IBD

Choose the option that works for your patients

Established Treatment[1,2] **Convenient Care**[3]

HEALTHCARE
CELLTRION

Remsima®
Infliximab
SUBCUTANEOUS

Remsima®
Infliximab
SUBCUTANEOUS

The only subcutaneous infliximab formulation approved in Australia[4]

Remsima® SC is indicated for the treatment of adult patients with moderate to severe and refractory fistulising CD and moderate to severe active UC[4*]

Infliximab IV is a well established treatment for patients with IBD, including those who failed treatment with conventional therapies, and has shown to be an efficacious treatment for IBD with a good safety profile.[1,2,5,6]

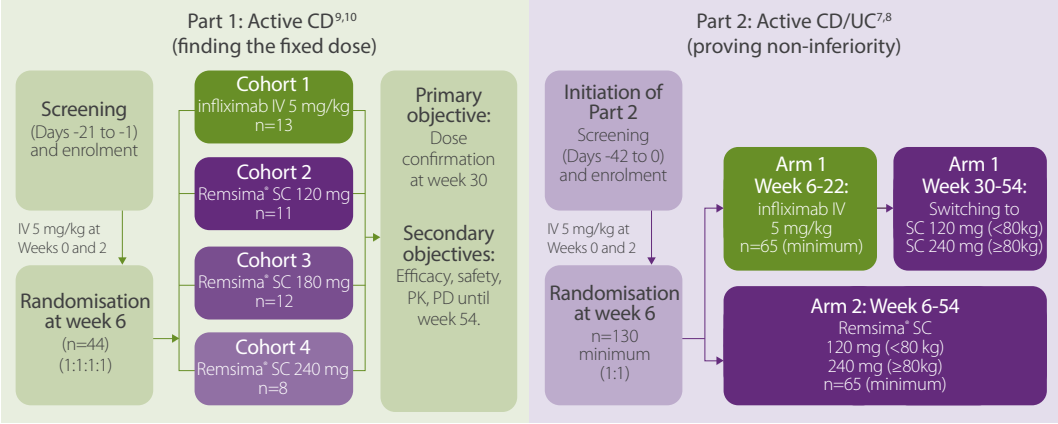
Availability of infliximab as dual formulation of IV and SC provides a treatment that can be tailored to the individual needs of your patients.

Remsima® SC demonstrates comparable efficacy, safety and immunogenicity with stable potency compared to IV administration.[7,8]

* Refer to the Australian Product Information for full indication wording.

Clinical trial with Remsima® SC in IBD

The Phase I study evaluated Remsima® SC in patients with active CD/UC[7,8,9,10]



Part 1

The primary objective of this Phase I study was to find the optimal dose of Remsima® SC over the first 30 weeks by pharmacokinetic (PK) comparability to IV dosing (AUCτ at steady state between Week 22 and Week 30). The secondary objectives were to evaluate efficacy, PK, PD, and overall safety of Remsima® SC in comparison with infliximab IV up to Week 54.[9,10]

Part 2

This randomized, multicenter, open-label, parallel-group phase I study compared PK, symptomatic and endoscopic efficacy, safety and immunogenicity of Remsima® SC vs infliximab IV in IBD patients. The primary objective was to demonstrate that Remsima® SC is non-inferior to infliximab IV in terms of $C_{trough,week\ 22}$ (pre-dose level at Week 22).[7,8]

The secondary objectives were to evaluate efficacy, PK, PD, and overall safety of Remsima® SC in comparison with infliximab IV.[7,8]

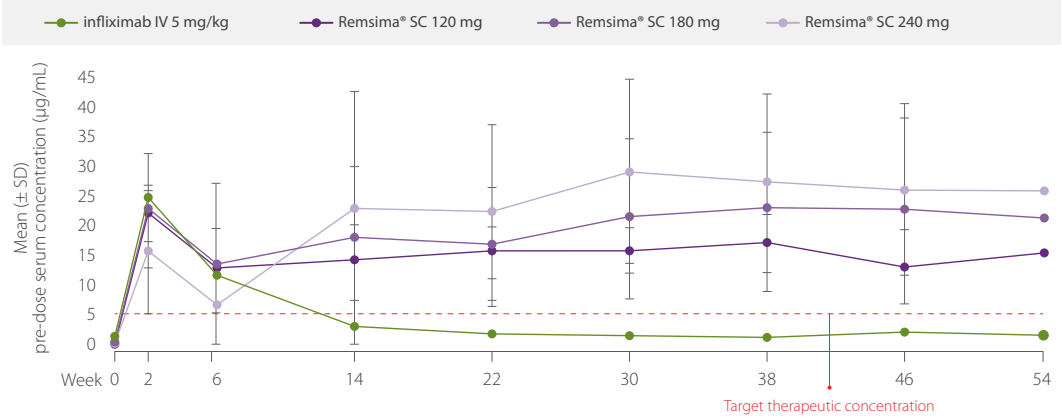
TNF-alpha inhibitor naive patients with UC (Mayo score 6-12 points with endoscopic subscore ≥ 2) or CD (CDAI index 220-450) from 50 centres were enrolled. After IV induction at week 0 and 2, patients were randomized to receive (1:1) Remsima® SC every 2 weeks or infliximab IV every 8 weeks. While Remsima® SC patients stayed on the treatment throughout the study (week 6-54), infliximab IV patients received IV in week 6-22 and then switched to SC every two weeks from week 30.[7,8]

AUC_{τ}, area under the curve at steady state, CD, Crohn's disease; CDAI, Crohn's disease activity index; C_{trough}, lowest serum concentration of a drug; IBD, inflammatory bowel disease; IV, intravenous; PD, pharmakodynamics; PK, pharmakokinetics; SC, subcutaneous; TNF-alpha, tumour necrosis factor alpha; UC, ulcerative colitis;

Established dose: 120mg

IBD Study Part 1 results[9,10]

Mean (± SD) **pre-dose** serum concentration of Remsima® by cohort — Figure 2



Adapted from Reinisch et al: Results from part 1 of a Phase I randomised controlled trial in patients with active CD.[9]

