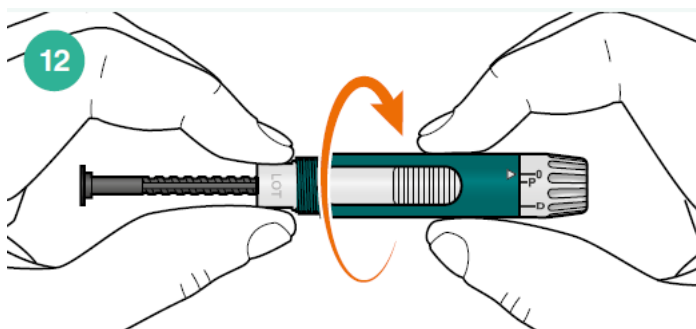
Reattach the outer pen needle cap and unscrew the pen needle (fig. 10). Always check your pen needle has been removed. Dispose of used pen needles carefully into an approved sharps container in accordance with the advice given by your healthcare professional or local regulations. Replace the pen cap on to the Kauliv pen and return it to the fridge for storage.

CHANGE THE CARTRIDGE (EVERY 28 DAYS)

Each cartridge contains enough teriparatide for 28 doses. After 28 days, dispose of the used cartridge and insert a new cartridge (fig. 1 to fig. 4.). Dispose of the used cartridge in accordance with the advice given by your healthcare professional/local regulations.



To change the cartridge, ensure the pen needle is removed. Unscrew the cartridge holder from the pen body and remove the cartridge (fig. 11).



Rewind the internal plunger by holding the grey rewind collar of the pen body between the thumb and finger (fig. 12). Turn the pen body until the internal plunger is fully retracted (fig. 2). Then return to step 3 to load the next cartridge.

PRIMING ADVICE

If during fig. 7 the arrow does not point to 0 (after pushing the release button) and no teriparatide appears, this may indicate one of two possibilities:

- A.** The pen needle that you are using could be blocked. If so, remove the pen needle from the pen and replace with a new one. Then return to fig. 5, fig. 6 and fig. 7.
- B.** The cartridge bung may require releasing. If so, follow these steps:
 - a.** Replace the outer pen needle cap onto the needle.
 - b.** Unscrew the cartridge holder.
 - c.** Push and hold down the release button towards the internal plunger until the arrow points to 0 on the dose selector.
 - d.** Dial up to D without screwing the pen back together. Push and hold down the release button towards the internal plunger until the arrow points to 0.
 - e.** Without rewinding the internal plunger, screw the cartridge holder and body firmly together. This will release the cartridge bung and expel some teriparatide, however, the pen will **not** be primed.
 - f.** Repeat fig. 6 and fig. 7 to prime the pen fully.

SAFETY PRECAUTIONS

- Wash hands thoroughly before use.
- When a Kauliv cartridge is loaded, the Kauliv pen should be stored in a refrigerator (2°C to 8°C) in between injections until 28 days of use from the date of first use. The cartridge/pen can additionally be placed in the pouch supplied with the pen in order to protect from light.
- The Kauliv pen should be stored with the arrow on the pen body pointing to 0 to avoid damage to the pen.
- Check the Kauliv cartridge. If the solution appears cloudy, then use a new cartridge.
- Always ensure the Kauliv pen has been primed before every use, in accordance with the instructions detailed in steps 6 and 7. Failure to follow the exact priming procedures could result in an inaccurate dose being delivered.
- Never attempt to dial back the dose selector as doing so may damage the Kauliv pen. Expel the incorrect dose into the air.
- Do not inject more than one dose (D) per day.
- If when removing the pen needle any leakage of teriparatide is found, it is possible that you may not have injected the full teriparatide dose. Do not try to make up for the shortfall in your teriparatide dose by giving a second injection.
- The needle should be removed and safely disposed of immediately after each injection. If the needle is left on the pen, it can get blocked and affect the next dose.
- Choking hazard – small parts. Keep away from children under 3.

STORAGE AND CLEANING

- To clean the Kauliv pen wipe with a damp cloth. Do not immerse in water. Do not use any other solutions to clean the pen, e.g. chemicals, alcohol wipes.

- The Kauliv pen should always be stored or carried with the pen needle removed and the pen cap on.
- Discard cartridge 28 days after the date of first use.
- Before disposing of the pen injector, be sure to remove the pen needle.
- Dispose of used pen needles carefully into a sharps container or in accordance with the advice given by your healthcare professional/local regulations.
- Do not throw needles directly into your household waste.
- Do not recycle the filled sharps container.