EU Risk Management Plan for Gotenfia (Golimumab)

RMP version to be assessed as part of this application:

RMP Version number: 0.2

Data lock point for this RMP: 2025-Jun-11

Date of final sign off: 2025-Jun-11

Rationale for submitting an updated RMP: RMP was updated to implement SmPC changes.

Summary of significant changes in this RMP: Wording of indication and dosage in Part I adapted to be in line with the reference medicinal product; inclusion of procedure number.

Other RMP versions under evaluation:

RMP Version number: Not applicable

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Details of the currently approved RMP:

Version number: Not applicable

Approved with procedure: Not applicable

Date of approval (opinion date): Not applicable

QPPV Name: Dr. Andreas Iwanowitsch

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)	Golimumab
Pharmacotherapeutic group(s) (ATC Code)	Immunosuppressants, tumour necrosis factor alpha (TNF-α) inhibitors, ATC code: L04AB06
Marketing Authorisation Applicant	STADA Arzneimittel AG
Medicinal products to which this RMP refers	1
Invented name(s) in the European Economic Area (EEA)	Gotenfia
Marketing authorisation procedure	Centralised (EMEA/H/C/006621/0000)
Brief description of the product	Chemical class: Immunosuppressant, TNF-α inhibitor.
	Summary of mode of action: Golimumab is a human monoclonal antibody that forms high affinity, stable complexes with both the soluble and transmembrane bioactive forms of human TNF-α, which prevents the binding of TNF-α to its receptors.
	Important information about its composition: Human IgG1κ monoclonal antibody produced by a murine hybridoma cell line with recombinant DNA technology (biosimilar medicinal product).
Hyperlink to the Product Information	The product information is included in Module 1.3.1 of the eCTD sequence.
Indication(s) in the EEA	Current: Rheumatoid arthritis (RA) Gotenfia, in combination with methotrexate (MTX), is indicated for: • the treatment of moderate to severe, active rheumatoid arthritis in adults when the response to disease-modifying anti-rheumatic drug (DMARD) therapy including MTX has been inadequate.

	• the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with MTX. Golimumab, in combination with MTX, has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function. <u>Juvenile idiopathic arthritis [only Gotenfia 50 mg]</u> *Polyarticular juvenile idiopathic arthritis (pJIA)* Gotenfia in combination with MTX is indicated for the treatment of polyarticular juvenile idiopathic arthritis in children 2 years of age and older, who have responded inadequately to previous therapy with MTX. <u>Psoriatic arthritis (PsA)</u> Gotenfia, alone or in combination with MTX, is indicated for the treatment of active and progressive psoriatic arthritis in adult patients when the response to previous DMARD therapy has been inadequate. Golimumab has been shown to reduce the rate of progression of peripheral joint damage as measured by X-ray in patients with polyarticular symmetrical subtypes of the disease and to improve physical function. <u>Axial spondyloarthritis</u> *Ankylosing spondylitis (AS)* Gotenfia is indicated for the treatment of severe, active ankylosing spondylitis in adults who have responded inadequately to conventional therapy. *Non-radiographic axial spondyloarthritis (nr-Axial SpA)* Gotenfia is indicated for the treatment of adults with severe, active non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI) evidence, who have had an inadequate response to, or are intolerant to nonsteroidal anti-inflammatory drugs (NSAIDs). <u>Ulcerative colitis (UC)</u> Gotenfia is indicated for treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies.

Dosage in the EEA	Current: Rheumatoid arthritis Gotenfia 50 mg given once a month, on the same date each month. Gotenfia should be given concomitantly with MTX. Polyarticular juvenile idiopathic arthritis [only Gotenfia 50 mg] Gotenfia 50 mg administered once a month, on the same date each month, for children with a body weight of at least 40 kg. There is no dosage form for Gotenfia that allows for a 45 mg/0.45 mL dose available for administration to children with polyarticular juvenile idiopathic arthritis weighing less than 40 kg. Thus, it is not possible to administer Gotenfia to patients that require a 45 mg/0.45 mL dose. If a 45 mg/0.45 mL dose is required, another golimumab product should be used instead. Psoriatic arthritis, ankylosing spondylitis, or non-radiographic axial spondyloarthritis Gotenfia 50 mg given once a month, on the same date each month. *Patients with body weight greater than 100 kg* For all of the above indications, in patients with RA, PsA, AS, or nr-Axial SpA with a body weight of more than 100 kg who do not achieve an adequate clinical response after 3 or 4 doses, increasing the dose of golimumab to 100 mg once a month may be considered, taking into account the increased risk of certain serious adverse reactions with the 100 mg dose compared with the 50 mg dose. Continued therapy should be reconsidered in patients who show no evidence of therapeutic benefit after receiving 3 to 4 additional doses of 100 mg. Ulcerative colitis *Patients with body weight less than 80 kg* Gotenfia given as an initial dose of 200 mg, followed by 100 mg at week 2. Patients who have an adequate response should receive 50 mg at week 6 and every 4 weeks thereafter. Patients who have an inadequate response may benefit from continuing with 100 mg at week 6 and every 4 weeks thereafter. *Patients with body weight greater than or equal to 80 kg* Gotenfia given as an initial dose of 200 mg, followed by 100 mg at week 2, then 100 mg every 4 weeks, thereafter.
Pharmaceutical form(s) and strengths	Current: Gotenfia 50 mg solution for injection in pre-filled syringe: Each 0.5 mL pre-filled syringe contains 50 mg of golimumab Gotenfia 100 mg solution for injection in pre-filled syringe: Each 1 mL pre-filled syringe contains 100 mg of golimumab
Is/will the product be subject to additional monitoring in the EU?	Yes

Part II: Safety specification

Gotenfia has been developed as a biosimilar to Simponi, containing golimumab as an active substance. Product name of Gotenfia during non-clinical and clinical development was BAT2506.

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

Gotenfia is indicated in

- Rheumatoid arthritis (RA)
- Polyarticular juvenile idiopathic arthritis (pJIA) [only Gotenfia 50 mg]
- Psoriatic arthritis (PsA)
- Axial spondyloarthritis (Axial SpA) including ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-Axial SpA)
- Ulcerative colitis (UC)

A detailed description of the epidemiology is not required as Gotenfia is a biosimilar.

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

Pharmacokinetic studies with single and multiple doses of BAT2506 and Simponi in cynomolgus monkeys demonstrated similar pharmacokinetic characteristics of the two drugs.

No BAT2506-related toxicity was observed in cynomolgus monkeys after repeated-dose SC injections of BAT2506 at 3, 10 and 50 mg/kg twice weekly for 9 consecutive doses. Blood samples were taken from these monkeys after the first and seventh dose. NOAEL was considered to be 50 mg/kg following BAT2506 repeated dose subcutaneously administered to cynomolgus monkeys. Immunogenicity studies performed as part of the repeated-dose toxicity studies in cynomolgus monkeys showed similar incidence and titer of the anti-drug antibody (ADA) in the BAT2506 and Simponi groups at a dose of 10 mg/kg. In summary, there were no significant differences in systemic toxicity, metabolic characteristics, and immunogenicity between BAT2506 and Simponi when administered at 10 mg/kg. In vitro haemolysis test demonstrated both BAT2506 and Simponi at 25 mg/mL had no haemolytic or aggregation effect on human red blood cells.

Genetic, reproductive, and carcinogenic toxicity studies were not required as no such toxicities have been observed with Simponi.

Part II: Module SIII - Clinical trial exposure

This Module summarizes all clinical trial exposure data of BAT2506 available to the applicant.

The clinical development program for the submission to EMA included three biosimilarity trials with BAT2506 as an SC administration compared to golimumab reference product Simponi (Table SIII.1). Of these, studies BAT-2506-001-CR and BAT-2506-003-CR are Phase 1 pharmacokinetics (PK) trials in healthy, male Chinese subjects and BAT-2506-002-CR is a Phase 3 comparative efficacy/safety trial in patients with active PsA.

General safety data was not pooled across studies since the study populations (i.e., healthy [BAT-2506-001-CR and BAT-2506-003-CR] versus diseased populations [BAT-2506-002-CR]) and dosing period (i.e., single [BAT-2506-001-CR and BAT-2506-003-CR] versus repeat dosing [BAT-2506-002-CR]) are not comparable.

In study **BAT-2506-001-CR**, all individuals (healthy subjects) in the safety set received a single, full dose of BAT2506 (n=90) or EU-Simponi (n=90) as a SC injection of 50 mg.

In study **BAT-2506-003-CR**, all individuals (healthy subjects) in the safety set received a single, full dose of BAT2506 (n=123), EU-approved Simponi (n=125) or US-licensed Simponi (n=121) as an SC injection of 50 mg.

