EU Risk Management Plan for Teriparatide BGW, 20 µg/80 µl, solution for injection in pre-filled pen (teriparatide)

RMP version to be assessed as part of this application:

RMP Version number:	01
Data lock point for this RMP:	16-July-2018
Date of final sign off:	31.01.2019

Rationale for submitting an updated RMP:	Not applicable for initial marketing authorisation application submission
Summary of significant changes in this RMP:	Not applicable for initial marketing authorisation application submission

RMP Version number:	Not applicable
Submitted on:	Not applicable
Procedure number:	Not applicable
Version number:	Not applicable
Approved with procedure:	Not applicable
Date of approval (opinion date):	Not applicable

QPPV name:

QPPV signature:

Table of content

Part I: Product(s) Overview

Table Part I.1 – Product Overview

Active substance(s) (INN or common name)	Teriparatide
Pharmacotherapeutic group(s) (ATC Code)	Calcium homeostasis, parathyroid hormones and analogues ATC code: H05 AA02
Marketing Authorisation Holder or Applicant	Welding GmbH & Co. KG, Esplanade 39, 20354 Hamburg, Germany
Medicinal products to which this RMP refers	1
Invented name(s) in the European Economic Area (EEA)	Teriparatide BGW, 20 µg/80 µl, solution for injection in pre-filled pen
Marketing authorisation procedure	DCP/H/6160/001/DC
Brief description of the product	Teriparatide BGW is a synthetically derived polypetide. It is identical to the 34 N-terminal amino acid sequence of endogenous human parathyroid hormone. Teriparatide is the active fragment of endogenous human parathyroid hormone. Molecular Formula: Molecular Weight: 4117.773 g/mol
	Endogenous 84-amino-acid parathyroid hormone (PTH) is the primary regulator of calcium and phosphate metabolism in bone and kidney. 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. 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.

Hyperlink to the Product Information	The proposed PI is available in the module 1.3.1
Indication(s) in the EEA	Current (if applicable): Not approved yet.
	Proposed (if applicable): TERIPARATIDE BGW is indicated in adults. Treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture. 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.
Dosage in the EEA	Current (if applicable): Not approved yet.
	Proposed (if applicable): The recommended dose of TERIPARATIDE BGW is 20 micrograms administered once daily. The maximum total duration of treatment with TERIPARATIDE BGW should be 24 months. The 24-month course of TERIPARATIDE BGW should not be repeated over a patient's lifetime. Patients should receive supplemental calcium and vitamin D supplements if dietary intake is inadequate. Following cessation of TERIPARATIDE BGW therapy, patients may be continued on other osteoporosis therapies. Dosage adjustment is not required in patients with mild renal impairment and in elderly. TERIPARATIDE BGW should be used with caution in patients with hepatic impairment or moderate renal impairment. TERIPARATIDE BGW should not be used in pediatric patients, or young adults with open epiphyses or in patients with severe renal impairment. <u>Method of administration</u> Before first use of the pen, a priming dose must be released. TERIPARATIDE BGW should be administered once daily by subcutaneous injection in the thigh or abdomen. Patients must be trained to use the proper injection techniques. A user manual is also available to instruct patients on the correct use of the pen.
Pharmaceutical form(s) and strengths	Current (if applicable): Not approved yet.
	Proposed (if applicable): solution for injection in pre-filled pen; 20 µg/80 µl
Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety specification

Part II: Module SI - Epidemiology of the indication(s) and target population(s)

Not applicable.

Part II: Module SII - Non-clinical part of the safety specification

Not applicable.

Part II: Module SIII - Clinical trial exposure

Not applicable.

Part II: Module SIV - Populations not studied in clinical trials

Not applicable.

Part II: Module SV - Post-authorisation experience

Not applicable.

Part II: Module SVI - Additional EU requirements for the safety specification

Not applicable.

Part II: Module SVII - Identified and potential risks

Not applicable.

Part II: Module SVIII - Summary of the safety concerns

A Summary of safety concerns presented below has been prepared based on the list of safety concerns published on the CMDh website for teriparatide.

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Hypercalcemia • Orthostatic Hypotension
Important potential risks	• Osteosarcoma • Non-uraemic calciphylaxis
Missing information	• None

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

No additional PhV activities applicable to generics were identified by the Applicant in the publicly available information on the reference product Forsteo and in the list of safety concerns published on the CMDh website for teriparatide.
The CHMP considered that the Pharmacovigilance system as described by the MAH fulfils the legislative requirements. No safety concerns requiring risk minimisation activities have been identified. Routine pharmacovigilance was adequate to monitor the safety of the product. Therefore, no additional PhV activities were proposed.

Part IV: Plans for post-authorisation efficacy studies

No additional post authorisation efficacy studies applicable to generics were identified by the Applicant in the publicly available information on the reference product Forsteo and in the list of safety concerns published on the CMDh website for teriparatide. Therefore, no additional post authorisation efficacy studies were proposed.

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan
The safety information in the proposed product information is aligned to the reference medicinal product.

V.1. Routine Risk Minimisation Measures
Not applicable.

V.2. Additional Risk Minimisation Measures
Not applicable.

V.3 Summary of risk minimisation measures
Not applicable.

Part VI: Summary of the risk management plan

Summary of risk management plan for on Teriparatide BGW, 20 µg/80 µl, solution for injection (teriparatide)

This is a summary of the risk management plan (RMP) for on Teriparatide BGW, 20 µg/80 µl, solution for injection. The RMP details important risks of on Teriparatide BGW, 20 µg/80 µl, solution for injection, how these risks can be minimised, and how more information will be obtained about Teriparatide BGW's risks and uncertainties (missing information).

Teriparatide BGW's summary of product characteristics (SmPC), its package leaflet as well as the Instructions for Use (IFU) give essential information to healthcare professionals and patients on how on Teriparatide BGW, 20 µg/80 µl, solution for injection should be used.

I. The medicine and what it is used for

The proposed indications for on Teriparatide BGW, 20 µg/80 µl, solution for injection are:

- treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture. 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.

It contains teriparatide as the active substance and it is given by subcutaneous route of administration.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Teriparatide BGW, together with measures to minimise such risks and the proposed studies for learning more about Teriparatide BGW's risks, are outlined below. Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet, IFU and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

II.A List of important risks and missing information

Important risks of Teriparatide BGW are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Teriparatide BGW. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

List of important risks and missing information	
Important identified risks	• Hypercalcemia • Orthostatic Hypotension
Important potential risks	• Osteosarcoma • Non-uraemic calciphylaxis
Missing information	• None

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference product Forsteo.

II.C Post-authorisation development plan

Not applicable.

Part VII: Annexes

Annex 1 – EudraVigilance Interface

Not applicable.

Annex 2 – Tabulated summary of planned, ongoing, and completed pharmacovigilance study programme

Not applicable.

Annex 3 - Protocols for proposed, on-going and completed studies in the pharmacovigilance plan

Not applicable.

Annex 4 - Specific adverse drug reaction follow-up forms

Not applicable.

Annex 5 - Protocols for proposed and on-going studies in RMP part IV

Not applicable.

Annex 6 - Details of proposed additional risk minimisation activities (if applicable)

Not applicable.

Annex 7 - Other supporting data (including referenced material)

Not applicable.

Annex 8 – Summary of changes to the risk management plan over time

Not applicable.

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QPPV name: Angelika Bredehorst

QPPV signature:

31.01.19