Part VI: Summary of the risk management plan

Summary of risk management plan for Remsima IV/SC and Inflectra IV (Infliximab)

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

Remsima IV/SC and Inflectra IV's summary of product characteristics (SmPCs) and its package leaflet (PL) give essential information to healthcare professionals (HCPs) and patients on how Remsima IV/SC and Inflectra IV should be used.

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

Important new concerns or changes to the current ones will be included in updates of Remsima IV/SC and Inflectra IV's RMP.

I. The medicine and what it is used for

Remsima/Inflectra IV is authorised in adults with the following diseases:

- Rheumatoid arthritis (RA) (an immune-system disease causing inflammation of the joints). Remsima/Inflectra IV is used with methotrexate (a medicine that acts on the immune system);
- Crohn's disease (CD) (a disease-causing inflammation of the digestive tract), when the disease is moderate to severe or fistulising (with the formation of fistulae, abnormal passageways between the gut and other organs);
- Ulcerative colitis (UC) (a disease-causing inflammation and ulcers in the lining of the gut);
- Ankylosing spondylitis (AS) (a disease-causing inflammation and pain in the joints of the spine);
- Psoriatic arthritis (PsA) (a disease causing red, scaly patches on the skin and inflammation of the joints);
- Psoriasis (a disease causing red, scaly patches on the skin).

Remsima/Inflectra IV is also used in patients aged between 6 and 17 years with severe, active CD or severely active UC, when they have not responded to or cannot take other medicines or treatments (see SmPC for the full indication). It contains infliximab as the active substance and it is given by intravenous route.

Remsima SC is authorised in adults with the following diseases:

- Rheumatoid arthritis (RA) (an immune-system disease causing inflammation of the joints). Remsima SC is used with methotrexate (a medicine that acts on the immune system);

- Crohn's disease (CD) (a disease-causing inflammation of the digestive tract), when the disease is moderate to severe or fistulising (with the formation of fistulae, abnormal passageways between the gut and other organs);
- Ulcerative colitis (UC) (a disease-causing inflammation and ulcers in the lining of the gut);
- Ankylosing spondylitis (AS) (a disease-causing inflammation and pain in the joints of the spine);
- Psoriatic arthritis (PsA) (a disease causing red, scaly patches on the skin and inflammation of the joints);
- Psoriasis (Ps) (a disease causing red, scaly patches on the skin).

Further information about the evaluation of Remsima IV/Inflectra IV/Remsima SC's benefits can be found in Remsima IV/Inflectra IV/Remsima SC's EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage.

Remsima

https://www.ema.europa.eu/en/medicines/human/EPAR/remsima

Inflectra

https://www.ema.europa.eu/en/medicines/human/EPAR/inflectra

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

Important risks of Remsima IV/SC and Inflectra IV, together with measures to minimise such risks and the proposed studies for learning more about these 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 HCPs;
- Different packaging for the different formulations (IV and SC)
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so as 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 case of Remsima IV/SC and Inflectra IV, 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 periodic safety update report (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 Remsima IV/SC and Inflectra IV is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Remsima IV/SC and Inflectra IV 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 Remsima IV/SC and Inflectra IV. 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 including sepsis BCG breakthrough infection and agranulocytosis in infants with *in utero* exposure to infliximab Demyelinating disorders Malignancy
Important potential risks	Colon carcinoma/dysplasia (in paediatric ulcerative colitis)
Missing information	Long term treatment with SC infliximab (SC only)