In study **BAT-2506-002-CR**, all individuals (subjects with PsA) in the safety set received at least one dose of study drug, including 351 subjects received BAT2506 only, 187 subjects received EU Simponi only and 166 subjects received EU-Simponi followed by BAT2506. The mean (Standard Deviation [SD]) actual total dose administered was 12.3 (1.9) injections with a range from 1 to 13 injections. Extent of exposure and treatment compliance is summarized in Table SIII.2.

Demographic characteristics for healthy subjects who were evaluated in studies BAT-2506-001-CR and BAT-2506-003-CR, and for subjects with PsA who were evaluated in study BAT-2506-002-CR, are summarized in Table SIII.3, Table SIII.4, and Table SIII.5, respectively. There were no meaningful differences in demographic characteristics across treatment groups in any study.

A further interventional study using BAT2506 (БАТ-2506-002-КИ) has been initiated in Russia by Pharmapark to cover the Russian MOH MAA requirements; no data from this ongoing study are available to the applicant.

Table SIII.1: Studies conducted with BAT2506 SC injection

Study ID	Study Centres	Enrolment Details	Design and Control Type	Study and Reference Products	Study Objective	Subjects by Arm FAS/SS	Duration	Gender (M/F); Age (Median [Range])	Study Population
BAT-2506-001-CR	China 1 site	Start/End 06 Aug 2019/ 31 Mar 2020 Status Complete Planned 182 subjects Analysed (SS) 180 subjects	Phase 1, randomized, double-blind, single-dose, 2-arm parallel, comparative study	Product: BAT2506 Reference Simponi Dosage Single SC injection of 50 mg	To compare PK biosimilarity between BAT2506 and Simponi in healthy Chinese male subjects	BAT2506 90/90 EU-golimumab 90/90	Total 71 days Screening period: Day -14 to Day -2 Hospitalization phase: Day 1 to Day 5 Follow-up phase: Day 3 to Day 71 Treatment Single-dose	Gender 180 M / 0 F 34.5 (20-50)	Healthy, adult male Chinese subjects (≥18 years)
BAT-2506-002-CR	Bulgaria, Czech Republic, Poland, Ukraine, China 60 sites total	Start/End 27 May 2021/ 06 Oct 2023 Status Complete Planned 700 Analysed (SS) 704	Phase 3, multicenter, randomized, double-blind, parallel-group, comparative study	Product BAT2506 Reference Simponi Dosage BAT2506: 50 mg (Week 0 to Week 48) EU-golimumab: 50 mg (Week 0 to Week 48) EU-golimumab 50 mg (Week 0 to Week 20) →BAT2506 50 mg (Week 24 to Week 48)	To demonstrate the equivalence of BAT2506 and Simponi on ACR 20 response in subjects with active PsA	BAT2506 351/351 EU-golimumab 179/187 EU-golimumab→ BAT2506 174/166	Total: 60 weeks Screening: 4 weeks TP1: Week 0 to Week 24 TP: Week 24 to Week 52 Follow up: Until Week 60 Treatment 50 mg administered once every 4 weeks	358 M/ 346 F 46.0 (18-78)	Adult subjects with active PsA (who had PsA for at least 6 months prior to the first administration of the study drug, the presence of ≥3 of 68 tender joint counts and ≥3 of 66 swollen joint counts and at least one active psoriatic lesion with a qualifying lesion of at least 2 cm in diameter at Screening and Randomization)

Study ID	Study Centres	Enrolment Details	Design and Control Type	Study and Reference Products	Study Objective	Subjects by Arm FAS/SS	Duration	Gender (M/F); Age (Median [Range])	Study Population
BAT-2506-003-CR	China 1 site	Start/End 01 Aug 2022/ 10 Jul 2023 Status Complete Planned 375 subjects Analysed (SS) 369 subjects	Phase 1, randomized, double-blind, single-dose, parallel three-arm comparative study	Product BAT2506 Reference Simponi Dosage Single SC injection of 50 mg	To compare the similarity of pharmacokinetics between BAT2506 Injection and Simponi after a single subcutaneous injection in healthy Chinese male subjects	BAT2506 123/123 EU-golimumab 125/125 US-golimumab 121/121	Total 78 days Screening: Day -14 to Day -2 Hospitalization phase: Day 1 to Day 5 Follow-up: Day 6 to Day 78 Treatment Single-dose	369 M/ 0 F 34.0 (18-54)	Healthy, adult male Chinese subjects (≥18 years)

Abbreviations: ECG = Electrocardiography; FAS = Full Analysis Set; SS = Safety Set; TEAEs = Treatment Emergent Adverse Events; TP = Treatment Period.

Table SIII.2: Extent of Exposure and Treatment Compliance (Study BAT-2506-002-CR)

	BAT2506 (N=351) n (%)	Simponi (N=187) n (%)	Simponi→ BAT2506 (N=166) n (%)	All subjects (N=704) n (%)
Treatment duration (Weeks) [1]				
Mean (SD)	50.5 (6.2)	48.1 (11.3)	51.5 (2.8)	50.1 (7.5)
Median	52.0	52.0	52.0	52.0
Actual dose administered (injections) overall				
Mean (SD)	12.4 (1.6)	11.8 (2.8)	12.7 (0.9)	12.3 (1.9)
Median	13.0	13.0	13.0	13.0
Min, Max	1, 13	1, 13	7, 13	1, 13
Actual dose administered (injections) in TP1				
n	351	187	166	704
Mean (SD)	5.9 (0.5)	5.7 (1.0)	5.9 (0.3)	5.8 (0.7)
Median	6.0	6.0	6.0	6.0
Min, Max	1, 6	1,6	3, 6	1, 6
Actual dose administered (injections) in TP2				
n	341	172	166	679
Mean (SD)	6.7 (0.8)	6.7 (1.0)	6.8 (0.9)	6.7 (0.9)
Median	7.0	7.0	7.0	7.0
Min, Max	2, 7	1, 7	1, 7	1, 7

[1] Treatment Duration = last administration visit/weeks + 4 weeks.
Source: CSR Study BAT-2506-002-CR CSR, Table 14.1.7.

Table SIII.3: Demographic Baseline Characteristics Study BAT-2506-001-CR (FAS, Phase 1, Healthy Subjects)

	BAT2506 (N = 90)	EU-Simponi (N=90)	Total (N=180)
Age (years)			
Mean (SD)	35.0 (8.18)	35.6 (8.10)	35.3 (8.12)
Median (Q1, Q3)	34.5 (28.0, 41.0)	34.5 (29.0, 42.0)	34.5 (28.5, 41.0)
Min, Max	20, 50	20, 50	20, 50
Gender [n (%)]			
Male	90 (100)	90 (100)	180 (100)
Female	0	0	0
Ethnicity [n (%)]			
Han ethnicity	84 (93.3)	87 (96.7)	171 (95.0)
Others	6 (6.7)	3 (3.3)	9 (5.0)
Weight (kg)			
Mean (SD)	66.39 (7.541)	65.20 (7.691)	65.80 (7.619)
Median (Q1, Q3)	65.45 (60.40, 72.50)	65.35 (59.90, 71.20)	65.45 (60.25, 71.95)
Min, Max	51.2, 79.8	50.1, 79.3	50.1, 79.8

	BAT2506 (N = 90)	EU-Simponi (N=90)	Total (N=180)
Body mass index (kg/m^2)			
Mean (SD)	23.10 (2.332)	23.14 (2.496)	23.12 (2.409)
Median (Q1, Q3)	23.00 (21.20, 25.20)	23.30 (21.20, 24.90)	23.10 (21.20, 25.05)
Min, Max	18.7, 28.0	18.1, 27.9	18.1, 28.0

Abbreviations: BMI = Body Mass Index; N = number of subjects, SD = Standard Deviation.
Source: CSR Study BAT-2506-001-CR CSR, Table 14.1.2.

Table SIII.4: Demographic Baseline Characteristics Study BAT-2506-003-CR (FAS, Phase 1, Healthy Subjects)

	BAT2506 (N = 123)	EU-approved Simponi (N=125)	US-licensed Simponi (N=121)	Total (N=369)
Age (years)				
Mean (SD)	35.2 (10.4)	34.8 (10.0)	35.1 (10.4)	35.0 (10.2)
Median	35.0	34.0	34.0	34.0
Min, Max	18, 54	18, 54	19, 54	18, 54
Gender [n (%)]				
Male	123 (100)	125 (100)	121 (100)	369 (100)
Female	0	0		0
Ethnicity [n (%)]				
Han ethnicity	113 (91.9)	117 (93.6)	110 (90.9)	340 (92.1)
Others	10 (8.1)	8 (6.4)	11 (9.1)	29 (7.9)
Weight (kg)				
Mean (SD)	65.76 (7.90)	66.13 (7.84)	66.23 (8.17)	66.04 (7.95)
Median	66.40	67.10	67.20	66.70
Min, Max	50.2, 79.9	50.0, 79.9	50.0, 79.8	50.0, 79.9
Body mass index (kg/m^2)				
Mean (SD)	23.06 (2.64)	23.35 (2.62)	23.22 (2.39)	23.21 (2.55)
Median	23.20	23.50	23.40	23.40
Min, Max	18.0, 27.9	18.1, 27.9	18.3, 27.9	18.0, 27.9

Abbreviations: BMI = Body Mass Index; N = number of subjects, SD = Standard Deviation.
Source: CSR Study BAT-2506-003-CR, Table 14.1.3.

Table SIII.5: Demographic Baseline Characteristics Study BAT-2506-002-CR (FAS1, Phase 3, PsA Subjects)

	BAT2506 (N = 351)	EU-Simponi (N=179)	Simponi→BAT2506 (N=174)	Combined Simponi (N=353)	Total (N=704)
Age (years)					
Mean (SD)	46.6 (11.8)	44.9 (12.1)	45.1 (12.7)	45.0 (12.4)	45.8 (12.1)
Median	47.0	45.0	46.0	45.0	46.0
Min, Max	18, 78	20, 74	19, 73	19, 74	18, 78
Region [n (%)]					
Asia	44 (12.5%)	25 (14.0%)	23 (13.2%)	48 (13.6%)	92 (13.1%)
Europe	307 (87.5%)	154 (86.0%)	151 (86.8%)	305 (86.4%)	612 (86.9%)
Gender [n (%)]					
Male	180 (51.3%)	97 (54.2%)	81 (46.6%)	178 (50.4%)	358 (50.9%)
Female	171 (48.7%)	82 (45.8%)	93 (53.4%)	175 (49.6%)	346 (49.1%)
Ethnicity [n (%)]					
Asian	44 (12.5%)	25 (14.0%)	24 (13.8%)	49 (13.9%)	93 (13.2%)
White	307 (87.5%)	154 (86.0%)	150 (86.2%)	304 (86.1%)	611 (86.8%)
Weight (kg)					
Mean (SD)	81.92 (17.01)	82.98 (19.03)	80.19 (19.04)	81.60 (19.06)	81.76 (18.05)
Median	80.70	80.00	78.50	79.60	80.00
Min, Max	47.0, 133.2	44.0, 140.0	46.0, 139.8	44.0, 140.0	44.0, 140.0
Body mass index (kg/m^2)					
Mean (SD)	27.87 (4.93)	28.37 (5.94)	27.60 (5.71)	27.99 (5.83)	27.94 (5.40)
Median	27.40	27.67	26.75	27.08	27.26
Min, Max	18.13, 49.24	18.52, 49.45	16.85, 46.65	16.85, 49.45	16.85, 49.45

Abbreviations: BMI = Body Mass Index; N = number of subjects, SD = Standard Deviation.
Note: Full Analysis Set 1 (FAS1) comprised all subjects randomised to a study treatment arm.
Source: CSR Study BAT-2506-002-CR, Table 14.1.4.1.1.

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

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

Table SIV.1: Important Exclusion Criteria in Pivotal Clinical Trials Across the Development Program

Exclusion criterion	Reason for exclusion	considered to be included as missing information	Rationale
Subjects with a history of allergies to the study drug, or subjects with allergic constitution (allergic to a variety of drugs and foods)	Individuals with a known hypersensitivity to human IgG proteins or any of the components of golimumab would be at a higher risk of subsequent serious systemic hypersensitivity reactions with re-exposure.	No	Gotenfia is contraindicated in patients with a history of hypersensitivity to golimumab or to any of the excipients (SmPC, section 4.3)
Subjects with clinically significant chronic or acute infections at screening/enrollment, or with active infections, including acute and chronic infections and local infections (bacteria, viruses, parasites, fungi or other pathogens of opportunistic infectious diseases)	Treatment with anti-TNFα agents may increase the risk of the development of infections or worsen an existing infection. Serious infections are considered a class effect of these agents.	No	*Serious infections* is an important identified risk. Information about infections is described in the SmPC. The risk to this patient population is adequately addressed in the SmPC and the Patient Card.
Subjects with a history of tuberculosis, or with latent tuberculosis infection or clinically suspected tuberculosis (including but not limited to pulmonary tuberculosis); and subjects who had contacted with tuberculosis patients or/and had symptoms and/or signs suspected of being tuberculosis within 3 months prior to screening			

Subjects positive for hepatitis B surface antigen at screening [or negative hepatitis B surface antigen and meeting all three of the following: positive hepatitis B core antibody, negative hepatitis B surface antibody, and hepatitis B virus deoxyribonucleic acid (HBV DNA) levels exceed the normal quantification range]; or positive hepatitis C antibody, hepatitis C core antigen, HIV antigen/antibody, or positive syphilis spirochete antibody			
Subjects whose abnormalities in past medical history were clinically significant or other clinical findings suggested the following clinically significant diseases (including but not limited to gastrointestinal, renal, hepatic, neurological, blood, endocrine, neoplastic, pulmonary, immune, psychiatric or cardiovascular and cerebrovascular diseases)	This is a typical, prudent, precautionary position applied to clinical trial subjects when a drug was not widely used in humans.	No	Given the severity of disease in these subjects, the risk/benefit balance of the use of Gotenfia should be carefully evaluated on a case-by-case basis. Guidance on the use of Gotenfia in subjects with hematologic and neurologic disorders is provided in section 4.4 of the SmPC (Special warnings and precautions for use).
Subjects who suffered from malignant tumours (excluding those with basal cell carcinoma which had been surgically resected)	Published medical literature suggests that certain types of malignancies may be adversely affected by TNFα blockade. The potential role of TNF-blocking therapy in the development of certain types of malignancies is not known.	No	*Malignancy* is an important identified risk. The risk to this patient population is adequately addressed in the SmPC.
Subjects who had received live/attenuated vaccine within 12 weeks prior to study administration or plan to receive live/attenuated vaccine during study period;	Treatment with anti-TNFα agents may increase the risk of the development of	No	*Breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero* is an important potential risk. The risk of live vaccinations is

Subjects who had received inactivated vaccine (including COVID-2019 inactivated vaccine) within 2 weeks prior to administration or planned to receive inactivated vaccine during study period	infections or worsen an existing infection.		adequately addressed in the SmPC and the Patient Card.
Subjects who had used Simponi, any anti-TNF-α biologic, or have used any biologics or monoclonal antibodies within 6 months prior to enrollment	These agents were prohibited or required a washout period to reduce the risk of concomitant immunosuppression or the risk of adverse events (AEs) after the use of these agents.	No	This risk is adequately addressed in the SmPC.
Subjects who had been treated with cytotoxic agents, (including but not limited to azathioprine, cyclosporine, cyclophosphamide), nitrogen mustard, chlorambucil, or other alkylating agents within 6 months prior to the first administration of the study drug	To reduce the risk of concomitant immunosuppressants or the risk of AEs after cytotoxic agent use, these agents were prohibited or required a washout period.	No	The concomitant use of biologics and other immunosuppressants for the treatment of autoimmune disease is associated with an increase in AEs with no increase in efficacy (Genovese 2004; Weinblatt 2006). The risk of immunosuppression with Gotenfia and interactions with other medicinal products is addressed in the SmPC (section 4.4).
Subjects who are pregnant, nursing, or planning a pregnancy or fathering a child within 6 months after receiving the last administration of trial medication	Per International Council for Harmonisation (ICH) guidelines, pregnant women should normally be excluded from clinical trials.	No	<u>Exposure during pregnancy</u> Guidance for the use of Gotenfia during pregnancy is provided in the SmPC (section 4.6). <u>Use during breastfeeding</u> Guidance for the use of Gotenfia during breastfeeding is provided in the SmPC (section 4.6).

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/cumulative exposure.

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

Table SIV.2 presents an overview of special populations in the completed clinical trials.

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

Type of special population	Exposure
Pregnant women	Although prohibited by protocol, 1 case of exposure to BAT2506 during pregnancy was reported in the clinical development program.
Breastfeeding women	Breastfeeding women were not included in the clinical development program.
Patients with relevant comorbidities: • Patients with hepatic impairment • Patients with renal impairment • Patients with cardiovascular impairment • Immunocompromised patients • Patients with a disease severity different from inclusion criteria in clinical trials	Generally, patients with relevant comorbidities were not included in the clinical development program. However, by default, subjects participating in BAT2506 clinical trials are immunocompromised as a result of their underlying disease, their concomitant medications, and by virtue of receiving treatment with a TNFα inhibitor.
Population with relevant different ethnic origin	BAT2506 clinical trials have been conducted globally in a variety of ethnic groups. The majority of subjects in clinical trials were white.
Subpopulations carrying relevant genetic polymorphisms	Not included in the clinical development program.
Children	Not included in the clinical development program.
Elderly	A total of 40 subjects ≥65 years old have been exposed to BAT2506 in the phase 3 trial in patients with active PsA (BAT-2506-002-CR).

Part II: Module SV - Post-authorisation experience

SV.1 Post-authorisation exposure

As Gotenfia is not yet authorized in the EU or another region outside the EU no post-authorisation data are available.

