EU Risk Management Plan for LIVOGIVA (Teriparatide)

RMP version to be assessed as part of this application:

RMP Version number: 0.3

Data lock point for this RMP: 20-Aug-2024

Date of final sign-off: 22-Aug-2024

Rationale for submitting an updated RMP: administrative updates taking the opportunity of renewal procedure

Other RMP versions under evaluation: None

QPPV name: Birger Fels

QPPV signature:

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Part I: Product(s) Overview

Table Part I.1 – Product(s) Overview

Active substance(s) **(INN or common name)**	Teriparatide (rhPTH [1-34])
Pharmacotherapeutic group(s) (ATC Code)	Calcium homeostasis, parathyroid hormones and analogues (H05AA02)
Marketing Authorisation Holder	Theramex Ireland Limited 3rd Floor Kilmore House, Park Lane, Spencer Dock Dublin 1 D01 YEG4
Medicinal products to which this RMP refers	1
Invented name(s) in the European Economic Area (EEA)	LIVOGIVA
Marketing authorisation procedure	Centralised procedure (EMEA/H/C/5087)
Brief description of the product	Chemical class The active ingredient in PF708 (teriparatide [rDNA origin] injection) is teriparatide, a 34-amino acid recombinant analog of human parathyroid hormone (rhPTH [1-34]). It has an identical sequence to the 34 N-terminal amino acids (the biologically active region) of the 84-amino acid human parathyroid hormone (PTH).

	Summary of mode of action Endogenous 84-amino acid PTH is the primary regulator of calcium and phosphate metabolism in bone and kidney. Teriparatide injection (rhPTH[1-34]) is the active fragment (1-34) of endogenous human PTH. Physiological actions of PTH include regulation of bone metabolism, renal tubular reabsorption of calcium and phosphate, and intestinal calcium absorption. The biological actions of PTH and teriparatide are mediated through binding to specific high-affinity cell-surface receptors. Teriparatide and PTH bind to these receptors with the same affinity and have the same physiological actions on bone and kidney. Teriparatide is not expected to accumulate in bone or other tissues. The skeletal effects of teriparatide depend upon the pattern of systemic exposure. Once-daily administration of teriparatide stimulates new bone formation on trabecular and cortical (periosteal and/or endosteal) bone surfaces by preferential stimulation of osteoblastic activity over osteoclastic activity. In monkey studies, teriparatide improved trabecular microarchitecture and increased bone mass and strength by stimulating new bone formation in both cancellous and cortical bone. In humans, the anabolic effects of teriparatide manifest as an increase in skeletal mass, an increase in markers of bone formation and resorption, and an increase in bone strength. By contrast, continuous excess of endogenous PTH, as occurs in hyperparathyroidism, may be detrimental to the skeleton because bone resorption may be stimulated more than bone formation.
	Important information about its composition *Pseudomonas fluorescens* is utilised in the production of a teriparatide injection, with an amino acid sequence identical to that of the originator. *P fluorescens* has been used to commercially produce a variety of proteins for over 20 years.
Hyperlink to the Product Information	Please see module 1.3.1
Indication(s) in the EEA	Current: Treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture. Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk for fracture.
	Proposed (if applicable): Not applicable.
Dosage in the EEA	Current: The recommended dose of teriparatide is 20 micrograms administered once daily. The maximum total duration of treatment with teriparatide should be 24 months.

	Proposed (if applicable): Not applicable.
Pharmaceutical form(s) and strengths	Current (if applicable): Solution for injection in pre-filled pen 20 micrograms/80 microliters
	Proposed (if applicable): Not applicable.
Is/will the product be subject to additional monitoring in the EU?	Yes

Part II: Safety specification

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

Key safety findings from non-clinical studies and relevance to human usage:

