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

Movymia 20 micrograms/80 microliters solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 80 microliters contains 20 micrograms of teriparatide*.

One cartridge of 2.4 mL of solution contains 600 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 with a pH of 3.8 – 4.5.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Movymia 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 Movymia 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

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.

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

Method of administration
Movymia should be administered once daily by subcutaneous injection in the thigh or abdomen.

It should be administered exclusively with the Movymia Pen reusable, multidose medicine delivery system and the injection needles which are listed as compatible in the instructions which are provided with the pen. The pen and injection needles are not included with Movymia. Movymia must not be used with any other pen.
Patients must be trained to use the proper injection techniques (see section 6.6). An instruction for use which is included in the carton of the delivery system is also available to instruct patients on the correct use of the pen.

The date of first injection should also be written on the outer carton of Movymia (see the provided space on the box: {First use:}).

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

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 studies with teriparatide, isolated episodes of transient orthostatic hypotension were observed. Typically, an event began within 4 hours of dosing and spontaneously resolved within a few minutes to a few hours. When transient orthostatic hypotension occurred, it happened within the first several doses, was relieved by placing subjects in a reclining position, and did not preclude continued treatment.

Renal impairment
Caution should be exercised in patients with moderate renal impairment.

Younger adult population
Experience in the younger adult population, including premenopausal women, is limited (see section 5.1). Treatment should only be initiated if the benefit clearly outweighs risks in this population.

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

Duration of treatment
Studies in rats indicate an increased incidence of osteosarcoma with long-term administration of teriparatide (see section 5.3). Until further clinical data become available, the recommended treatment time of 24 months should not be exceeded.

Documentation
Batch (Lot) number of each cartridge and the date of its first injection should be recorded by the patient on a calendar.

Excipient
This medicinal product contains less than 1 mmol sodium (23 mg) per dosage unit, 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, Movymia should be discontinued.

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

Breast-feeding
Movymia 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

Teriparatide 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 limb, 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 (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), and rare (≥1/10,000 to <1/1,000).

Organ System Class	**Very common**	**Common**	**Uncommon**	**Rare**
Blood and lymphatic system disorders		Anaemia		
Immune system disorders				Anaphylaxis
Metabolism and nutrition disorders		Hypercholesterol-aemia	Hypercalcaemia greater than 2.76 mmol/L, hyperuricaemia	Hypercalcaemia greater than 3.25 mmol/L
Psychiatric disorders		Depression		
Nervous system disorders		Dizziness, headache, sciatica, syncope		
Ear and labyrinth disorders		Vertigo		
Cardiac disorders		Palpitations	Tachycardia	

Organ System Class	Very common	Common	Uncommon	Rare
Vascular disorders		Hypotension		
Respiratory, thoracic and mediastinal disorders		Dyspnoea	Emphysema	
Gastrointestinal disorders		Nausea, vomiting, hiatus hernia, gastro-oesophageal reflux disease	Haemorrhoids	
Skin and subcutaneous tissue disorders		Sweating increased		
Musculoskeletal and connective tissue disorders	Pain in limb	Muscle cramps	Myalgia, arthralgia, back cramp/pain*	
Renal and urinary disorders			Urinary incontinence, polyuria, micturition urgency, nephrolithiasis	Renal failure/impairment
General disorders and administration site condition		Fatigue, chest pain, asthenia, mild and transient injection site events, including pain, swelling, erythema, localised bruising, pruritus and minor bleeding at injection site	Injection site erythema, injection site reaction	Possible allergic events soon after injection: acute dyspnoea, oro/facial oedema, generalised urticaria, chest pain, oedema (mainly peripheral)
Investigations			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 ≥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.

In a large clinical trial, antibodies that cross-reacted with teriparatide were detected in 2.8% of women receiving teriparatide. Generally, antibodies were first detected following 12 months of treatment and diminished after withdrawal of therapy. 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 800 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

Movymia 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 (rhPTH(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
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/cm^2 (equivalent to a T-score = - 2.6). All patients were offered 1000 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 1). To prevent one or more new vertebral fractures, 11 women had to be treated for a median of 19 months.

Table 1

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 (≥2) [a]	4.9	1.1 [b]	0.23 (0.09, 0.60)
Non-vertebral fragility fractures [c]	5.5%	2.6% [d]	0.47 (0.25, 0.87)
Major non-vertebral fragility fractures[c] (hip, radius, humerus, ribs and pelvis)	3.9%	1.5% [d]	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.
[d] $p \leq 0.025$ compared with placebo.

After 19 months (median) treatment, bone mineral density (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, randomized, 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 1433 IU/day (1400 IU/day) and for the risedronate arm was 1191 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 bone mineral density 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 1000 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 1000 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). Dosage 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 1000 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
Sodium acetate trihydrate
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

2 years.

Chemical in-use stability has been demonstrated for 28 days at 2 – 8 °C.
From a microbiological point of view, once opened, the product may be stored for a maximum of 28 days within its shelf life at 2 °C to 8 °C.
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). After insertion of the cartridge into the pen, the combined pen and cartridge should be returned to the refrigerator immediately after use.
Do not freeze. Keep the cartridge in the outer carton in order to protect from light.

Do not store the injection device with the needle attached. Do not remove the cartridge from the pen after first use.

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

6.5 Nature and contents of container

3 mL cartridge (siliconised Type I glass), with a plunger stopper (bromobutyl) and disc seal (aluminium and rubber liner seals), packed in a plastic tray sealed with lid foil and a carton.