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

Potential for misuse for illegal purposes

No trials have been conducted to evaluate the dependence potential of golimumab. Drugs with abuse potential generally include drugs that affect the central nervous system, drugs that are chemically or pharmacologically similar to other drugs with known abuse potential, and drugs that produce psychoactive effects such as sedation, euphoria, or mood change (Food and Drug Administration 2017).

As a class, therapeutic mAbs are not associated with dependence; their chemical structure differs from central nervous system-active drugs associated with dependence. The pharmaceutical characteristics and pharmacokinetic (PK)/pharmacodynamic (PD) characteristics of golimumab are not characteristic of drugs with high dependence potential (eg, rapid onset/short-acting active substances).

Part II: Module SVII - Identified and potential risks

Gotenfia has been developed as a biosimilar to Simponi, which has been marketed in the EU since 01 October 2009. The safety concerns of Gotenfia are based on the originator's RMP. For the list of safety concerns please see section SVIII.

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

The safety concerns of Gotenfia are based on the originator's RMP. All of the risks were included in this RMP. For the list of safety concerns please see section SVIII.

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

The safety concerns of Gotenfia are based on the originator's RMP. All of the risks were included in this RMP. For the list of safety concerns please see section SVIII.

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

Not applicable as this section applies to RMP updates after the granting of the marketing authorisation.

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

Serious infections:

Potential mechanisms:
Tumour necrosis factor alpha is a mediator of cellular immune responses and inflammation, which are important in host defence against certain pathogens, especially intracellular pathogens. Anti-TNFα agent therapy reduces the ability to mount an inflammatory response against such pathogens. Gotenfia may therefore inhibit protective immune responses to intracellular bacteria (including mycobacteria) and opportunistic pathogens and may also allow HBV reactivation.

Evidence source(s) and strength of evidence:
Because they suppress the immune system, drugs that inhibit TNFα have been associated with an increased risk of serious infections (some fatal), including opportunistic infections, TB, and invasive fungal infections. Drugs that inhibit TNFα have also been associated with HBV reactivation in patients who are chronic carriers of the virus.

In the comparability studies of BAT2506, events of “infections and infestations” were common TEAEs (≥4%) and were observed across all the treatment groups in both healthy subjects (Study BAT-2506-001-CR: 8/180 [4.4%], overall; Study BAT-2506-003-CR 109/369 [29.5%] overall) and PsA patients (Study BAT-2506-002-CR 242/704 [34.4%] overall).

Serious infections is considered an important identified risk because of the consistency of evidence across multiple sources, including data from products in the same class.

Characterisation of the risk:
The impact of this risk on the individual patient is potentially significant. Patients who are exposed to and subsequently infected with an infectious agent may have a more severe course due to use of the product.

Risk factors and risk groups:
Serious Infections

Risk factors for the development of serious infections include the use of steroids, other immunosuppressive drugs (including MTX), or other biologics at the same time as Gotenfia.

Opportunistic Infections

People whose immune status is compromised are susceptible to opportunistic infections. Risk factors for opportunistic infections may therefore include HIV disease, increased age, having an organ transplant, immunosuppressive drug therapy (corticosteroids, MTX, azathioprine, and biologic agents), chronic pulmonary disease, and chronic renal failure.

Invasive Fungal Infections

People who have resided in or travelled to regions where invasive fungal infections are common are at increased risk.

Tuberculosis

The most common risk factors for the development of TB include conditions that weaken the immune system such as advanced age, HIV infection, alcohol abuse, malignancy, use of

corticosteroids or other immunosuppressive drugs such as MTX, connective tissue disease, renal failure, diabetes, and pregnancy.

Other risk factors for the development of TB include contact with a person with active TB infection and having been born in, lived in, or travelled to countries where the incidence of TB is high. Exposure to TB may occur through various health care settings (eg, hospitals and nursing homes) or high-density institutions (eg, prisons).

Hepatitis B Virus Reactivation

Risk factors for the acquisition of HBV include being born to a mother from a highly endemic area, emigration from a highly endemic area, history of IV drug use, and a history of multiple sexual partners. Patients at risk for HBV reactivation are those who are chronic carriers of this virus (ie, surface antigen-positive), especially those who become immunosuppressed. Approximately 14% to 50% of immunosuppressed patients who are chronic carriers of HBV will experience acute reactivations during the natural history of their disease (Shibolet 2002). Thus, risk factors for HBV reactivation in patients with a history of HBV infection include the concomitant use of medications that suppress the immune system (eg, chemotherapy, corticosteroids, MTX, azathioprine, TNFα inhibitors). Other risk factors that may contribute to HBV reactivation include HIV infection, transplantation (especially bone marrow), and withdrawal from immunosuppressive therapies (Ocama 2005).

Preventability:
Gotenfia is contraindicated in patients with active TB or other severe infections such as sepsis and opportunistic infections (SmPC Section 4.3 [Contraindications]). The risk of serious infections is described in the Patient Card (see Part V.2).

Serious Infections and Opportunistic Infections

Section 4.4 of the SmPC (Special warnings and precautions for use) states that golimumab should not be given to patients with a clinically important, active infection. Caution should be exercised when considering the use of golimumab in patients with a chronic infection or a history of recurrent infection. Patients should be advised of, and avoid exposure to, potential risk factors for infection as appropriate. Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, they should be closely monitored and golimumab should not be administered until the infection resolves.

Invasive Fungal Infections

Section 4.4 of the SmPC (Special warnings and precautions for use) states that for patients who have resided in or travelled to regions where invasive fungal infections are endemic, the benefits and risks of golimumab treatment should be carefully considered before initiation of therapy.

Tuberculosis

Patients who are being considered for golimumab therapy should be evaluated for TB infection. Golimumab should not be given to patients with active TB. Golimumab should not be given to patients with latent TB unless treatment for latent TB is initiated prior to administering golimumab, including those patients with a past history of latent TB in whom an adequate course of treatment cannot be confirmed. Patients receiving golimumab should be monitored closely for signs and symptoms of active TB during and after treatment (SmPC Section 4.4 [Special warnings and precautions for use]).

Hepatitis B Virus Reactivation

All patients should be screened for HBV infection prior to initiation of Gotenfia. In patients who test positive for hepatitis B surface antigen, consultation with a physician with expertise in the treatment of HBV infection is recommended. Chronic carriers of HBV should be appropriately evaluated and monitored prior to initiation of, during treatment with, and for several months following discontinuation of Gotenfia (SmPC Section 4.4 [Special warnings and precautions for use]).

Impact on the risk-benefit balance of the product:
The observed incidence of serious infections has not had a significant impact on the risk-benefit balance of the product. Risk minimization measures are in place and considered adequate and proportionate to the risk; the SmPC and PL provide information to the prescriber and patient on how to manage this important identified risk. In addition, the safety concern is addressed in the Patient Card.

Public health impact:
The public health impact of the development of serious infections during treatment with Gotenfia is not known.

Demyelinating disorders:

Potential mechanisms:
The role that TNFα plays as an immunomodulator suggests that TNFα blockade may promote the development of drug-induced neuropathies by augmenting the number of activated peripheral T cells and thereby enhancing autoimmune responses by altering antigen presenting cell function, potentiating T-cell receptor signalling, and/or decreasing apoptosis of autoreactive T cells. These autoreactive T cells might also drive the maturation of B cells into cells secreting autoantibodies to neuronal-specific antigens (Stübgen 2008).

Evidence source(s) and strength of evidence:
Demyelinating disorders (both central and peripheral) have been associated with the use of TNFα inhibitors.

Demyelinating disorders is considered an important identified risk because of the consistency of evidence across multiple sources, including data from products in the same class.

Characterisation of the risk:
Demyelinating disorders are considered a class effect for anti-TNFα agents. Demyelinating disorders are listed in the Gotenfia SmPC (Section 4.4 [Special warnings and precautions for use] and Section 4.8 [Undesirable effects]).

The impact of this risk on the individual patient can vary from minimal to significant. Patients with pre-existing or recent onset of demyelinating disorders may have a more severe course due to use of the product. This risk needs to be carefully weighed against the benefit conferred by use of the medication.

Risk factors and risk groups:
Multiple sclerosis (MS) and other autoimmune diseases have been linked to genetic and environmental factors. First-degree relatives of MS patients are at greater risk of developing MS than the general population (Didonna 2015). Whites, particularly of northern European descent, are also more likely to develop MS (Ascherio 2016).

Several studies have suggested an association between smoking and MS (Ascherio 2016). Obesity in early life and Epstein-Barr virus have also been identified as risk factors for MS (Ascherio 2016).

Preventability:
Predictability and preventability of the development of demyelination is not known. In patients with pre-existing or recent onset of demyelinating disorders, the benefits and risks of anti-TNFα agents should be carefully considered before initiation of Gotenfia therapy (SmPC Section 4.4 [Special warnings and precautions for use]).