II.B Summary of important risks

Important identified risk: Serious infections including sepsis	
Evidence for linking the risk to the medicine	A United States of America (USA) incidence cohort showed that RA patients were at risk of developing infections compared with non-RA patients. The hazard ratios for objectively confirmed infections, infections requiring hospitalisation and any documented infection in patients with RA were 1.70 (95% confidence interval [CI] 1.42–2.03), 1.83 (95% CI 1.52–2.21), and 1.45 (95% CI 1.29–1.64), respectively, after adjustment for age, sex, smoking status, leukopenia, corticosteroid use, and diabetes mellitus. Since RA patients are treated with immunosuppressive drugs, it is not clear whether this is related to the underlying disease or the treatment. Before the methotrexate and anti-tumour necrosis factor (TNF) era, studies showed a general increase in mortality due to infection in RA patients. RA appears to increase the risk for bacterial, tubercular, fungal, opportunistic, and viral infections, with all infections being more common in more active and severe RA. TNF acts to regulate and enhance appropriate inflammatory, innate and adaptive immune responses to pathogenic organisms and hence inhibition of TNF by Remsima IV/SC and Inflectra IV may suppress these beneficial activities of TNF and increase the potential for serious infections. Sepsis constitutes a systemic

Important identified risk: Serious infections including sepsis	
	response to infection which is characterised by both a pro-inflammatory response mediated by cytokines such as TNF and Interleukins (IL)-l and an anti-inflammatory indicated by the expression of IL-10 and transforming growth factor-β (TGF-β). Remsima IV and Inflectra IV is a biosimilar medicinal product and Remsima SC has the same INN. The reference product for Remsima IV and Inflectra IV is Remicade. The evidence of the above-mentioned risk is derived from Remicade RMP and hence the strength of the evidence is good.
Risk factors and risk groups	Risk factors for serious infections including sepsis includes immunosuppressive medications (such as transplant recipients), including steroids, treatment with chemotherapy drugs or radiation, splenectomy, longstanding diabetes, acquired immune deficiency syndrome (AIDS), or cirrhosis, large burns or severe trauma and infections such as pneumonia, meningitis, cellulitis, urinary tract infection. Very young people and elderly people are at risk of these infections.
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.2 where advice is given that Remsima/Inflectra treatment is to be initiated and supervised by qualified physicians experienced in the diagnosis and treatment of conditions for which Remsima/Inflectra is indicated.* *SmPC section 4.2 where advice is given that patients treated with Remsima/Inflectra should be given the PL and the patient reminder card.* *SmPC section 4.4 where a warning is given that the patients must be monitored closely for infections including TB before, during and after treatment with infliximab.* *SmPC section 4.4 where warning is given that the suppression of TNF-α may mask symptoms of infection such as fever. Severe infections such as sepsis is listed as a contraindication in SmPC section 4.3.* *Serious infections including sepsis is listed as special warnings and precautions for use in SmPC section 4.4.* *Serious infections including sepsis is listed as an adverse reaction in SmPC section 4.8.* *PL section 2 where a warning is given that, tell your doctor if you have an infection or if you have ever lived in or travelled to an area where infections called histoplasmosis, coccidioidomycosis, or blastomycosis are common before you are given Remsima/Inflectra.* *Serious infection is listed as contraindication and warning and precautions in PL section 2.*

Important identified risk: Serious infections including sepsis	
	Legal status: Medicinal product subject to restricted medical prescription. Additional risk minimisation measures: *Patient reminder card.*
Additional pharmacovigilance activities	*CT-P13 4.2* *CT-P13 4.3* *CT-P13 4.4* *BSRBR-RA (Sponsor: Celltrion Inc.)* *BSRBR-RA (Sponsor: Pfizer Inc.)* *RABBIT (Sponsor: Celltrion Inc.)* *RABBIT (Sponsor: Pfizer Inc.)* *CT-P13 SC 3.7* *CT-P13 SC 3.8* *CT-P13 SC 4.8* *CT-P13 SC 4.9* See Section II.C of this summary for an overview of the post-authorisation development plan.