Toxicity

- Key issues identified from acute or repeat-dose toxicity studies: In single-dose rodent studies using subcutaneous injection of teriparatide, no mortality was seen in mice given 10,000 mcg/kg (2700-times the human dose based on surface area, mcg/m^2) or in rats given doses of 1000 mcg/kg (540-times the human dose based on surface area, mcg/m^2).
  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 tumors were observed in ovariectomized monkeys treated for 18 months or during a 3-year follow-up period after treatment cessation.
- Reproductive/developmental toxicity: No effects on fertility were observed in male and female rats given subcutaneous teriparatide doses of 30, 100, or 300 mcg/kg/day prior to mating and in females continuing through gestation day 6 (16- to 160-times the human dose of 20 mcg based on surface area, mcg/m^2). In animal studies, teriparatide increased skeletal deviations and variations in mouse offspring at doses more than 60-times the equivalent human dose, produced mild growth retardation, and reduced motor activity in rat offspring at doses more than 120-times the equivalent human dose.
  In animal studies, pregnant mice received teriparatide during organogenesis at subcutaneous doses 8- to 267-times the human dose. At doses ≥ 60-times the human dose, the fetuses showed an increased incidence of skeletal deviations or variations (interrupted rib, extra vertebra or rib). When pregnant rats received subcutaneous teriparatide during organogenesis at doses 16- to 540-times the human dose, the fetuses showed no abnormal findings.
  In a perinatal/postnatal study, pregnant rats received subcutaneous teriparatide from organogenesis through lactation. Mild growth retardation in female offspring at doses ≥ 120-times the human dose (based on surface area, mcg/m^2). Mild growth retardation in male offspring and reduced motor activity in both male and female offspring occurred at maternal doses 540-times the human dose. There were no developmental or reproductive effects in mice or rats at doses 8-or 16-times the human dose, respectively. Exposure multiples were normalized based on body surface area (mcg/m^2). Actual animal doses: mice (30 to 1000 mcg/kg/day); rats (30 to 1000 mcg/kg/day).
- Genotoxicity: Teriparatide was not genotoxic in any of the following test systems: the Ames test for bacterial mutagenesis; the mouse lymphoma assay for mammalian cell mutation; the chromosomal aberration assay in Chinese hamster ovary cells, with and without metabolic activation; and the *in vivo* mouse micronucleus test.
- Carcinogenicity: Two carcinogenicity bioassays were conducted in Fischer 344 rats. In the first study, male and female rats were given daily subcutaneous teriparatide injections of 5, 30, or 75 mcg/kg/day for 24 months from 2 months of age. These doses resulted in systemic exposures that were 3-, 20-, and 60-times higher, respectively, than the systemic exposure observed in humans following a subcutaneous dose of 20 mcg (based on AUC comparison).

Teriparatide treatment resulted in a marked dose-related increase in the incidence of osteosarcoma, a rare malignant bone tumor, in both male and female rats. Osteosarcomas were observed at all doses and the incidence reached 40% to 50% in the high-dose groups. Teriparatide also caused a dose-related increase in osteoblastoma and osteoma in both sexes. No osteosarcomas, osteoblastomas or osteomas were observed in untreated control rats. The bone tumors in rats occurred in association with a large increase in bone mass and focal osteoblast hyperplasia.

The second 2-year study was carried out in order to determine the effect of treatment duration and animal age on the development of bone tumours. Female rats were treated for different periods between 2 and 26 months of age with subcutaneous doses of 5 and 30 mcg/kg (equivalent to 3 and 20 times the human exposure at the 20-mcg dose, based on AUC comparison). The study showed that the occurrence of osteosarcoma, osteoblastoma, and osteoma was dependent upon dose and duration of exposure. Bone tumours were observed when immature 2-month-old rats were treated with 30 mcg/kg/day for 24 months or with 5 or 30 mcg/kg/day for 6 months. Bone tumours were also observed when mature 6-month-old rats were treated with 30 mcg/kg/day for 6 or 20 months. Tumours were not detected when mature 6-month-old rats were treated with 5 mcg/kg/day for 6 or 20 months. The results did not demonstrate a difference in susceptibility to bone tumour formation, associated with teriparatide treatment, between mature and immature rats.

The relevance of these animal findings to humans is uncertain.

In a long-term study, skeletally mature ovariectomized female monkeys (N = 30 per treatment group) were given either daily subcutaneous teriparatide injections of 5 mcg/kg or vehicle. Following the 18-month treatment period, the monkeys were removed from teriparatide treatment and were observed for an additional 3 years. The 5-mcg/kg dose resulted in systemic exposures that were approximately 6-times higher than the systemic exposure observed in humans following a subcutaneous dose of 20 mcg (based on AUC comparison). Bone tumours were not detected by radiographic or histologic evaluation in any monkey in the study.