Impact on the risk-benefit balance of the product:
Demyelinating disorders is an unusual risk. Risk minimization measures are in place and considered adequate and proportionate to the risk. The SmPC and PL provide information to the prescriber and patient on how to manage this important identified risk.

Public health impact:
The public health impact of the development of demyelinating disorders during treatment with Gotenfia is not known.

Malignancy:

Potential mechanisms:
Immunomodulation by TNFα may be important in tumour surveillance, although the literature is not consistent on this point (Torre-Amione 1996). While TNFα was shown to exert cytotoxic and/or cytostatic effects on a number of human and murine tumour cell lines, some malignant cell lines are TNFα-resistant or even proliferate in the presence of low levels of TNFα and TNFα may behave as a tumour promoter particularly in the setting of unresolved, chronic inflammation (Balkwill 2006). Therefore, the effects attributed to TNFα in published medical literature suggesting that certain types of malignancies may be adversely affected by TNFα blockade may apply to Gotenfia.

Of note, HSTCL is a rare and rapidly progressive subtype of peripheral T-cell lymphoma and has been reported following TNFα-blocker therapy. Most patients who developed HSTCL were adolescent or young adult males. Almost all these patients had also received azathioprine or 6-mercaptopurine. Hypothetical mechanisms include (1) inhibition of TNF signalling resulting in impaired immune surveillance particularly affecting the detection and elimination of cells with chromosomal abnormalities resulting from azathioprine or 6-mercaptopurine therapy and (2) alterations in azathioprine or 6-mercaptopurine metabolism in patients receiving anti-TNF therapy (Shale 2008).

Evidence source(s) and strength of evidence:
In Phase 3 Study BAT-2506-002-CR AEs by SOC “Neoplasms benign, malignant and unspecified (including cysts and polyps)” were reported in 15 subjects, most of AEs were considered not related or unlikely related to the study drug.

The development of malignancy is considered an important identified risk because the effects attributed to TNFα in published medical literature, suggesting that certain types of malignancies may be adversely affected by TNFα blockade, may apply to Gotenfia.

Characterisation of the risk:
The risk of malignancy is addressed in the Gotenfia SmPC (Section 4.4 [Special warnings and precautions for use] and/or Section 4.8 [Undesirable effects]) and certain subtypes of malignancies are listed as ADRs.

The impact of this risk on the individual patient is potentially significant, particularly in patients with an existing malignancy, a history of malignancy, or significant risk factors for malignancy such as a history of heavy smoking.

Risk factors and risk groups:
Because disease severity, cumulative disease activity, and disease duration may also contribute to an increased risk of malignancy in patients with immune-mediated diseases, it is difficult to distinguish the individual contribution of immunosuppressive medications, including those like Gotenfia that inhibit TNFα, from other risk factors for the development of malignancy (Jones 1996; Tennis 1993; Silman 1988). This is further complicated by the fact that patients with severe disease are more likely to have been treated with one or more immunosuppressive medications.

There are a number of conflicting studies related to the risk of malignancies with the use of MTX. A retrospective analysis of 16,263 RA patients registered at the Mayo Clinic between 1976 and 1992 showed no relationship between the development of malignancy and the dose or duration of MTX compared with any other DMARD (Moder 1995).

Information regarding additional risk factors for the malignancy subtypes included in the broad category of malignancy is given below.

Lymphoma

- Lymphoma: Risk factors for the development of lymphoma include older age, male gender, family history, immunosuppression (due to medications [such as immunosuppression for organ transplants, chemotherapy for cancer or treatment for autoimmune diseases], infection with HIV, or from immune deficiencies due to an inherited syndrome), autoimmune diseases with chronic inflammation (RA, systemic lupus erythematosus, Sjögren's syndrome, celiac disease), infections that directly transform lymphocytes (human T-cell lymphotropic virus, Epstein-Barr virus, human herpes virus 8), infections that cause chronic immune stimulation (Helicobacter pylori, Chlamydophila psittaci, Campylobacter jejuni, chronic hepatitis C infection), radiation exposure, and exposure to certain chemicals among others (Baecklund 2006; Smedby 2006; Hartge 2007; Cerhan 2014; American Cancer Society 2018).
- Hepatosplenic T-cell lymphoma: young men, the immunocompromised, and patients undergoing solid organ transplantation appear to be at a higher risk for HSTCL (Belhadj 2003).

Skin Cancer

- Melanoma: Risk factors for the development of melanomas can be categorized as environmental or host factors. Exposure to ultraviolet (UV) light, especially in patients with a fair complexion, history of sunburns, and poor ability to tan, is the most strongly correlated environmental risk factor with the development of melanoma. Patients with xeroderma pigmentosum who do not have the ability to repair UV light-induced DNA damage are particularly susceptible. Family or personal history of melanoma and/or certain gene mutations are strong host risk factors. Additional host risk factors include the presence of 5 or more

dysplastic nevi, a large number of nevi, and giant congenital nevus. Patients with conditions that are associated with immune suppression (ie, HIV, organ transplantation) are at higher risk of developing melanomas (American Cancer Society 2016).

- Nonmelanoma skin cancer: The risk factors for basal cell or squamous cell skin cancer include UV light exposure, increasing age, arsenic exposure, radiation exposure, previous skin cancer, long-term or severe skin inflammation or injury, specific genetic syndromes, and a weakened immune system (American Cancer Society 2023). With respect to patients with RA, epidemiological trials have generally shown that skin cancers are increased in this group, and immunosuppression may potentiate this risk by shortening the time taken to develop a malignancy (Wolfe 2007). With respect to psoriasis patients, a higher risk of NMSC is seen in those with prior coal tar, UVB therapy, psoralen plus UVA light, retinoids, and cyclosporine therapy (Stern 1998; Nijsten 2003; Curtin 2005).
- Merkel cell carcinoma (MCC): Although the cause of MCC remains unclear, risk factors associated with its development include exposure to UV radiation, immunosuppression, and possibly viral causes. Most MCCs are located on sun exposed areas, particularly the head and neck, extremities, and trunk. Merkel cell carcinoma occurs most frequently in elderly white patients and affects males more commonly than females (Duprat 2011; Wang 2011). Immunosuppression increases the risk of MCC in patients with HIV and in solid organ transplant patients. Patients with other tumours, such as SCC and chronic lymphocytic leukaemia, also have an increased risk of MCC (Wang 2011).

Leukaemia

- Risk factors for the development of leukaemia include genetic abnormalities, family history, radiation exposure, chemotherapy, autoimmune diseases with chronic inflammation and exposure to certain chemicals among others (Choi 2014; Elbæk 2016).

Preventability:
Predictability and preventability of the development of malignancy is not known. Caution should be exercised when considering the use of Gotenfia in patients with a history of malignancy or when considering continuing treatment in patients who develop a malignancy (SmPC Section 4.4 [Special warnings and precautions for use]).

For skin cancer, specific preventive measures can be taken such as limiting sun exposure, especially in the middle of the day (between the hours of 10 am and 4 pm). Also, use of sunscreen, protective clothing, and hats are recommended to limit exposure to UV light. Periodic skin examinations are recommended for all patients, particularly for patients with risk factors for skin cancer.

Impact on the risk-benefit balance of the product:
The observed incidence of malignancy (including lymphoma, HSTCL, skin cancer and leukemia) has not had a significant impact on the risk-benefit balance of the product. It is expected that the risk of malignancy will be further characterized by the PV activities outlined in this RMP. Leukemia is well characterized and based upon the small number of events reported to date, there is limited possibility of further characterization. Risk minimization measures are in place and considered adequate and proportionate to the risk; the SmPC and PL provide information to the prescriber and patient on how to manage the important identified risk of malignancy.

Public health impact:
The public health impact of the development of malignancy during treatment with Gotenfia is not known.

Serious depression including suicidality:

Potential mechanisms:
The exact biological mechanism of depression is not known. Cytokines may be involved with serotonin metabolism (Dantzer 1999). More specifically, pro-inflammatory cytokines such as TNFα are associated with major depression; reducing the effect of these cytokines may reverse depressive symptoms (Tyring 2006). The mechanism by which Gotenfia could affect mood is not known.

Evidence source(s) and strength of evidence:
Depression has been reported in clinical trials and in the postmarketing setting of Simponi and is described in published medical literature.

Although serious depression has been reported in patients treated with golimumab, a causal association between the development or worsening of serious depression (including suicidality) and golimumab has not been established. Complicating the assessment is evidence that patients with RA, AS, and PsA have increased rates of depression compared to the general population (Isik 2007; Sundquist 2008; Kotsis 2012). Additionally, while some researchers have found no evidence of an association between depression and UC, others have suggested that depression and anxiety are common in patients with IBD (Sajadinejad 2012; Román 2011).

Characterisation of the risk:
Depression is listed in the Gotenfia SmPC (Section 4.8 [Undesirable effects]).

The impact of this risk on the individual patient can vary from minimal to considerable. This risk needs to be carefully weighed against the benefit conferred by use of the medication.

Risk factors and risk groups:
Risk factors for depression include older age and associated neurologic conditions, recent childbirth, stressful life events, a personal or family history of depression, and selected medical comorbid conditions. Suicide rates are twice as high in families of suicide victims (Fancher 2007).

Preventability:
There is no known means of preventing depression. There are screening tools available to identify patients with depression. Patients with a history of untreated or inadequately treated depression should be treated for such.

Impact on the risk-benefit balance of the product:
The observed incidence of serious depression, including suicidality has not had a significant impact on the risk-benefit balance of the product. Routine risk minimization measures that are considered adequate and proportionate to the risk are in place.

Public health impact:
The public health impact of the development of serious depression (including suicidality) during treatment with Gotenfia is not known.

Breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero:

Potential mechanisms:
Following treatment with a TNFα-blocking mAb during pregnancy, the antibody was detected for up to 6 months in the serum of the infant born to the treated woman. Because TNFα inhibitors reduce the immune response, administration of a TNFα inhibitor during pregnancy may predispose infants to breakthrough infections when receiving live (attenuated) vaccines within 6 months after birth. It is known that Gotenfia crosses the placenta during pregnancy and so this risk may also apply to Gotenfia.

Evidence source(s) and strength of evidence:
A small number of cases of breakthrough infection have occurred after administration of live vaccines in infants exposed to another TNFα-blocking agent in utero (REMICADE SmPC Section 4.4). No cases have been identified in originator's product Simponi and the biosimilar Gotenfia.

Characterisation of the risk:
There have been no reported cases of breakthrough infections following administration of live (attenuated) vaccines in infants born to women who received Gotenfia.

Women who were pregnant, nursing, or planning a pregnancy were excluded from Gotenfia clinical trials. In addition, if a woman became pregnant while participating in a clinical trial, the study agent was discontinued.

Breakthrough infection after administration of live (attenuated) vaccines in infants exposed to TNFα inhibitors in utero, including Gotenfia, is considered a class effect. It is considered an important potential risk because the impact of this risk is potentially significant.

Risk factors and risk groups:
Infants exposed to Gotenfia in utero and who receive live (attenuated) vaccines within 6 months after birth may be at risk for developing breakthrough infection.

Preventability:
Administration of live (attenuated) vaccines to infants exposed to Gotenfia in utero is not recommended for 6 months following the mother's last Gotenfia injection during pregnancy (SmPC Section 4.6 [Fertility, pregnancy and lactation]). The risk of breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero is described in the Patient Card (see Part V.2).

Impact on the risk-benefit balance of the product:
As there are no reported cases, breakthrough infection after administration of live (attenuated) vaccines in infants with in utero exposure to Gotenfia has not had a significant impact on the risk-benefit balance of the product. Risk minimization measures are in place and considered adequate and proportionate to the risk; the SmPC, PL, and Patient Card provide information to the prescriber and patient on how to manage this important potential risk.

Public health impact:
The potential public health impact is not known.

SVII.3.2. Presentation of the missing information

Long-term safety in pediatric patients:

Evidence source:
Comorbidities of patients with pJIA differ from those of non-pJIA patients and therefore the long-term safety profile of golimumab in patients with pJIA may differ from that in other indications.

A relatively small number of children ≥2 to <18 years of age (173) were exposed to golimumab in the originator's pJIA trial CNTO148JIA3001, in which the average duration of follow-up for randomized subjects was 107 weeks. Although no risks of clinical significance were identified in golimumab-treated subjects, the effect of long-term treatment with golimumab in this patient population has not been studied.

Population in need of further characterisation:
Pediatric patients ≥2 years of age who have been treated with Gotenfia long term. An observational postauthorisation safety study (PASS) conducted by the originator to investigate the long-term safety of golimumab in pJIA subjects using the German Biologics JIA Registry (BiKeR), in which patients are followed for up to 5 years, is ongoing.

Part II: Module SVIII - Summary of the safety concerns

Gotenfia has been developed as a biosimilar to Simponi, which has been marketed in the EU since 2009. The safety concerns of Gotenfia are based on the originator's RMP (Simponi: EPAR – Risk management plan, last updated on 15 December 2023, available on Simponi | European Medicines Agency (EMA) (europa.eu)).

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Serious infections • Demyelinating disorders • Malignancy
Important potential risks	• Serious depression including suicidality • Breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero
Missing information	• Long-term safety in pediatric patients

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

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:

Specific adverse reaction follow-up questionnaires for the safety concerns:

- **Serious infections**
    - TOI TFUQ to collect information on serious infections and opportunistic infections
    - TOI TFUQ to collect information on TB
    - TOI TFUQ to collect information on progressive multifocal leukoencephalopathy/reversible posterior leukoencephalopathy syndrome
- **Malignancy**
    - TOI TFUQ to collect information on malignancy events (including lymphoma, second and secondary malignancies). Particular attention is paid to subjects ≤30 years of age.

The specific adverse reaction follow-up questionnaires are provided in Annex 4.

Other forms of routine pharmacovigilance activities:

Not applicable.

III.2 Additional pharmacovigilance activities

No additional pharmacovigilance activities are planned.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable.

Part IV: Plans for post-authorisation efficacy studies

No post-authorisation efficacy studies have been imposed or are planned.

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

Table Part V.1: Description of routine risk minimisation measures by safety concern

Safety concern	Routine risk minimisation activities
Serious infections	**Routine risk communication:** SmPC sections - 4.3 (Contraindications), - 4.4 (Special warnings and precautions for use), - 4.5 (Interaction with other medicinal products and other forms of interaction), and - 4.8 (Undesirable effects) Package Leaflet (PL) sections 2 and 4 **Routine risk minimization activities recommending specific clinical measures to address the risk:** SmPC section 4.4 (Special warnings and precautions for use) • Guidance on evaluating patients for infections prior to treatment initiation, monitoring patients for infections during and after treatment, and managing patients who develop infections SmPC section 4.5 (Interaction with other medicinal products and other forms of interaction) • Recommendations regarding the administration of live vaccines to patients receiving Gotenfia PL sections 2 and 4 • Patients are advised to notify their doctor if they have an infection before using Gotenfia or if they experience symptoms of an infection during Gotenfia treatment **Other routine risk minimization measures beyond the Product Information:** Legal status: Restricted medical prescription
Demyelinating disorders	**Routine risk communication:** SmPC sections - 4.4 (Special warnings and precautions for use) and

	- 4.8 (Undesirable effects) PL sections 2 and 4 **Routine risk minimization activities recommending specific clinical measures to address the risk:** SmPC section 4.4 (Special warnings and precautions for use) • Guidance to discontinue use of Gotenfia if demyelinating disorders develop PL sections 2 and 4 • Patients are advised to notify their doctor if they have been diagnosed with nervous system disease before using Gotenfia or if they experience any symptoms of nervous system disease **Other routine risk minimization measures beyond the Product Information:** Legal status: Restricted medical prescription
Malignancy	**Routine risk communication:** SmPC sections - 4.4 (Special warnings and precautions for use) and - 4.8 (Undesirable effects) PL sections 2 and 4 **Routine risk minimization activities recommending specific clinical measures to address the risk:** SmPC section 4.4 (Special warnings and precautions for use) • Recommendation to screen patients with UC who are at increased risk for or have a history of colon dysplasia or colon carcinoma for dysplasia before treatment initiation and throughout their disease course • Recommendation to perform periodic skin examination PL section 2 • Patients are advised to notify their doctor have been diagnosed with lymphoma or any other cancer before using Gotenfia or if they experience symptoms of lymphoma, skin cancer, or leukaemia; patient who may be at increased risk for cancer should discuss with their doctor whether treatment with a TNF blocker is appropriate PL section 4 • Patients are advised to notify their doctor if they experience symptoms of lymphoma, skin cancer, or leukaemia

	Other routine risk minimization measures beyond the Product Information: Legal status: Restricted medical prescription
Serious depression including suicidality	**Routine risk communication:** SmPC section 4.8 (Undesirable effects) PL section 4 **Routine risk minimization activities recommending specific clinical measures to address the risk:** None **Other routine risk minimization measures beyond the Product Information:** Legal status: Restricted medical prescription
Breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero	**Routine risk communication:** SmPC sections - 4.4 (Special warnings and precautions for use) and - 4.6 (Fertility, pregnancy, and lactation) PL section 2 **Routine risk minimization activities recommending specific clinical measures to address the risk:** SmPC section 4.6 (Fertility, pregnancy, and lactation) • Recommendations regarding the administration of live vaccines to infants exposed to golimumab in utero PL section 2 • Patients who take Gotenfia while pregnant are advised tell their baby's doctor and other HCPs about their use of Gotenfia before their baby receives any vaccine **Other routine risk minimization measures beyond the Product Information:** Legal status: Restricted medical prescription
Long-term safety in pediatric patients	**Routine risk communication:** None **Routine risk minimization activities recommending specific clinical measures to address the risk:** None **Other routine risk minimization measures beyond the Product Information:** Legal status: Restricted medical prescription

V.2. Additional Risk Minimisation Measures

Patient Card

Objectives:

The goal of the Patient Card is to educate patients on important safety information that they need to be aware of before and during treatment with Gotenfia.

The Patient Card addresses the following important risks:

- Serious infections (including opportunistic infections, tuberculosis, hepatitis B virus reactivation)
- Breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero

Rationale for the additional risk minimisation activity:

To enhance patient knowledge regarding the risk of infection associated with Gotenfia treatment and to remind patients who received Gotenfia during pregnancy to inform their infant's physician before the infant receives any live vaccine.

Target audience and planned distribution path:

The Patient Card is provided as part of the product packaging.

Plans to evaluate the effectiveness of the interventions and criteria for success:

The Marketing Authorisation Holder will evaluate the effectiveness of risk minimisation measures on ongoing basis within continuous risk-benefit evaluation (routine pharmacovigilance).

V.3. Summary of risk minimisation measures

Table Part V.3: Summary table of pharmacovigilance activities and risk minimisation activities by safety concern

Safety concern	Risk minimisation measures	Pharmacovigilance activities
Serious infections	**Routine risk minimization measures:** - SmPC sections 4.3 (Contraindications), 4.4 (Special warnings and precautions for use), 4.5 (Interaction with other medicinal products and other forms of interaction), and 4.8 (Undesirable effects) - Package Leaflet (PL) sections 2 and 4 **Additional risk minimization measures:** Patient Card	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** TOI TFUQ for Serious Infections and Opportunistic Infections TOI TFUQ for TB TOI TFUQ for Progressive Multifocal Leukoencephalopathy (PML)/Reversible Posterior Leukoencephalopathy Syndrome (RPLS) **Additional pharmacovigilance activities:** None

Safety concern	Risk minimisation measures	Pharmacovigilance activities
Demyelinating disorders	**Routine risk minimization measures:** - SmPC sections 4.4 (Special warnings and precautions for use) and 4.8 (Undesirable effects) - PL sections 2 and 4 **Additional risk minimization measures:** None	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None
Malignancy	**Routine risk minimization measures:** - SmPC sections 4.4 (Special warnings and precautions for use) and 4.8 (Undesirable effects) - PL sections 2 and 4 **Additional risk minimization measures:** None	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** TOI TFUQ for Malignancies (including Lymphoma, Second and Secondary Malignancies) **Additional pharmacovigilance activities:** None
Serious depression including suicidality	**Routine risk minimization measures:** - SmPC section 4.8 (Undesirable effects) - PL section 4 **Additional risk minimization measures:** None	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None
Breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero	**Routine risk minimization measures:** - SmPC sections 4.4 (Special warnings and precautions for use) 4.6 (Fertility, pregnancy, and lactation) - PL section 2 **Additional risk minimization measures:** Patient Card	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None

Safety concern	Risk minimisation measures	Pharmacovigilance activities
Long-term safety in pediatric patients	**Routine risk minimization measures:** None **Additional risk minimization measures:** None	**Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:** None **Additional pharmacovigilance activities:** None

Part VI: Summary of the risk management plan

Summary of risk management plan for Gotenfia (Golimumab)

This is a summary of the risk management plan (RMP) for Gotenfia. The RMP details important risks of Gotenfia, how these risks can be minimised, and how more information will be obtained about Gotenfia's risks and uncertainties (missing information).

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

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

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

I. The medicine and what it is used for

Gotenfia is authorised for rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (pJIA) [only Gotenfia 50 mg], psoriatic arthritis (PsA), axial spondyloarthritis (Axial SpA) including ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-Axial SpA), and ulcerative colitis (UC) (see SmPC for the full indication). It contains golimumab as the active substance and it is given by subcutaneous (SC) injection using a prefilled syringe.

Further information about the evaluation of Gotenfia's benefits can be found in Gotenfia's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage <link to the EPAR summary landing page>.

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

Important risks of Gotenfia, together with measures to minimise such risks and the proposed studies for learning more about Gotenfia'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 the case of Gotenfia, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

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*.

If important information that may affect the safe use of Gotenfia is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Gotenfia 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 Gotenfia. 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	• Serious infections • Demyelinating disorders • Malignancy
Important potential risks	• Serious depression including suicidality • Breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero
Missing information	• Long-term safety in pediatric patients

II.B Summary of important risks

Important identified risk: Serious infections	
Risk minimisation measures	*Routine risk minimisation measures:* SmPC sections 4.3 (Contraindications), 4.4 (Special warnings and precautions for use), 4.5 (Interaction with other medicinal products and other forms of interaction), and 4.8 (Undesirable effects) Package Leaflet sections 2 and 4 *Additional risk minimisation measures:* Patient Card

Important identified risk: Demyelinating disorders	
Risk minimisation measures	*Routine risk minimisation measures:* SmPC sections 4.4 (Special warnings and precautions for use) and 4.8 (Undesirable effects) Package Leaflet sections 2 and 4 *Additional risk minimisation measures:* None

Important identified risk: Malignancy	
Risk minimisation measures	*Routine risk minimisation measures:* SmPC sections 4.4 (Special warnings and precautions for use) and 4.8 (Undesirable effects) Package Leaflet sections 2 and 4 *Additional risk minimisation measures:* None

Important potential risk: Serious depression including suicidality	
Risk minimisation measures	*Routine risk minimisation measures:* SmPC section 4.8 (Undesirable effects) Package Leaflet section 4 *Additional risk minimisation measures:* None

Important potential risk: Breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero	
Risk minimisation measures	*Routine risk minimisation measures:* SmPC sections 4.4 (Special warnings and precautions for use) and 4.6 (Fertility, pregnancy, and lactation) Package Leaflet section 2 *Additional risk minimisation measures:* Patient Card

Missing information: Long-term safety in pediatric patients	
Risk minimisation measures	*Routine risk minimisation measures:* Not applicable *Additional risk minimisation measures:* Not applicable

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 Gotenfia.

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

There are no studies required for Gotenfia.

Part VII: Annexes

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Annex 4 – Specific adverse drug reaction follow-up forms

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Follow-up forms

- Topic of Interest Targeted Follow-up Questionnaire (TOI TFUQ) for Serious Infections and Opportunistic Infections
- Topic of Interest Targeted Follow-up Questionnaire (TOI TFUQ) for Tuberculosis (TB)
- Topic of Interest Targeted Follow-up Questionnaire (TOI TFUQ) for Progressive Multifocal Leukoencephalopathy (PML)/Reversible Posterior Leukoencephalopathy Syndrome (RPLS)
- Topic of Interest Targeted Follow-up Questionnaire (TOI TFUQ) for Malignancies (including Lymphoma, Second and Secondary Malignancies)

Topic of Interest Targeted Follow-up Questionnaire (TOI TFUQ)
for Serious Infections and Opportunistic Infections

Manufacturer Control Number: _____ Drug generic (TRADENAME): _____
Date of Report: _____ [dd-MMM-yyyy]

1. Medical History and Concurrent Conditions

☐ Prior history of exposure to TB

Details: _____

☐ Prior history of exposure to Hepatitis B/C

Details: _____

Details of vaccination history: _____

☐ The patient was considered immunocompromised (underlying diagnoses, immunosuppressive therapy etc.)

Details: _____

Other relevant medical history or any known risk factors for acquiring specific infection in question: _____

2. Adverse Event Details

☐ The infection was present prior to starting the product

☐ There were unusual features of the patient's presentation or clinical course

Details: _____

Type of infection (e.g., pneumonia, endocarditis, etc.) and location if relevant (e.g., subcutaneous abscess of the forearm or TB of the CNS): _____

Topic of Interest Targeted Follow-up Questionnaire (TOI TFUQ)
for Tuberculosis (TB)

Manufacturer Control Number: _____ Drug generic (TRADENAME): _____

Date of Report: _____ [dd-MMM-yyyy]

1. Relevant medical/occupational history ***(Check all that apply and provide details below.)***

☐ Weight loss ≥ 10% of ideal body weight
☐ Diabetes
☐ Gastrectomy or jejunal bypass
☐ Organ/Tissue transplant
☐ Prior BCG vaccination
☐ Recent travel to endemic area
☐ Head/Neck carcinoma
☐ Leukaemia/Lymphoma
☐ Household contact/Exposure to TB
☐ Prior/Prolonged steroid use
☐ IV drug abuse
☐ Prior/Prolonged immunosuppressant use
☐ Silicosis
☐ Positive HIV test
☐ Resident/Employee at high risk setting (e.g., correctional institute, homeless shelter, nursing home, refugee camp, etc.)

Details: _____

2. Diagnostics

☐ Purified Protein Derivative (PPD) testing was performed. Indicate test used:

☐ Intradermal skin test
☐ Multipuncture skin test
Number of units administered: _____
PPD Result: ☐ mm of induration (0, if no induration)
Date of PPD: _____ [dd-MMM-yyyy]
2nd PPD results (if applicable): _____ mm of induration
Date of second PPD: _____ [dd-MMM-yyyy]
☐ False negative test (e.g., time of injection to time of evaluation too long/short, evaluator of induration, etc.)? Explain reasons: _____

☐ The subject had active TB

☐ Prophylactic therapy was given

Time elapsed from onset of TB symptoms to institution of treatment: _____

Type of tuberculosis: ☐ Pulmonary
☐ Extrapulmonary; Location: _____
☐ Disseminated; Location: _____
☐ Multi-drug Resistant TB

Other laboratory results

Laboratory Test		**Test Result**	**Date [dd-MMM-yyyy]**
AFB Smear	**Sputum**		
	Other (specify)		
Culture	**Sputum**		
	Other (specify)		
PCR MTb			
Quantiferon TB Gold			

Topic of Interest Targeted Follow-up Questionnaire (TOI TFUQ)
for Progressive Multifocal Leukoencephalopathy (PML)/
Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

Manufacturer Control Number: _____ Drug generic (TRADENAME): _____

Date of Report: _____ [dd-MMM-yyyy]

1. Medical History and Concurrent Conditions

List relevant concurrent/pre-existing conditions (e.g., Hodgkin's CLL, CML, AML, ongoing GVHD, long term immunosuppression, pre-existing neurological features/disorders, and any relevant previous imaging or laboratory test results.) List the details with dates of diagnosis: _____

History of pre-existing conditions *(Check all that apply)*:
☐ Systemic hypertension
☐ Renal disease (e.g., renal failure)
☐ Preceding history of infection (e.g., HIV and/or sepsis)
☐ Immune mediated disease (e.g., Systemic lupus erythematosus, Polyarteritis nodosa etc.)
Other relevant medical history (e.g., transplantation, neurological disorders, pre-eclampsia, chemotherapy etc.): _____

2. Diagnostics

Laboratory/Radiographic evaluation results as appropriate and accompanying normal ranges, if available. *(Note date performed and other test results as appropriate.)*

☐ MRI: Date: _____ [dd-MMM-yyyy], Results: _____

☐ JC Virus DNA test was performed: Date: _____ [dd-MMM-yyyy], Results: _____

☐ CSF Fluid: Date: _____ [dd-MMM-yyyy), Results: _____

☐ Brain tissue biopsy: Date: _____ [dd-MMM-yyyy], Results: _____

☐ Non-CSF sources for JCV DNA testing: Date: _____ [dd-MMM-yyyy], Results: _____

☐ Imaging studies (e.g., CT scan, etc.): Date: _____ [dd-MMM-yyyy], Results: _____

☐ Histopathology of brain biopsy finding: Date: _____ [dd-MMM-yyyy]
- ☐ Demyelination
- ☐ Enlarged oligodendroglial nuclei
- ☐ Bizarre astrocytes
- ☐ other findings: _____

☐ Evidence of JC virus in brain tissue by:
- ☐ Electron microscopy
- ☐ Immunohistochemistry
- ☐ In situ Hybridization
- ☐ PCR

☐ Other relevant test results: _____

☐ Neurological evaluation was performed. *(Include the neurology report)*: _____

☐ Other findings, including dates *(e.g., clinical features observed - central nervous system and other symptoms and their progression, including dates [these could include neurological deficits such as motor symptoms (e.g., hemiparesis), cognitive dysfunction or changes in behaviour or personality, language or speech disturbances (e.g., aphasia/dysarthria), visual disturbances (e.g., hemianopsia), ataxia/loss of motor coordination, seizures, etc.]):* _____

MCN:

3. Prior or Concurrent Immunosuppressant Medications *(e.g., chemotherapy agents, radiation, transplant regimens; immunotherapy with monoclonal antibodies such as anti-CD-20 monoclonal antibodies and include over-the-counter and herbal medications).*

Medication	Indication	Total Daily Dose	Start Date [dd-MMM-yyyy]	Stop Date [dd-MMM-yyyy]

Topic of Interest Targeted Follow-up Questionnaire (TOI TFUQ) for Malignancies (including Lymphoma, Second and Secondary Malignancies)

Manufacturer Control Number: _____ Drug generic (TRADENAME): _____

Date of Report: _____ [dd-MMM-yyyy]

1. Relevant Medical/Family History *(Provide prior diagnoses and details for checked items below)*

☐ Previous malignancy (Provide specific diagnosis): _____

☐ Occupational/Exposure history: _____

☐ Excessive sun exposure (Describe): _____

☐ History of PUVA (Psoralen + Ultraviolet-A rays)

☐ History of radiation
Dose of radiation: _____
Area treated: _____
Age (or date of therapy) of the patient when they were treated with radiation: _____
Indication for radiation: _____
Any radiation induced changes? _____

☐ Pre-malignant lesions, e.g., Barret's oesophagus, Bowen's disease. Details: _____

Viral infections: ☐ EBV ☐ HIV ☐ HPV ☐ HBV or HCV

☐ Other relevant risk factors for malignancy (Excluding medications): _____

☐ Family history of malignancy (Provide specific diagnoses for each):
☐ In first degree relatives: _____
☐ In more distant relatives: _____

☐ Previous history of tumour necrosis factor (TNF) blocker therapy (With medication names, dates of exposure and the total number of doses or an approximation): _____

Age at first exposure to any TNF blocker: _____

☐ Previous administration of other immunosuppressive medications, antineoplastic medications, or other drugs, which have a risk for malignancy stated in their label. (e.g., other biologics, methotrexate, azathioprine, cyclosporine, 6-mercaptopurine, prednisone or other)

Include drug indication, dose levels, and treatment duration (e.g., methotrexate·, cyclophosphamide, vincristine, doxorubicin, cyclosporine, biologics)

Medication	Indication	Dose/Route of Administration	Start Date/Stop Date [dd-MMM-yyyy]

☐ Cytogenetic abnormalities detected at any point in time? *(Include those relevant for any malignancy including myeloma - this could be germline genetic diseases predisposing for malignancy e.g., Down's syndrome, neurofibromatosis etc., or cytogenetic abnormalities relevant to myeloma)* _____

2. Diagnostics

Histopathologic diagnosis *(Include the histopathology report)*: _____

Include malignancy stage, location of primary tumour, metastases, lymph node involvement and staging system used: _____

Additional diagnostic information, including finding that support specified staging; speciality consultations *(Attach reports, if available)*: _____ Final diagnosis: _____

☐ **Lymphoma**

☐ Non-Hodgkin's lymphoma

Histologic subtype: _____ Immunophenotype: _____ Cytogenetics: _____

☐ Hodgkin's lymphoma

Histologic subtype: _____

Was the lymphoma tissue tested for Epstein-Barr virus (EBV) (e.g., by in situ hybridization and/or immunohistology analysis)? ☐ No ☐ Yes *(Attach report)*

If Yes, Test Result: ☐ EBV positive ☐ EBV negative

☐ **Second malignancy** (A cancer that is unrelated to the treatment of a prior malignancy and is not a metastasis from the initial malignancy) *(List)*:

_____

☐ **Secondary malignancy** (A cancer caused by treatment for a previous malignancy e.g., Treatment with radiation or chemotherapy. It is NOT considered a metastasis of the initial malignancy) *(List)*:

_____

(Ref. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/aeguidelines.pdf)

Malignancy screening/Preventive measures (Include those that are relevant to the specific malignancy that is being reported, e.g., recent mammography, breast exam, Pap smear, sigmoidoscopy or colonoscopy, faecal occult blood, Prostatic Specific Antigen, digital rectal exam, HPV vaccine etc.)

Screening Test/ Preventive Measure	Date (dd-MMM-yyyy)	Results (Including units and reference ranges where applicable)

3. Treatment

What was the response to the first treatment for malignancy?

☐ Complete response ☐ Partial response ☐ Stable disease ☐ Progressive disease

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

Draft Key Messages of the Additional Risk Minimization Measures

Patient Card

The educational program consists of a Patient Card to be held by the patient. The card is aimed at both serving as a reminder to record the dates and outcomes of specific tests and to facilitate the patient sharing of special information with healthcare professionals (HCPs) treating the patient about ongoing treatment with the product.

The Patient Card shall contain the following key messages:

- A reminder to patients to show the Patient Card to all treating HCPs, including in conditions of emergency, and a message for HCPs that the patient is using Gotenfia.
- A statement that the brand name and batch number should be recorded.
- Provision to record the type, date and result of TB screenings.
- That treatment with Gotenfia may increase the risks of serious infection, opportunistic infections, tuberculosis, hepatitis B reactivation, and breakthrough infection after administration of live vaccines in infants exposed to golimumab in utero; and when to seek attention from a HCP.
- Contact details of the prescriber.

The language of the respective Patient Card can be found in the Gotenfia Product Information, Appendix IIIA.