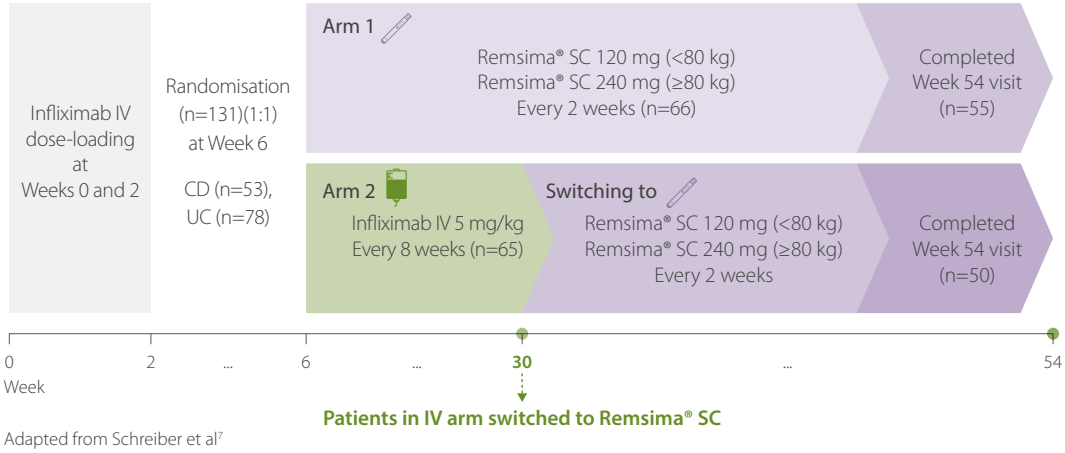
- C_{trough} levels of Remsima® SC consistently exceeded the threshold of target therapeutic concentration (5 µg/mL) up to the 1-year treatment period.[9]

Tested dose regimen[10]	C_{trough} (µg/mL)	$AUC_{22\text{-}30wk}$ (hr*µg/mL)	$C_{max,ss}$ (µg/mL)
Cohort 1: Infliximab IV 5 mg/kg every 8 weeks	2.3 (0.14 - 8.57)	25,599.73 (12,973.98 - 41,202.48)	103.69 (78.58 - 136.63)
Cohort 2: Remsima® SC 120 mg every 2 weeks	13.27 (5.62 - 26.77)	21,923.15 (11,227.54 - 41,085.68)	18.24 (10.14 - 32.63)
Cohort 3: Remsima® SC 180 mg every 2 weeks	19.91 (8.43 - 40.01)	32,882.88 (16,841.3 - 61,505.99)	27.36 (15.21 - 48.88)
Cohort 4: Remsima® SC 240 mg every 2 weeks	26.54 (11.23 - 53.24)	43,842.61 (22,455.07 - 81,926.30)	36.48 (20.28 - 65.15)

Adapted from Schreiber et al[10]

- PK modeling showed SC bioavailability of 60% (95% CI, 52-66%).[10]

IBD Study Part 2 design[7,8]

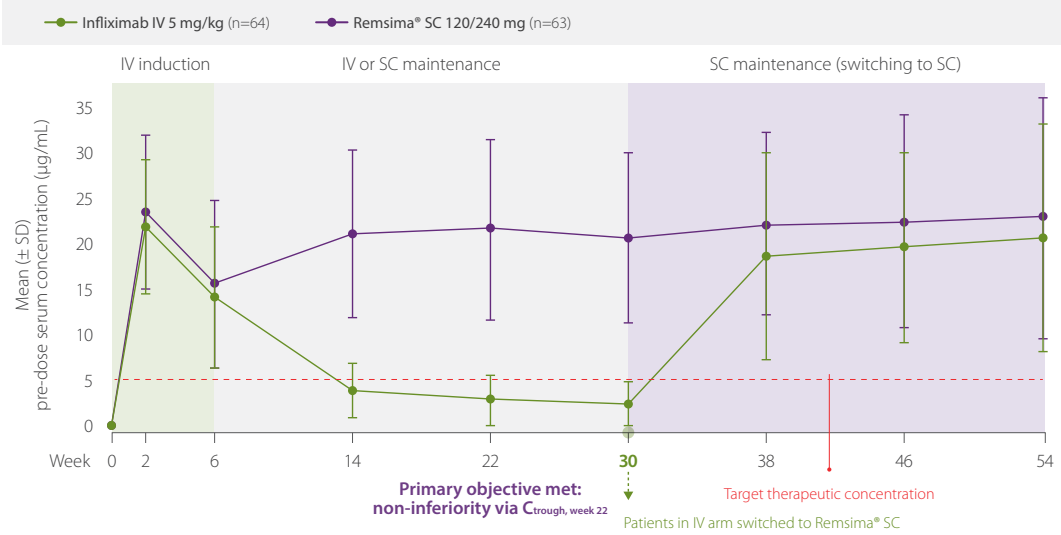


Adapted from Schreiber et al[7]

Administration of Remsima® SC every two weeks provides a stable pharmacokinetic profile[7,8,10]

Pharmacokinetic of SC vs IV administration

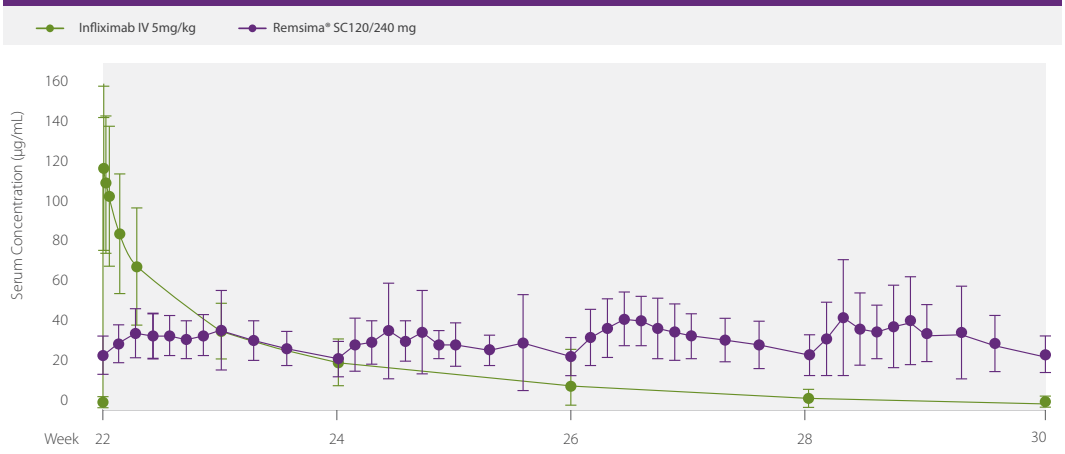
Mean (± SD) pre-dose serum concentration Figure 3



Adapted from Schreiber et al.[7]
Six CD patients and 8 UC patients in the SC and IV arms, respectively, had at least one escalated SC dose from 120mg to 240mg on or after Week 30.[8]

- Remsima® SC demonstrated non-inferiority to infliximab IV in terms of pre-dose concentration at Week 22 and therefore, met the primary outcome of the study.[7]
- In the Remsima® SC arm, the mean serum concentration before study drug administration increased from Week 6 and maintained a consistent level from Weeks 14 to 54.[8]
- After switching from IV to SC treatment at Week 30, the serum concentration gradually increased from Week 30 and maintained a consistent level up to Week 54.[8]
- Remsima® SC provides stable serum concentration with less fluctuation between C_{max} and C_{trough}, compared to IV administration, while maintaining levels constantly above the target therapeutic concentration of 5µg/mL.[8]

Serum Concentration at Steady State (Week 22 ~ 30) Figure 4



Adapted from Schreiber et al.[7]

AUC_{ss8w} (µg*h/mL)	SC 120/240mg (N=63)	IV 5mg/kg (N=64)
Mean ± SD	35467.2 ± 12000.94	28284.0 ± 10254.56
CV%	33.8	36.3

AUC, area under the curve; AUC_{ss8W}, area under the concentration-time curve for 8 weeks at steady state; CD, Crohn's disease; CI, confidence interval; C_{max}, maximum concentration; C_{trough}, trough serum concentration; CV, coefficient of variation; IBD, inflammatory bowel disease; IV, intravenous; SC, subcutaneous; SD, standard deviation; UC, ulcerative colitis

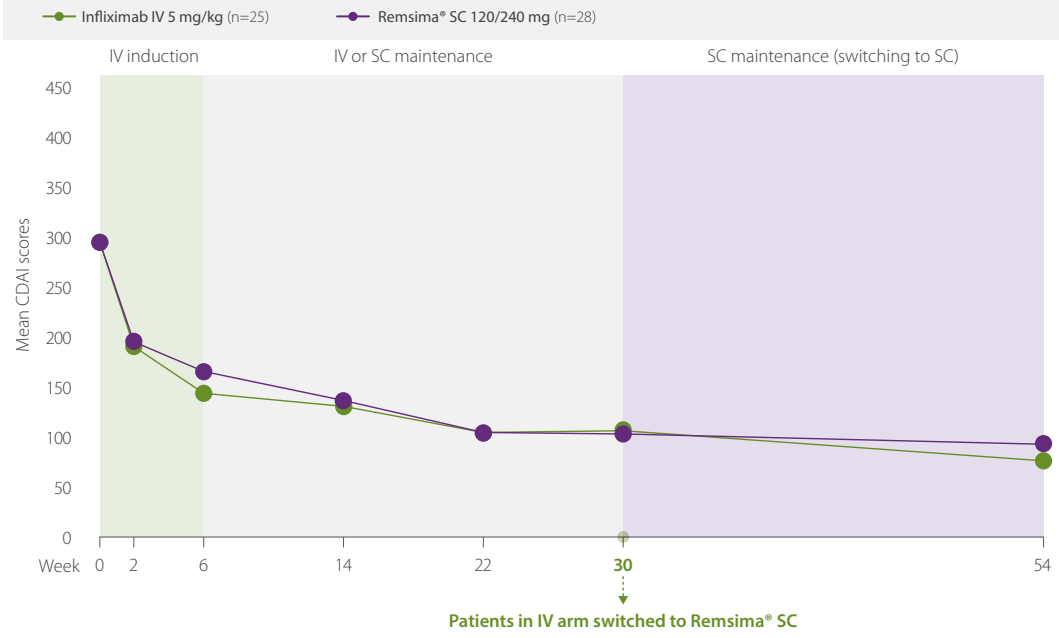
Administration of Remsima® SC every two weeks provides a stable pharmacokinetic profile[7,8,10]

Comparable efficacy to IV administration

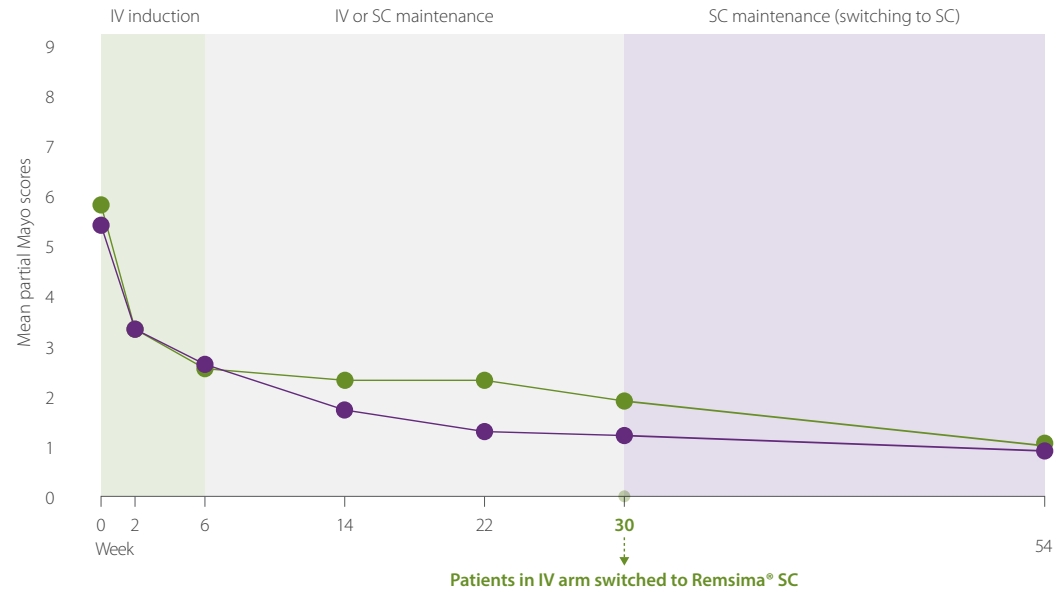
Efficacy

- The mean CDAI and partial Mayo scores decreased over time in both arms until Week 30 and comparable improvement in clinical activity was observed at Week 54 after switching.[8]

Mean CDAI scores up to Week 54 in patients with active CD Figure 5



Mean partial Mayo scores up to Week 54 in patients with active UC Figure 6



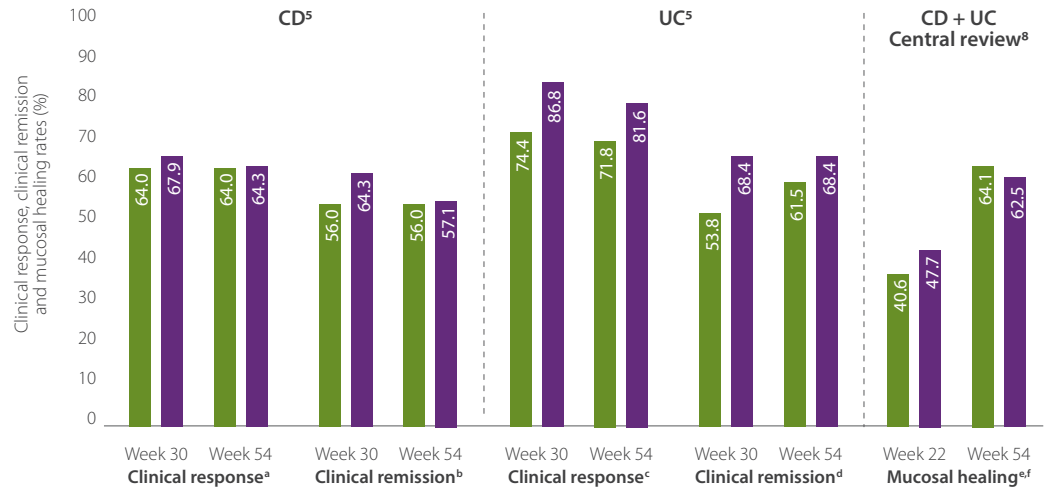
CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; IV, intravenous; SC, subcutaneous; SE, standard error; UC, ulcerative colitis

Remsima® SC offers comparable efficacy, including after switching from IV to SC[8]

Comparable response and remission rates to infliximab IV

- Clinical response and remission rates up to Week 54 were similar across both Remsima® SC and infliximab IV study arms and did not change after switching the administration route at Week 30.[7,8]

Long-term clinical response, clinical remission and mucosal healing in CD and UC Figure 7

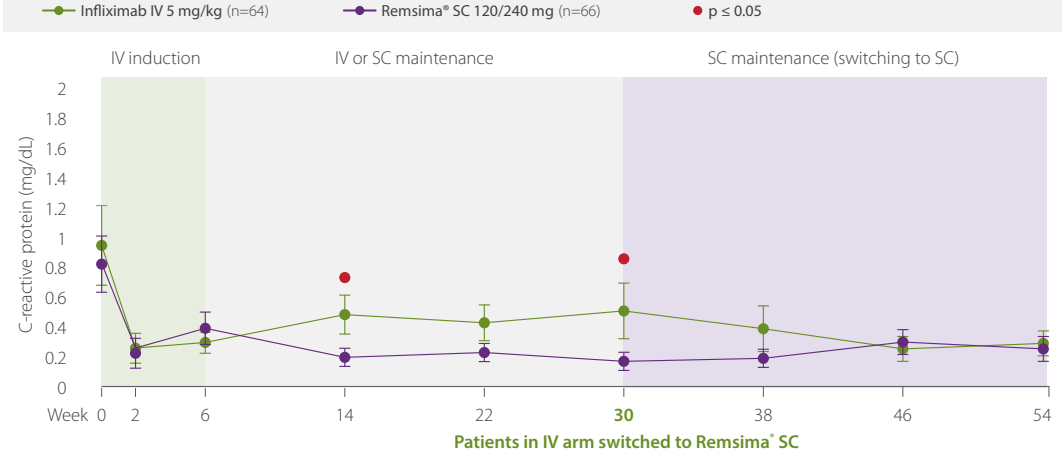


Adapted from Schreiber et al.[7]

[a] Decrease in CDAI score ≥100 from the baseline value (efficacy population) / [b] Absolute CDAI score <150 / [c] Decrease in partial Mayo score from baseline ≥2, with an accompanying decrease in the subscore for rectal bleeding of ≥1, or an absolute subscore for rectal bleeding of 0 or 1/[d] Partial Mayo score of ≤1 / [e] Absolute SES-CD score ≤2 for CD / [f] Absolute Mayo endoscopic subscore ≤1 for UC

- C-reactive protein levels decreased following IV induction and were maintained at comparable lowered levels throughout the 54 weeks with Remsima® SC and intravenous infliximab.[8]

C-reactive protein (mean, SE) Figure 8



Adapted from Ben-Horin et al.[8]

Six CD and 8 UC patients in the IV arm had at least one escalated SC dose from 120mg to 240mg on or after Week 30.[8]

Clinical response and remission rates were comparable with Remsima® SC and infliximab IV[7,8]

Comparable safety to IV administration

Safety

The overall safety profile of Remsima SC and infliximab IV was comparable during the maintenance phase and after switching to SC.[7,8]

Safety summary Table 1

Number (%) of patients		Maintenance phase (W6~54)		On or after Week 30[a] (W30~54)	
		IV 5 mg/kg (n=65)	Remsima® SC 120/240 mg (n=66)	IV 5 mg/kg (n=65)	Remsima® SC 120/240 mg (n=66)
TEAEs	Total	38 (58.5)	49 (74.2)	21 (32.3)	31 (47.0)
	Related	20 (30.8)	28 (42.4)	11 (16.9)	13 (19.7)
TEASEs	Total	6 (9.2)	5 (7.6)	2 (3.1)	3 (4.5)
	Related	2 (3.1)	1 (1.5)	1 (1.5)	1 (1.5)
IRR/SIR/DEL	Total (=Related)	2 (3.1)	3 (4.5)	0	2 (3.0)
	IRR[b]	2 (3.1)	N/A	N/A	N/A
	SIR[c]	0	1 (1.5)	0	1 (1.5)
	DEL[d]	0	2 (3.0)	0	1 (1.5)
Localised Injection Site Reaction	Total	3 (4.6)	15 (22.7)	2 (3.1)	7 (10.6)
	Related	3 (4.6)	14 (21.2)	2 (3.1)	7 (10.6)
Infection	Total	19 (29.2)	21 (31.8)	9 (13.8)	12 (18.2)
	Related	6 (9.2)	9 (13.6)	2 (3.1)	3 (4.5)
Study drug discontinuation due to AE	Total	3 (4.6)	1 (1.5)	0	1 (1.5)
	Related	3 (4.6)	1 (1.5)	0	1 (1.5)

Injection site reactions were grade 1 or 2 in intensity and the majority recovered without treatment.[8]

[a] All patients in the Remsima® IV 5 mg/kg treatment arm switched to receive either 120mg or 240mg of Remsima® SC treatment from Week 30
[b] Infusion related reaction (IRR): Occurred between start of administration and 24 hours from the IV infusion
[c] Systemic injection reaction (SIR): Occurred between start of administration and 24 hours from the SC injection
[d] Delayed hypersensitivity (DEL): Occurred after 24 hours from the study drug administration

ADA, anti-drug antibodies; AE, adverse event; CD, Crohn's disease; IV, intravenous; N/A, not applicable; EOS, end of study; NAb, neutralizing antibody; SC, subcutaneous; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event; UC, ulcerative colitis; W, week

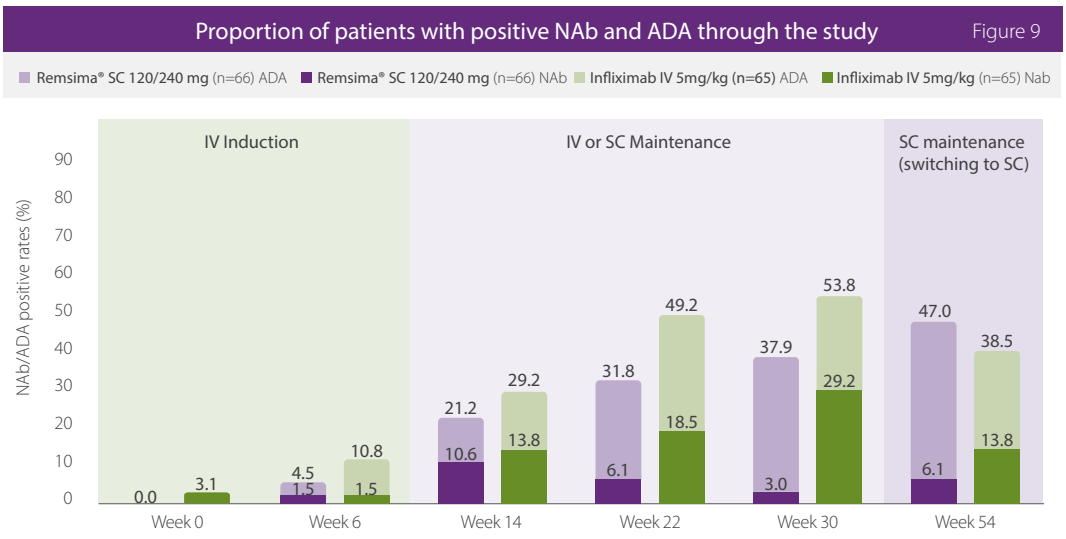
Remsima® SC has a comparable safety profile to infliximab IV in patients with active CD or UC[8]

Immunogenicity profile

Immunogenicity

- During the entire study (W0-54), similar proportions of patients in each arm converted to ADA-positive status.[7]
- Initial lower rate of NAb with Remsima® SC were maintained up to Week 54 with an overall comparable status of total ADA (NAb and non-NAb).[8]
- A smaller proportion of patients in the Remsima SC arm converted to NAb-positive status compared with the infliximab arm (p=0.0194; 18.2% [n=12/66] vs 36.9% [n=24/65] respectively).[7]

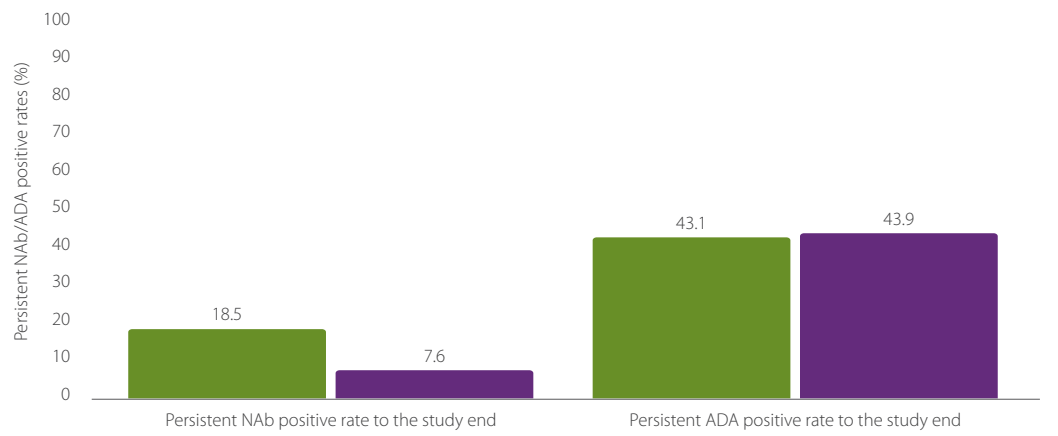
Proportion of patients with positive NAb and ADA through the study Figure 9



Adapted from the EMA Public Assessment Report for Remsima, p111.[12]

Immune respones against Remsima® SC in human serum were detected using an electrochemiluminescence (ECL) platform with an affinity capture elution (ACE) step. More than 25 ng/mL of ADA can be detected in the presence of 120 µg/mL of Remsima® in CD and UC serum.

Patients with positive NAb and ADA at Week 54 Figure 10



Adapted from Ben-Horin et al.[8]

Persistent ADA/NAb: Patients who had persistent ADA to the study end once being detected. All immunogenicity results up to Week 54 excluding results at EOS and unscheduled visits were considered. Immune responses against Remsima® SC in human serum were detected using an electrochemiluminescence (ECL) platform with an affinity capture elution (ACE) step. More than 25 ng/mL of ADA can be detected in the presence of 120 µg/mL of Remsima® in CD and UC serum.

Remsima® SC has a comparable immunogenicity profile to Infliximab IV administration[7,8,11]

Indications

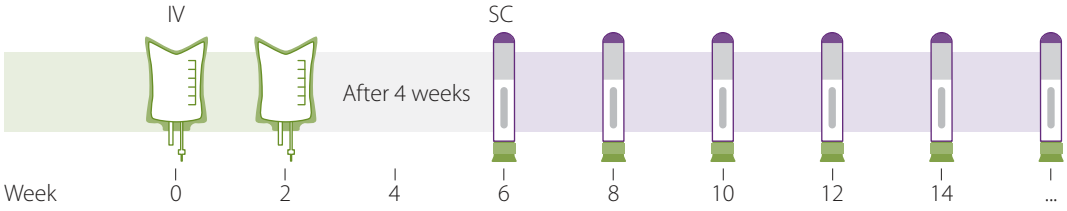
Remsima® SC is indicated for adult patients[4]

Indication	Posology
• Moderate to severe Crohn's Disease • Refractory fistulising Crohn's Disease • Moderately severe to severe active Ulcerative Colitis	**Initiation** • **IV induction with 5 mg/kg** at Week 0, 2 • **SC maintenance with120 mg dose every 2 weeks,** starting from Week 6 **Maintenance therapy** • Last dose of infliximab IV given at week 0. • SC maintenance with 120mg dose every 2 weeks, starting from week 8.

Dosing schedules[4]

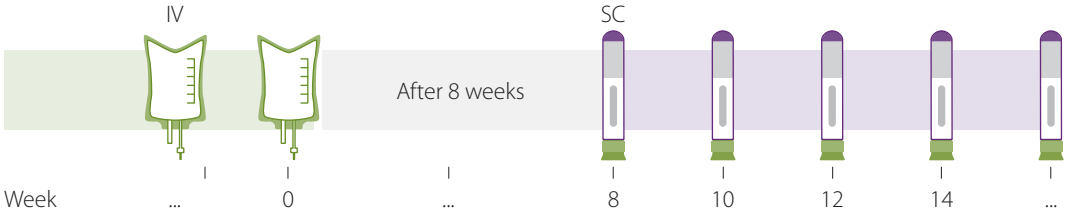
Remsima® SC initiation

- 4 weeks after last administration of the infliximab IV at week 0 and 2.
- Administration of Remsima® SC starting from week 6, every two weeks.



Switching from the maintenance therapy of infliximab intravenous

- 8 weeks after last administration of the infliximab IV
- Administration of Remsima® SC starting from week 8, every two weeks



IV, intravenous; SC, subcutaneous

Administration of Remsima® SC every two weeks provides a stable pharmacokinetic profile[7,8,10]

Remsima®
Infliximab

SUBCUTANEOUS

Remsima® SC contains infliximab, a time tested and clinically established TNF-alpha blocker, with a well-known safety and efficacy profile[1,2]

The only subcutaneous infliximab approved in Australia[4]

Comparable efficacy and safety to infliximab IV[7,8]

Convenient care through self-administration[3]

Comparable immunogenicity profile of Remsima® SC to infliximab IV[7, 8,11]

120mg is the recommended dose[4]

References: 1. Molloy, J. W., Stengel, J. Z. and Arnold, H. L. (2009) 'Infliximab: A Review of its Use in the Treatment of Crohn's Disease', Clinical Medicine. Therapeutics. **2.** Rutgeerts, P, Van Assche, G. and Vermeire, S. (2006), Review article: infliximab therapy for inflammatory bowel disease – seven years on. Alimentary Pharmacology & Therapeutics, 23: 451-463. **3.** Cha JM et al., Journal Korean Med Sci 2017;32:85–9. **4.** Remsima® Product Information. Available at: https://www.ebs.tga.gov.au/ebs/picmi/ picmirepository.nsf/pdf?OpenAgent&id=CP-2020-PI-02540-1. **5.** Lamb CA et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut 2019;68:s1–s106. **6.** Papamichael K et al., Infliximab in inflammatory bowel disease. Ther Adv Chronic Dis. 2019;10:2040622319838443. **7.** Schreiber, S et al. (in press) Randomized Controlled Trial: Subcutaneous vs Intravenous Infliximab CT-P13 Maintenance in Inflammatory Bowel Disease; J. Gastroenterol. DOI: https://doi.org/10.1053/j.gastro.2021.02.068 Accessed 10 May 2021. **8.** Ben-Horin S et al. A novel subcutaneous infliximab (CT-P13): 1-year results including a switch from intravenous infliximab (CT-P13) in patients with active Crohn's Disease and Ulcerative Colitis. OP24. Presented at ECCO 2020, 12–15 February, Vienna. **9.** Reinisch W et al. A Novel Formulation of CT-P13 (Infliximab Biosimilar) for Subcutaneous Administration: 1-Year Result from a Phase I Open-label Randomised Controlled Trial in Patients with Active Crohn's Disease. DOP62. Presented at ECCO 2019, 6–9 March, Copenhagen. **10.** Schreiber S et al. Novel Formulation of CT-P13 (Infliximab Biosimilar) for Subcutaneous Administration: Initial Results from a Phase I Open-Label Randomized Controlled Trial in Patients with Active Crohn's Disease. Gastroenterology 2018;154(6):S1371. **11.** Schreiber S et al. Non-inferiority of Novel Subcutaneous Infliximab (CT-P13) to Intravenous Infliximab (CT-P13) in Patients with Active Crohn's Disease and Ulcerative Colitis: Week 30 Results from a Multicentre, Randomised Controlled Pivotal Trial. LB02. Presented at UEGW 2019, 19–23 October, Barcelona. **12.** EMA Public Assessment Report for Remsima (EMA/376884/2020). Available at: https://www.ema.europa.eu/en/ documents/variation-report/remsima-h-c-2576-ii-0082-epar-assessment-report-variation_en.pdf. Accessed on 10-Jun-2021.

PBS Information: Authority required. Refer to PBS Schedule for full authority information. This product is not listed on the PBS for the treatment of refractory fistulising Crohn's Disease.

Before prescribing, please review full product information available on request from the Celltrion Healthcare Australia Pty Ltd Medical Information Service (Phone: 1800 325 228) or www.ebs.tga.gov.au.

MINIMUM PRODUCT INFORMATION REMSIMA® SC (infliximab) containing 120mg infliximab for subcutaneous injection in a 1mL single dose pre-filled pen or syringe. **INDICATIONS (Adults ≥18 years):** Rheumatoid arthritis (RA), in combination with methotrexate, for the reduction of signs and symptoms and prevention of structural joint damage (erosions and joint space narrowing) in patients with active disease despite treatment with methotrexate, and patients with active disease who have not previously received methotrexate. Should be combined with methotrexate (Efficacy and safety in RA only demonstrated in combination with methotrexate); Ankylosing spondylitis (AS), to reduce signs and symptoms and improve physical function in patients with active disease; Psoriatic arthritis (PsA), to treat signs and symptoms, as well as for the improvement in physical function in patients with active and progressive disease who responded inadequately to disease-modifying anti-rheumatic drug (DMARD) therapy (may be combined with methotrexate); Psoriasis, in patients with moderate to severe plaque psoriasis for whom phototherapy or conventional systemic treatments were inadequate or are inappropriate. Safety and efficacy beyond 12 months is not established; Moderate to severe crohn's disease (CD), to reduce the signs and symptoms and to induce and maintain clinical remission in patients who have an inadequate response to conventional therapies; Refractory fistulising crohn's disease, to reduce the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure; Moderately severe to severe active ulcerative colitis (UC) in patients who had an inadequate response to conventional therapy. **CONTRAINDICATIONS:** Severe infections (e.g. sepsis, abscesses, tuberculosis and opportunistic infections); History of hypersensitivity to infliximab, other murine proteins or any excipient; Concurrent administration with anakinra; Congestive heart failure or moderate or severe heart failure (NYHA class III/IV). **PRECAUTIONS:** Systemic injection reaction/localized injection site reaction/hypersensitivity: Systemic injection reactions, anaphylactic shock and delayed hypersensitivity reactions occurred, and differ in time of onset. Initiate IV dose where medications (such as adrenaline, antihistamines, corticosteroids and/or paracetamol) and artificial airway are available. Pre-treatment with e.g., antihistamine, hydrocortisone and/or paracetamol may prevent mild and transient effects. Localised injection site reactions incl. erythema, pain, pruritus, swelling, induration, bruising, haematoma, oedema, coldness, irritation, paraesthesia, ulcer, urticaria, haemorrhage, rash and scab occured following SC dose. If re-treatment after prolonged period, monitor closely for symptoms of delayed hypersensitivity. **Malignancies and lymphoproliferative disorders:** Risk of development of lymphomas/other malignancies can't be excluded. Caution with history of malignancy, with increased risk for malignancy, and treating patients who develop a malignancy. Possible increased risk of cervical cancer; periodic screening should continue in women, incl. ≥60 years. Post-marketing cases of hepatosplenic T-cell lymphoma and leukaemia occured. Most hepatosplenic T-cell lymphoma cases occurred in patients with CD or UC treated concomitantly with AZA or 6-MP. Melanoma and Merkel cell carcinoma occured, periodic skin examination is recommended, particularly with risk factors for skin cancer. Patients with UC at increased risk for, or with a prior history of dysplasia or colon carcinoma, should be screened for dysplasia before therapy and regularly. Infections: Monitor closely for infections, including tuberculosis, before, during and up to 6 months after treatment. Caution with chronic infection or a history of recurrent infection. Suppression of TNF may mask symptoms of infection such as fever. Tuberculosis, bacterial infections (including sepsis and pneumonia), invasive fungal, viral and other opportunistic infections, were observed, some were fatal. Active tuberculosis in patients receiving infliximab was observed. Before treatment, evaluate for active or latent tuberculosis. Therapy must not be initiated if active tuberculosis. If latent tuberculosis, consult physician with expertise in tuberculosis treatment and consider benefit/risk. Treatment of tuberculosis must be initiated before initiation of Remsima®. Suspect an invasive fungal infection such as aspergillosis, candidiasis, pneumocystosis or listeriosis if serious systemic illness develops. Consult a physician with expertise in treatment of invasive fungal infections at an early stage. Fistulising CD patients with acute suppurative fistulas must not initiate Remsima® until possible source of infection is excluded. Should not be given when chronic viral infections such as HIV, Hepatitis B or C. Hepatitis B (HBV) reactivation: Reactivation of HBV occurred in chronic carriers when receiving infliximab. Some were fatal. Test for HBV infection before initiating treatment and closely monitor for symptoms of active HBV. Hepatobiliary events: Jaundice and non-infectious hepatitis, some with features of autoimmune hepatitis, was observed. Isolated cases of liver failure resulting in liver transplantation or death occurred. Discontinue if jaundice and/or ALT elevations ≥5 times the upper limit of normal develop. Vaccinations/therapeutic infectious agents: Prior to therapy vaccinations should be up to date. May use concurrent vaccinations, but live vaccines or therapeutic infectious agents not recommended. In infants exposed in utero to infliximab, fatal outcome due to disseminated Bacillus Calmette Guérin (BCG) infection occured following administration of BCG vaccine after birth. Min. six month waiting period after birth before use of live vaccines to infants exposed in utero to infliximab. Autoimmune processes: Discontinue treatment if symptoms suggestive of a lupus-like syndrome and positive for antibodies against double-stranded DNA. Neurological events: Anti-TNF agents are associated with new onset or exacerbation of clinical symptoms and/or radiographic evidence of peripheral and CNS demyelinating disorders, including Guillain-Barré syndrome and multiple sclerosis. Caution in patients with these disorders and consider discontinuation if these develop. Heart failure: Caution with mild heart failure (NYHA class I/II) and discontinue when new or worsening symptoms of heart failure develope. Hematologic reactions: Consider discontinuation when significant hematologic abnormalities, including pancytopenia, leukopenia, neutropenia and thrombocytopenia. Others: When surgery whilst on therapy closely monitor for infections. Use in the elderly: Caution in the treatment of elderly patients (Elderly patients have a greater frequency of decreased hepatic, renal and/or cardiac function and, concomitant disease and/or other drug therapy). Fertility, pregnancy and lactation/Women of childbearing potential should consider adequate contraception to prevent pregnancy and continue use for ≥6 months after treatment. Not recommended for use during pregnancy and lactation. Breastfeeding should be discontinued for ≥6 months after treatment. Paediatric use: Safety and efficacy of subcutaneous therapy in children <18 years is not established, and is recommended for use only in adults. **INTERACTIONS:** No specific drug interaction studies conducted. Combination with anakinra is contraindicated, use with abatacept as well as other biological therapeutics used to treat the same conditions not recommended. Majority of patients in clinical trials received concomitant medications normally used in Crohn's disease. No interactions were reported. In RA, PsA and CD patients, concomitant use of methotrexate/other immunomodulators may reduce antibody formation and increase plasma concentration of infliximab. May use concurrent vaccinations, but use of live vaccines or therapeutic infectious agents not recommended. Min. six month waiting period after birth before use of live vaccines to infants exposed in utero to infliximab. **ADVERSE EFFECTS:** Very common: localised injection site reactions (e.g. injection site erythema, pain, pruritus, bruising). Common: viral infection (e.g. influenza, herpes infection), fever, serum-sickness-like reactions, headache, vertigo/dizziness, flushing, upper respiratory tract infection, lower respiratory tract infection (e.g., bronchitis, pneumonia), dyspnoea, sinusitis, nausea, diarrhoea, abdominal pain, dyspepsia, abnormal hepatic function, rash, pruritus, urticaria, increased sweating, dry skin, fatigue, chest pain, infusion-related reactions. For other less common and rarely reported adverse reactions please refer to the full PI. **DOSAGE AND ADMINISTRATION: Subcutaneous injection (Adults ≥18 years). The recommended dose is 120mg every 2 weeks. Initiate as maintenance therapy 4 weeks after the last of two IV doses of 3 mg/kg (in RA) and 5mg/kg (all other indications) given 2 weeks apart.** Treatment to be initiated and supervised by qualified physicians experienced in the treatment of Remsima® approved indications. Remsima® SC to be administered by subcutaneous injection only. During treatment, concomitant therapies, e.g. corticosteroids and immunosuppressants should be optimised. RA: Must be given in combination with methotrexate. Consider discontinuation if no therapeutic benefit after 12 weeks. Moderately to severely active CD and AS: Discontinue if no response after 6 weeks (i.e. 2 IV doses). Fistulising active CD: Discontinue if no response after 6 doses (i.e. 2 IV doses and 4 SC doses). UC: If no response after 14 weeks, i.e. 2 IV doses and 4 SC doses, consider discontinuation. PsA: Initiate as stated above. Psoriasis: Discontinue treatment if no response after 14 weeks (i.e. 2 IV doses and 5 SC doses). **Re-Administration:** CD and RA: Safety and efficacy of re-administration after treatment free interval of >16 weeks not established. In clinical studies with IV, delayed hypersensitivity reactions were uncommon and occurred after infliximab-free intervals <1 year. AS: Data supporting re-administration, other than every 6 to 8 weeks, not available (based on experience with IV). UC and PsA: Data supporting re-administration, other than every 8 weeks, not available (based on experience with IV). Psoriasis: Limited experience from re-treatment with single dose after interval of 20 weeks suggests reduced efficacy and a higher incidence of mild to moderate infusion reactions compared to the initial induction regimen. Limited experience from re-treatment of IV following disease flare by a re-induction regimen suggests higher incidence of infusion reactions, including serious ones, when compared to 8-weekly maintenance treatment (based on experience with IV). Across indications: If maintenance therapy is interrupted, use of IV re-induction regimen not recommended. Re-initiate as a single IV dose followed by SC maintenance as described above given 4 weeks after the IV dose. **Switching from IV maintenance to SC across indications:** If switch from IV maintenance to SC, administer SC dose 8 weeks after last IV dose. There is insufficient data switching patients on IV higher than 3 mg/kg for RA or 5 mg/kg for CD 8 weekly. **Missed dose:** Delayed ≤7 days, administer missed dose, continue original bi-weekly schedule. Delayed ≥8 days, skip missed dose, remain on original bi-weekly schedule.

Celltrion Healthcare Australia Pty Ltd.
Suite 13.03, 31 Market Street, Sydney NSW 2000, Australia
www.celltrionhealthcare.com.au www.remsimate.com.au

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