Safety pharmacology

- Immunogenicity: The results of a 4-week repeat-dose bridging rat toxicity study carried out by the Applicant, including the lack of immunogenicity responses, provides further support regarding the safety of the excipients and qualification of impurities in PF708.
- Renal toxicity: Subcutaneous administration of teriparatide at a dose of 40 mcg/kg/day to monkeys for approximately 4 months caused renal histologic changes, which were largely reversible and had a limited impact on kidney function. However, no drug-related histopathologic changes were observed in the kidneys of mature, ovariectomized monkeys administered teriparatide doses up to 5 mcg/kg/day for 12 or 18 months.
- Other findings: Subcutaneous administration of 30 mcg/kg/day PF708 for 4-weeks resulted in responses that were comparable to the originator, including non-adverse effects on haematology and clinical chemistry, no gender differences in systemic exposure, no detectable ADA findings, increased bone in the sternum and distal femur and proximal tibia of the femoro-tibial joint, and increased extramedullary hematopoiesis in the spleen.

Other toxicity-related information or data

Studies conducted by the Applicant and those available in the public domain do not raise concerns in relation to human safety.

Part II: Module SIII - Clinical trial exposure

The Applicant conducted two studies in the pre-approval phase. The first study (PF708-101) evaluated the pharmacokinetics of PF708 and the originator (Forteo) in healthy adult subjects after a single subcutaneous (SC) dose. The secondary objective was to evaluate the pharmacodynamics (PD) of PF708 and Forteo in healthy adult subjects after a single SC 20 mcg dose.

The second trial was a multicentre parallel-group, open-label study in 27 study centres in the United States. The primary objective of this study was to compare the effects of PF708 and Forteo on immunogenicity after 24 weeks of subcutaneous (SC) daily dosing in patients with osteoporosis. The secondary objective was to compare the pharmacokinetics and pharmacodynamics of PF708 and Forteo in patients with osteoporosis. Each study patient received 24 weeks of 20 mcg PF708 or Forteo by daily SC self-injection in the abdomen or thigh.

Due to the differences in subjects, design and objective of these two studies, the following tabulations have been clearly separated to add clarity.

Table SIII.1: Duration of exposure

Cumulative for all indications (person time)		
Duration of exposure	Patients	Person time
<1 m	70 (healthy volunteers)	Single dose
3 to <6 m	181	168 days
Total person time	168 days	
Osteoporosis		
Duration of exposure	Patients	Person time
3 to <6 m	181	168 days
Total person time for indication	168 days	

Table SIII.2: Age group and gender

Age group	Healthy volunteers		Person time	
	M	F	M	F
Adults (e.g. 18 to 64 years)	43	27	Single dose	Single dose
Total	43	27	Single dose	Single dose
Osteoporosis				
Age group	Patients		Person time	
	M	F	M	F
Adults (e.g. 18 to 64 years)			168 days	168 days
Elderly people (65 to 85 years				

Age group	Healthy volunteers		Person time	
	M	F	M	F
Total	50	131	168 days	168 days

Table SIII.3: Dose

Dose of exposure	Patients	Person time
20 mcg	70	Single dose
Total	70	Single dose
Osteoporosis		
Dose of exposure		
20 mcg/day	181	168 days
Total	181	168 days

Table SIII.4: Ethnic origin

Ethnic origin	Healthy volunteers	Person time
Healthy volunteers		
White	34	Single dose
Black or African American	33	Single dose
Other	3	Single dose
Total	181	Single dose

Ethnic origin	Patients	Person time
Osteoporosis		
White	163	168 days
Black or African American	13	168 days
Asian	1	168 days
American Indian or Alaska native or native Hawaiian or other Pacific islander	1	168 days
Other	3	168 days
Total	181	168 days

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

SIV.1 Exclusion criteria in pivotal clinical studies within the development programme

Study PF708-101

This study was conducted in male or female healthy adult subjects aged 18-55 years. Usual exclusion criteria for a bioequivalence study were:

History of or positive test result for human immunodeficiency virus,

Hepatitis C virus or hepatitis B virus,

History of severe allergic reactions to any drug or anaphylactic reactions,

Known allergy to teriparatide or any other components of the products,

History of malignant disease,

Major surgery within the previous 12 months,

Pregnancy, blood donation,

Clinically significant cardiac, endocrinological, haematologic, hepatic, immunologic, metabolic, urologic, pulmonary, neurologic, dermatologic, psychiatric, renal, or other major disease, alcohol, tobacco or substance abuse).

Other exclusion criteria in Study PF708-101 were:

Paget's disease of bone

Reason for exclusion: Per protocol. Paget's disease is a contraindication to the use of teriparatide in the proposed SmPC. In rats, teriparatide caused an increased incidence of osteosarcoma; this is of uncertain relevance to human subjects. Therefore, patients with increased baseline risk of osteosarcoma (e.g., Paget's disease of bone, or unexplained elevations of alkaline phosphatase, pediatric and young adult patients with open epiphyses, or prior external beam or implant radiation therapy involving the skeleton) should not be prescribed PF708 drug product pen injector.

Is it considered to be included as missing information? No

Rationale: Paget's disease of bone shows an increased baseline risk of osteosarcoma. This latter has been identified as an important potential risk).

Prior external beam or implant radiation therapy involving the skeleton

Reason for exclusion: Per protocol. External beam or implant radiation therapy involving the skeleton is a contraindication to the use of teriparatide in the proposed SmPC. In rats, teriparatide caused an increased incidence of osteosarcoma; this is of uncertain relevance to human subjects. Therefore, patients with increased baseline risk of osteosarcoma (e.g., Paget's disease of bone, or unexplained elevations of alkaline phosphatase, pediatric and young adult patients with open epiphyses, or prior external beam or implant radiation therapy involving the skeleton) should not be prescribed PF708 drug product pen injector.

Is it considered to be included as missing information? No

Rationale: External beam or implant radiation therapy involving the skeleton show an increased baseline risk of osteosarcoma. This latter has been identified as an important potential risk).

Active urolithiasis or primary hyperparathyroidism

Reason for exclusion: Per protocol. Pre-existing hypercalcaemia (as a cause of acute urolithiasis) and metabolic bone disease (including hyperparathyroidism) are contraindications to the use of teriparatide in the proposed SmPC. Teriparatide has not been studied in individuals with active urolithiasis or with pre-existing hypercalcemia, such as primary hyperparathyroidism, and should not be administered in such individuals because of the potential for exacerbation.

Is it considered to be included as missing information? No

Rationale: Patients with pre-existing hypercalcemia should not be treated with teriparatide because of the possibility of exacerbating hypercalcemia. This latter is a well-known adverse effect of teriparatide. In clinical trials, at least one episode of transient hypercalcemia in the 4 to 6 hours after administration of teriparatide was observed in 11% of women and 6% of men treated with teriparatide, compared to 2% of women and none of the men receiving placebo. The number of patients with transient hypercalcemia verified on consecutive measurements was 3% of women and 1% of men treated with teriparatide.

Study PF708-301

In this randomized, multi-centre, parallel group, open-label study conducted in the United States to compare the effects of PF708 and Forteo after 24 weeks of treatment. A total of 182 men and women with osteoporosis were randomly assigned to treatment. Adult male and female patients with osteoporosis aged 30 to 85 years were included in the study. Females had to be ≥5 years postmenopausal and have a screening DXA-derived BMD value of intact, non-fractured vertebrae or of the hip that was either 1.0 to 2.5 standard deviation (SD) below the average of young, healthy women (with documentation of osteoporotic fracture required), or more than 2.5 SD below the average. Males had to have a DXA-derived BMD value of intact, non-fractured vertebrae or of the hip, that was at least 2 SD below the average of young, healthy men.

Standard exclusion criteria were similar to these for study PF708-301. An additional exclusion criterion included the following.

Severe renal impairment (CrCl ≤ 30 mL/min)

Reason for exclusion: Per protocol. In patients with severe renal impairment (CrCl < 30 mL/min), the area under the concentration time curve (AUC) and $T_{1/2}$ of teriparatide were increased by 73% and 77%, respectively. Maximum serum concentration (C_{max}) of teriparatide was not increased. This may cause overexposure to teriparatide.

Is it considered to be included as missing information? No

Rationale: In patients with severe renal impairment (CrCl < 30 mL/min), the increased AUC might raise the possibility of exacerbating hypercalcemia. This latter is a well-known adverse effect of teriparatide.

SIV.2 Limitations to detect adverse reactions in clinical trial development programmes

The clinical development programme is unlikely to detect certain types of adverse reactions such as rare adverse reactions, adverse reactions with a long latency, or those caused by prolonged exposure.

SIV.3 Limitations in respect to populations typically under-represented in clinical trial development programmes

Table SIV.2: Exposure of special populations included or not in clinical trial development programmes

Type of special population	**Exposure**
Pregnant women	not included in the clinical development program
Breastfeeding women	
Patients with relevant comorbidities: • Patients with hepatic impairment • Patients with renal impairment (CrCl ≤ 30 mL/min) • Patients with cardiovascular impairment • Immunocompromised patients • Patients with a disease severity different from inclusion criteria in clinical trials	not included in the clinical development program
Population with relevant different ethnic origin	18 non-white Caucasian patients (168 days)
Subpopulations carrying relevant genetic polymorphisms	not included in the clinical development program

Part II: Module SV - Post-authorisation experience

Theramex acquired the licence for Livogiva (teriparatide) on 27th August 2020, which is the date from which the exposure data was calculated. Exposure data have been obtained from internal Theramex sources and PV licensing partners if relevant.

Livogiva 20 micrograms/80 microliters is a solution for injection in pre-filled pen. Each dose of 80 microliters contains 20 micrograms (µg) of teriparatide. Each pre-filled pen of 2.7 mL contains 675 micrograms of teriparatide (corresponding to 250 micrograms per mL). Each pen contains 28 doses of 20 micrograms for use.

An estimate of patient-years was calculated based on the recommended/designated daily dose (WHO DDD), which is 20 µg (0.02 mg) of teriparatide administered daily for 28 days (1 pen used per treatment cycle). It is assumed 13 treatment cycles (13 pens of teriparatide/28 doses) per year of exposure.

Cumulative Exposure to teriparatide from post marketing experience during the period from product launch till the end of June-2024 is estimated to be 7,340 patient-years.

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

Potential for misuse for illegal purposes

Teriparatide is indicated in the following conditions:

- 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 have been demonstrated.

- Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk for fracture.

Teriparatide was developed to stimulate the bone formation. It contains a recombinant 1-34 N-terminal fragment of endogenous human parathyroid hormone (rhPTH (1-34)). As such, teriparatide has no potential for misuse for illegal purposes, e.g. as a recreational drug or to facilitate assault.

Part II: Module SVII - Identified and potential risks

SVII.1 Identification of safety concerns in the initial RMP submission

SVII.1.1. Risks not considered important for inclusion in the list of safety concerns in the RMP

Not applicable, since the summary of the safety concerns is in line with the originator product.

SVII.1.2. Risks considered important for inclusion in the list of safety concerns in the RMP

None

SVII.2 New safety concerns and reclassification with a submission of an updated RMP

Not applicable, since the summary of the safety concerns is in line with the originator product.

SVII.3 Details of important identified risks, important potential risks, and missing information

SVII.3.1. Presentation of important identified risks and important potential risks

Not applicable, since the summary of the safety concerns is in line with the originator product.

Part II: Module SVIII - Summary of the safety concerns

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

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

III.1 Routine pharmacovigilance activities

There are no routine pharmacovigilance activities beyond adverse reactions reporting and signal detection.

III.2 Additional pharmacovigilance activities

None proposed. The applicant did not identify outstanding needs for pharmacovigilance investigations at the time of their application. There are no safety studies imposed as condition of the marketing authorisation (category 1), as specific obligations in the context of a marketing authorisation under exceptional circumstances or conditional marketing authorisation (category 2), or required by the competent authority (category 3).

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable.

Part IV: Plans for post-authorisation efficacy studies

Not applicable.

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

No additional risk minimisation measures are included in this RMP.

V.3 Summary of risk minimisation measures

Not applicable.

Summary of risk management plan for LIVOGIVA injection (Teriparatide)

This is a summary of the risk management plan (RMP) for LIVOGIVA injection. The RMP details important risks of LIVOGIVA injection.

LIVOGIVA injection's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how LIVOGIVA injection should be used.

This summary of the RMP for LIVOGIVA injection should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all that is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of LIVOGIVA injection's RMP.

I. The medicine and what it is used for

LIVOGIVA injection is authorised for treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture. Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk for fracture (see SmPC for the full indication). It contains teriparatide as the active substance and it is given by the subcutaneous route of administration.

Further information about the evaluation of LIVOGIVA injection’s benefits can be found in LIVOGIVA injection’s EPAR, including in its plain-language summary, available on the EMA website, under the medicine’s webpage.

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

Important risks of LIVOGIVA injection, together with measures to minimise such risks and the proposed studies for learning more about LIVOGIVA injection'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 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, including PSUR assessment - 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 LIVOGIVA injection are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 LIVOGIVA injection. 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).

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

II.B Summary of important risks

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

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies, which are conditions of the marketing authorisation or specific obligation of LIVOGIVA injection.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for LIVOGIVA injection.

Part VII: Annexes

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Annex 4 - Specific adverse drug reaction follow-up forms

Not applicable.

[redacted]

[redacted]

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

Not applicable.

[redacted]

[redacted]

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]