Important identified risk: BCG breakthrough infection and agranulocytosis in infants with in utero exposure to infliximab	
Evidence for linking the risk to the medicine	In infants exposed *in utero* to infliximab, fatal outcome due to disseminated Bacillus Calmette-Guérin (BCG) infection has been reported following administration of BCG vaccine after birth. Remsima IV and Inflectra IV is a biosimilar medicinal product and Remsima SC has the same INN. The reference product for Remsima IV and Inflectra IV is Remicade. The evidence of the above-mentioned risk is derived from Remicade RMP and hence the strength of the evidence is good.
Risk factors and risk groups	Risk factors for Bacillus Calmette–Guérin (BCG) breakthrough infection and agranulocytosis includes administration of live vaccines to infants in utero which are at risk of BCG breakthrough infection and agranulocytosis.
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.2 where advice is given that patients treated with Remsima/Inflectra should be given the PL and the patient reminder card.* *SmPC section 4.4 where a warning is given that infants exposed in utero to infliximab, fatal outcome due to disseminated BCG*

Important identified risk: BCG breakthrough infection and agranulocytosis in infants with in utero exposure to infliximab	
	infection has been reported following administration of BCG vaccine after birth. *SmPC section 4.6 where guidance is given that administration of live vaccines (e.g. BCG vaccine) to infants exposed to infliximab in utero is not recommended for at least 6 months after birth and cases of agranulocytosis have also been reported.* *Agranulocytosis is listed as an adverse reaction in SmPC section 4.8.* *PL section 2 where a warning is given that, talk to your doctor if you have recently received or are scheduled to receive treatment with a therapeutic infectious agent (such as BCG instillation used for the treatment of cancer).* *Legal status: Medicinal product subject to restricted medical prescription.* Additional risk minimisation measures: *Patient reminder card.*
Additional pharmacovigilance activities	*None*

Important identified risk: Demyelinating disorders	
Evidence for linking the risk to the medicine	Demyelinating disorders were identified as a class effect on review of the post-marketing data for all TNF inhibitors. After demyelinating disorders were identified as a risk, subjects with a history of demyelinating disorders were excluded form clinical trials. The role that TNF plays as an immunomodulator suggests that TNF blockade may promote the development of drug-induced neuropathies by augmenting the number of activated peripheral T cells and thereby enhance 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. A recent report in a murine model of experimental autoimmune encephalomyelitis suggests that membrane TNF is neuroprotective. Since TNF inhibitors can neutralise both soluble and membrane TNF, they may remove the neuroprotection provided by membrane TNF. Remsima IV and Inflectra IV is a biosimilar medicinal product and Remsima SC has the same INN. The reference product for Remsima IV and Inflectra IV is Remicade. The evidence of the above-mentioned risk is derived from Remicade RMP and hence the strength of the evidence is good.
Risk factors and risk groups	Patients with a history of demyelinating disorders, or a family history
Risk minimisation measures	Routine risk minimisation measures:

Important identified risk: Demyelinating disorders	
	SmPC section 4.4 where a warning is given that use of TNF-blocking agents, including infliximab, has been associated with cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of central nervous system demyelinating disorders, including multiple sclerosis, and peripheral demyelinating disorders, including Guillain-Barré syndrome. *SmPC section 4.4 where guidance is given that the in patients with pre-existing or recent onset of demyelinating disorders, the benefits and risks of anti-TNF treatment should be carefully considered before initiation of infliximab therapy. Discontinuation of infliximab should be considered if these disorders develop.* *Demyelinating disorders is listed as an adverse reaction in SmPC section 4.8.* *Legal status: Medicinal product subject to restricted medical prescription.* Additional risk minimisation measures: *None.*
Additional pharmacovigilance activities	*CT-P13 4.2* *CT-P13 4.3* *CT-P13 4.4* *BSRBR-RA (Sponsor: Celltrion Inc.)* *BSRBR-RA (Sponsor: Pfizer Inc.)* *RABBIT (Sponsor: Celltrion Inc.)* *RABBIT (Sponsor: Pfizer Inc.)* *CT-P13 SC 3.7* *CT-P13 SC 3.8* *CT-P13 SC 4.8* *CT-P13 SC 4.9* See section II.C of this summary for an overview of the post-authorisation development plan.

Important identified risks: Malignancy	
Evidence for linking the risk to the medicine	According to the Remsima IV/SC and Inflectra IV SmPC, malignancies (some fatal) have been reported among children, adolescents and young adults (up to 22 years of age) treated with TNF-blocking agents (initiation of therapy ≤18 years of age), including infliximab in the post-marketing setting. A risk for the development of malignancies in patients treated with TNF-blockers cannot be excluded.

Important identified risks: Malignancy	
	In clinical studies with infliximab in which 5,780 patients were treated, representing 5,494 patient years, 26 non-lymphoma malignancies were detected as compared with 1 non-lymphoma malignancy in 1,600 placebo-treated patients representing 941 patient years. In long-term safety follow-up of clinical studies with infliximab of up to 5 years, representing 6,234 patients-years (3,210 patients), 38 cases of non-lymphoma malignancies were reported. TNF has been shown to exert cytotoxic and/or cytostatic effects on a number of human and murine tumour cell lines. Low doses of TNF can increase tumour blood vessel permeability, thus augmenting tissue concentrations of chemotherapeutic agents, as well as enhance the cytolytic effect of NK and CD8+ T cell killing of immunogenic tumour cells. Therefore, the neutralisation of TNF by infliximab may allow some types of tumour cells to survive. Remsima IV/SC and Inflectra IV is a biosimilar medicinal product and Remsima SC has the same INN. The reference product for Remsima IV and Inflectra IV is Remicade. The evidence of the above-mentioned risk is derived from Remicade RMP and hence the strength of the evidence is good.
Risk factors and risk groups	Risk factor of malignancy in patients includes history of malignancy, immunosuppressant therapy, HIV infection. Additionally, phototherapy for psoriasis increases the risk of skin cancer. Moreover, UC is associated with a higher risk of colon cancer.
Risk minimisation measures	Routine risk minimisation measures: *SmPC section 4.4 where warning is given that there is an increased background risk for lymphoma and leukaemia in RA patients with long-standing, highly active, inflammatory disease, which complicates risk estimation.* *Malignancy is listed in SmPC section 4.8.* *PL section 2 where a warning is given that, Patients taking Remsima/Inflectra may have an increased risk of developing lymphoma or another cancer. Tell your doctor if you have or have ever had lymphoma (a type of blood cancer) or any other cancer before you are given Remsima/Inflectra.* *Cancer in children and adults is listed in PL section 4.* *Legal status: Medicinal product subject to restricted medical prescription.* Additional risk minimisation measures: *None.*
Additional pharmacovigilance activities	*CT-P13 4.2* *CT-P13 4.3* *CT-P13 4.4*

Important identified risks: Malignancy	
	BSRBR-RA (Sponsor: Celltrion Inc.) *BSRBR-RA (Sponsor: Pfizer Inc.)* *RABBIT (Sponsor: Celltrion Inc.)* *RABBIT (Sponsor: Pfizer Inc.)* *CT-P13 SC 3.7* *CT-P13 SC 3.8* *CT-P13 SC 4.8* *CT-P13 SC 4.9* See section II.C of this summary for an overview of the post-authorisation development plan.

Important potential risks: Colon carcinoma/dysplasia (in paediatric ulcerative colitis)	
Evidence for linking the risk to the medicine	In a review of published studies concerning the risk of colon carcinoma in UC patients. The crude annual incidence rate of colon carcinoma in UC patients ranges from approximately 0.006 to 0.16%. It is assumed that the more widespread use of maintenance therapy for UC and surveillance colonoscopy are the causes of the risk decrease. TNF has been shown to exert cytotoxic and/or cytostatic effects on a number of human and murine tumour cell lines. Low doses of TNF can increase tumour blood vessel permeability, thus augmenting tissue concentrations of chemotherapeutic agents, as well as enhance the cytolytic effect of NK and CD8+ T cell killing of immunogenic tumour cells. Therefore, the neutralisation of TNF by infliximab may allow some types of tumour cells to survive. Remsima/Inflectra IV is a biosimilar medicinal product. The reference product is Remicade. The evidence of the above-mentioned risk is derived from Remicade RMP and hence the strength of the evidence is good.
Risk factors and risk groups	Patient with UC who have a history of previous colonic malignancy are at risk, as are patients with longstanding disease.
Risk minimisation measures	Routine risk minimisation measures (Not applicable for SC): *SmPC section 4.4 where a warning is given that all patients with UC who are at increased risk for dysplasia or colon carcinoma (for example, patients with long-standing UC or primary sclerosing cholangitis), or who had a prior history of dysplasia or colon carcinoma should be screened for dysplasia at regular intervals before therapy and throughout their disease course.* *SmPC section 4.4 where guidance is given that this evaluation should include colonoscopy and biopsies per local recommendations. Current data do not indicate that*

Important potential risks: Colon carcinoma/dysplasia (in paediatric ulcerative colitis)	
	Remsima/Inflectra treatment influences the risk for developing dysplasia or colon cancer. *Abnormal tissue swelling or growth is listed in PL section 4.* *Legal status: Medicinal product subject to restricted medical prescription.* Additional risk minimisation measures: *None.*
Additional pharmacovigilance activities	*CT-P13 4.3* See section II.C of this summary for an overview of the post-authorisation development plan.

Missing information: Long term treatment with SC infliximab (SC only)	
Risk minimisation measures	Routine risk minimisation measures: • Legal status: Medicinal product subject to restricted medical prescription. Additional risk minimisation measures: None.
Additional pharmacovigilance activities	*CT-P13 SC 3.7* *CT-P13 SC 3.8* *CT-P13 SC 4.8* *CT-P13 SC 4.9* See Section II.C of this summary for an overview of the post-authorisation development plan.

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 obligations of Remsima IV/SC and Inflectra IV.

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

CT-P13 4.2: An Observational, Prospective Cohort Study to Evaluate Safety and Efficacy of Remsima® in Patients with Rheumatoid Arthritis

Purpose of the study:

Rationale:

The proposed study is a prospective registry cohort study to compare safety and efficacy over 5 years (2 years initially, followed by an additional 3 years for patients who consent to participate in an extension study), between patients with RA who are recipients of Remsima® and reference cohorts of other anti-TNF drugs and 50 biologic naïve patients (in Korea only). Data generated in this study will built upon the safety data already generated in the PLANETAS and PLANETRA studies in patients with AS and RA.

Study objectives:

The primary objective of this study is to assess the long-term safety of Remsima® in RA patients by evaluation of events of special interest (ESI) up to 5 years and to exploratory compare patients receiving Remsima® with patients receiving non-biologic treatments or other anti-TNF drugs.

The secondary objectives of this study are to evaluate efficacy. Further, additional safety of Remsima® in RA patients, in comparison with patients receiving non-biologic treatments or other anti-TNF drugs will be assessed. Health-economics parameters will also be assessed.

CT-P13 4.3: An observational, prospective cohort study to evaluate the safety and efficacy of Remsima® in patients with Crohn's disease (CD) or Ulcerative Colitis (UC)

Purpose of the study:

Rationale:

This study is initiated to evaluate and further characterise the long-term safety and efficacy of Remsima® treatment in patients with CD or UC as part of routine clinical practice. Data generated in this study will built upon the safety data already generated in the PLANETAS and PLANETRA studies in patients with AS and RA.

Study objectives:

The primary objective of this study is to assess the safety of Remsima® by evaluation of ESI in IBD patients, who have active CD, fistulising CD, or UC for up to 5 years for each patient. The secondary objectives of this study are to evaluate additional safety and efficacy of Remsima® in IBD patients. Health-economic parameters will also be assessed.

CT-P13 4.4: An Observational, Prospective Cohort Study to Evaluate Safety and Efficacy of Remsima® in Patients with Ankylosing Spondylitis

Purpose of the study:

Rationale:

The proposed study is a prospective registry cohort study to compare safety and efficacy over 5 years (2 years initially, followed by an additional 3 years for patients who consent to participate in an extension study), between patients with AS who are recipients of Remsima® and patients receiving other TNF blockers. Data generated in this study will built upon the safety data already generated in the PLANETAS and PLANETRA studies in patients with AS and RA.

Study objectives:

The primary objective of this study is to assess the safety of Remsima® in AS patients, in comparison with patients receiving other anti-TNF drugs, by evaluation of ESI for up to 5 years from the first visit of each patient.

The secondary objectives of this study are to evaluate efficacy and additional safety of Remsima® in AS patients, in comparison with patients receiving other TNF blockers. Health-economics parameters will also be assessed.

BSRBR-RA: A longitudinal observational study of patients with rheumatoid arthritis treated with biologic and other new advanced targeted therapies (UK) (Sponsor: Celltrion Inc.)

Purpose of the study:

Rationale:

There is an increased risk of premature mortality, serious infection and lymphoproliferative malignancy in RA patients. It is therefore important to compare their occurrence in patients on new treatments compared to patients on more established treatment. Because long term immunosuppressive agents such as infliximab have the potential to impact all-cause mortality and lymphoproliferative malignancy, long term tracking of this is important.

Study objectives:

The major hypotheses to be tested are as follows:

1. Primary: That any new biologic or other new advanced targeted therapy (defined as a biologic or other new targeted therapy not previously studied by the BSRBR and which the BSRBR is currently recruiting) in patients with RA is associated with a similar risk of developing serious infections compared to patients with similar disease activity receiving established anti-TNF drugs (i.e. patients receiving Humira, Enbrel, or Remicade).

2. Secondary: That any new biologic or other new advanced therapy (defined as a biologic or other new targeted therapy not previously studied by the BSRBR and which the BSRBR is currently recruiting) in patients with RA is associated with a similar risk of developing malignancy and other specified outcomes (such as myocardial infarction) compared to patients with similar disease activity receiving established anti-TNF drugs (i.e. patients receiving Humira, Enbrel, or Remicade).

RABBIT: Long-term Observation of Treatment with Biologics in Rheumatoid Arthritis (Sponsor Celltrion Inc.)

Purpose of the study:

Rationale:

The German biologics register RABBIT is an independent long-term observational cohort study of the safety and effectiveness of biologic agents in RA. The aim of the register is to provide safety and effectiveness. Data on all licensed biologic drugs available for the treatment of RA are collected in this Registry since 2012.

Study objectives:

To study the long-term safety of biologic agents. This includes the observation of all adverse events (serious and non-serious) in order to assess the overall safety profile. Specific emphasis will be laid on “events of interest".

BSRBR-RA: **A longitudinal observational study of patients with rheumatoid arthritis treated with biologic and other new advanced targeted therapies (UK) (Sponsor Pfizer Inc.)**

Purpose of the study:

Rationale:

There is an increased risk of premature mortality, serious infection and lymphoproliferative malignancy in RA patients. It is therefore important to compare their occurrence in patients on new treatments compared to patients on more established treatment. Because long term

immunosuppressive agents such as infliximab have the potential to impact all-cause mortality and lymphoproliferative malignancy, long term tracking of this is important.

Study objectives:

The major hypotheses to be tested are:

1. Primary: That any new biologic or other new advanced targeted therapy (defined as a biologic or other new targeted therapy not previously not previously studied by the BSRBR and which the BSRBR is currently recruiting) in patients with RA is associated with a similar risk of developing serious infections compared to patients with similar disease activity receiving established anti-TNF drugs (i.e. patients receiving adalimumab [ADA], etanercept [ETA] or infliximab [INF]).

2. Secondary: That any new biologic or other new advanced therapy (defined as a biologic or other new targeted therapy not previously studied by the BSRBR and which the BSRBR is currently recruiting) in patients with RA is associated with a similar risk of developing malignancy and other specified outcomes (such as myocardial infarction) compared to patients with similar disease activity receiving established anti-TNF drugs (i.e. patients receiving ADA, ETA, or INF).

RABBIT: **Long-term Observation of Treatment with Biologics in Rheumatoid Arthritis (Germany) (Sponsor: Pfizer Inc.)**

Purpose of the study:

Rationale:

The German biologics register RABBIT is an independent long-term observational cohort study of the safety and effectiveness of biologic agents in RA. The aim of the register is to provide safety and effectiveness. Data on all licensed biologic drugs available for the treatment of RA are collected in this Registry since 2012. Hospira (Pfizer) entered the registry in 2015.

Study objectives:

Major aims are:

1. To study the long-term safety of biologic agents. This includes the observation of all adverse events (serious and non-serious) in order to assess the overall safety profile. Specific emphasis will be laid on “events of interest”.
2. To describe the long-term effectiveness of treatment with biologic agents (disease outcomes on therapy as well as after terminating therapy). Major outcomes are: disease activity score (DAS) 28 response, ACR 20/50/70 response, time under therapy, and functional status.
3. To describe selected direct and indirect costs of therapy with biologics compared to conventional DMARD therapy. This includes the description of health care consumption and work disability.

Study CT-P13 SC 4.8: An observational, prospective cohort study to evaluate safety of CT-P13 Subcutaneous in patients with Rheumatoid Arthritis

Purpose of the study:

Rationale:

To collect further safety information on patients treated with Remsima® SC with regard to long-term safety.

Study objectives:

Primary Objective:

To assess the safety of Remsima® Subcutaneous (SC) in Rheumatoid Arthritis (RA) patients by evaluation of Adverse events of special interest (AESI)

Secondary Objective:
To evaluate additional safety of Remsima® SC in RA patients

Study CT-P13 SC 3.8: A Randomized, Placebo-Controlled, Double-Blind, Phase 3 Study to Evaluate the Efficacy and Safety of the Subcutaneous Injection of CT-P13 (CT-P13 SC) as Maintenance Therapy in Patients with Moderately to Severely Active Crohn's Disease.

Purpose of the study:

Rationale:

This Phase 3 randomized, placebo-controlled, double-blind, multicenter, parallel-group study is designed to evaluate the efficacy, PK, PD, usability and safety of CT-P13 SC as a maintenance therapy in patients with moderately to severely active CD who have had an inadequate response to conventional therapy.

Study objectives:

Primary objective:

To demonstrate superiority of CT-P13 SC over Placebo SC based on clinical remission and endoscopic response at Week 54

Secondary objectives:

To evaluate additional efficacy, PK, PD, usability, and overall safety including immunogenicity

Study CT-P13 SC 4.9: An observational, prospective cohort study to evaluate safety of Remsima® Subcutaneous in patients with Ankylosing Spondylitis, Psoriatic Arthritis and Psoriasis

Purpose of the study:

Rationale:

To collect further safety information on patients with AS, PsA and PS treated with Remsima® SC with regards to long-term safety.

Study objectives:

Primary Objective:

To assess the safety of Remsima® subcutaneous (SC) in Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA) and Psoriasis (PS) patients by evaluation of adverse events of special interest (AESI)

Secondary Objective:

To evaluate additional safety of Remsima® SC in AS, PsA and PS patients.

Study CT-P13 SC 3.7: A Randomized, Placebo Controlled, Double-Blind, Phase 3 Study to Evaluate the Efficacy and Safety of the Subcutaneous Injection of CT-P13 (CT-P13 SC) as Maintenance Therapy in Patients with Moderately to Severely Active Ulcerative Colitis

Purpose of the study:

Rationale:

This Phase 3 randomized, Placebo Controlled, Double-Blind, multicentre, parallel group study is designed to evaluate the efficacy, PK, PD and safety of CT-P13 SC as a maintenance therapy in patients with moderately to severly active ulcerative colitis.

Study objectives:

Primary Objective:

To demonstrate superiority of CT-P13 SC over Placebo SC based on clinical remission at Week 54

Secondary Objective:

To evaluate additional efficacy, PK, PD, and overall safety including immunogenicity