Each cartridge contains 2.4 mL of solution corresponding to 28 doses of 20 micrograms (per 80 microliters).
Pack sizes: 1 or 3 cartridges.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Movymia is supplied in a cartridge. Movymia cartridges are to be used in Movymia Pen reusable, multidose pen device exclusively and must not be used with any other pen. No injecting pen and needles are supplied with this medicinal product.
Each cartridge and pen should be used by only one patient. The pen can be used with compatible pen needles. These are listed in the instruction for use for the pen. A new, sterile pen needle must be used for every injection.

The expiry date on the cartridge label must always be checked before inserting the cartridge into Movymia 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 device 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.
Movymia must not be transferred to a syringe.
Empty cartridges must not be refilled.

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

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

7. MARKETING AUTHORISATION HOLDER

STADA Arzneimittel AG
Stadastrasse 2-18
61118 Bad Vilbel
Germany

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1161/001 [1 cartridge]
EU/1/16/1161/002 [3 cartridges]

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 January 2017

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 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 RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Richter-Helm BioLogics GmbH & Co. KG
Dengelsberg
24796 Bovenau
GERMANY

Name and address of the manufacturer responsible for batch release

Gedeon Richter Plc.
Gyömrői út 19-21
1103 Budapest
HUNGARY

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**

The requirements for submission of periodic safety update reports 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 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

1. NAME OF THE MEDICINAL PRODUCT

Movymia 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, sodium acetate trihydrate, mannitol, metacresol, water for injections, hydrochloric acid (for pH adjustment) and sodium hydroxide (for pH adjustment).

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

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

8. EXPIRY DATE

EXP

Discard the cartridge 28 days after the first use.

First use: 1. ...../2. ...../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

STADA Arzneimittel AG
Stadastrasse 2-18
61118 Bad Vilbel
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/16/1161/001 [1 cartridge]
EU/1/16/1161/002 [3 cartridges]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

Use only with Movymia Pen.

16. INFORMATION IN BRAILLE

Movymia

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier 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

Movymia 20 micrograms/80 microliters solution for injection
teriparatide

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STADA Arzneimittel AG

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Subcutaneous use *{1x}*
SC *{3x}*

Store in a refrigerator.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL

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

Movymia 20 mcg/80 mcL injection
teriparatide

SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

2.4 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Movymia 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 Movymia is and what it is used for

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

Movymia 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 Movymia

Do not use Movymia:
- 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 (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.

Warning and precautions
Movymia may increase calcium in your blood or urine.

Talk to your doctor before or while using Movymia:
- 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 Movymia. For the first doses, inject Movymia 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 Movymia Pen write down the batch (Lot) number of the cartridge and its first injection date on a calendar. The date of first injection should also be recorded on the outer carton of Movymia (see the provided space on the box: {First use:}) (see section 3.).

Movymia should not be used in growing adults.

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

Other medicines and Movymia
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 Movymia 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 Movymia. If you become pregnant while using Movymia, Movymia should be discontinued. Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Some patients may feel dizzy after injecting Movymia. If you feel dizzy you should not drive or use machines until you feel better.

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

3. How to use Movymia

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 take your medicine, inject it at about the same time each day. Movymia can be injected at meal times. Inject Movymia each day for as long as your doctor prescribes it for you.
The total duration of treatment with Movymia 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 take Movymia with calcium and vitamin D. Your doctor will tell you how much you should take each day.

Movymia can be given with or without food.

Movymia cartridges are designed to be used only with the Movymia Pen reusable, multidose delivery system and compatible pen needles. The pen and injection needles are not included with Movymia.

Before the first use, insert the cartridge into the pen (which is supplied separately). For the correct use of this medicine it is very important to closely follow the detailed Instructions for Use 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 Movymia Pen to inject any other medicine (e.g. insulin).
The pen is customised for use with Movymia only.
Do not refill the cartridge.
Do not transfer the medicine into a syringe.

You should inject Movymia 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. Store it in the cartridge sleeve during the whole 28-day treatment period.

Preparing the pen for use
- To ensure the correct administration of Movymia always read the Instructions for Use of Movymia 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 Movymia (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. Do not prime again after the first dose.

Injecting Movymia
- Before you inject Movymia, 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 six 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. This will keep the remaining Movymia sterile and prevent leaking from the pen. It will also stop air going back into the cartridge and the needle from clogging.
- Replace the cap on your pen. Leave the cartridge in the pen.

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

If you forget to use Movymia
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 Movymia

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

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

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 occured 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 in up to 1 in 10 people), this should clear up in a few days or weeks. Otherwise tell your doctor.

Rarely, 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)
- 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 Movymia

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 Movymia 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).

Avoid placing the cartridge close to the ice compartment of the refrigerator to prevent freezing. Do not use Movymia 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.

Movymia contains a clear and colourless solution. Do not use Movymia 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 Movymia contains
- The active substance is teriparatide. Each dose of 80 microliters contains 20 micrograms of teriparatide. One cartridge of 2.4 mL contains 600 micrograms of teriparatide (corresponding to 250 micrograms per mL).
- The other ingredients are: glacial acetic acid, mannitol, metacresol, sodium acetate trihydrate, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment), water for injections.

What Movymia looks like and contents of the pack
Movymia is a colourless and clear solution. It is supplied in a cartridge. Each cartridge contains 2.4 mL of solution, enough for 28 doses.

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

Not all pack sizes may be marketed.

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Manufacturer
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Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu