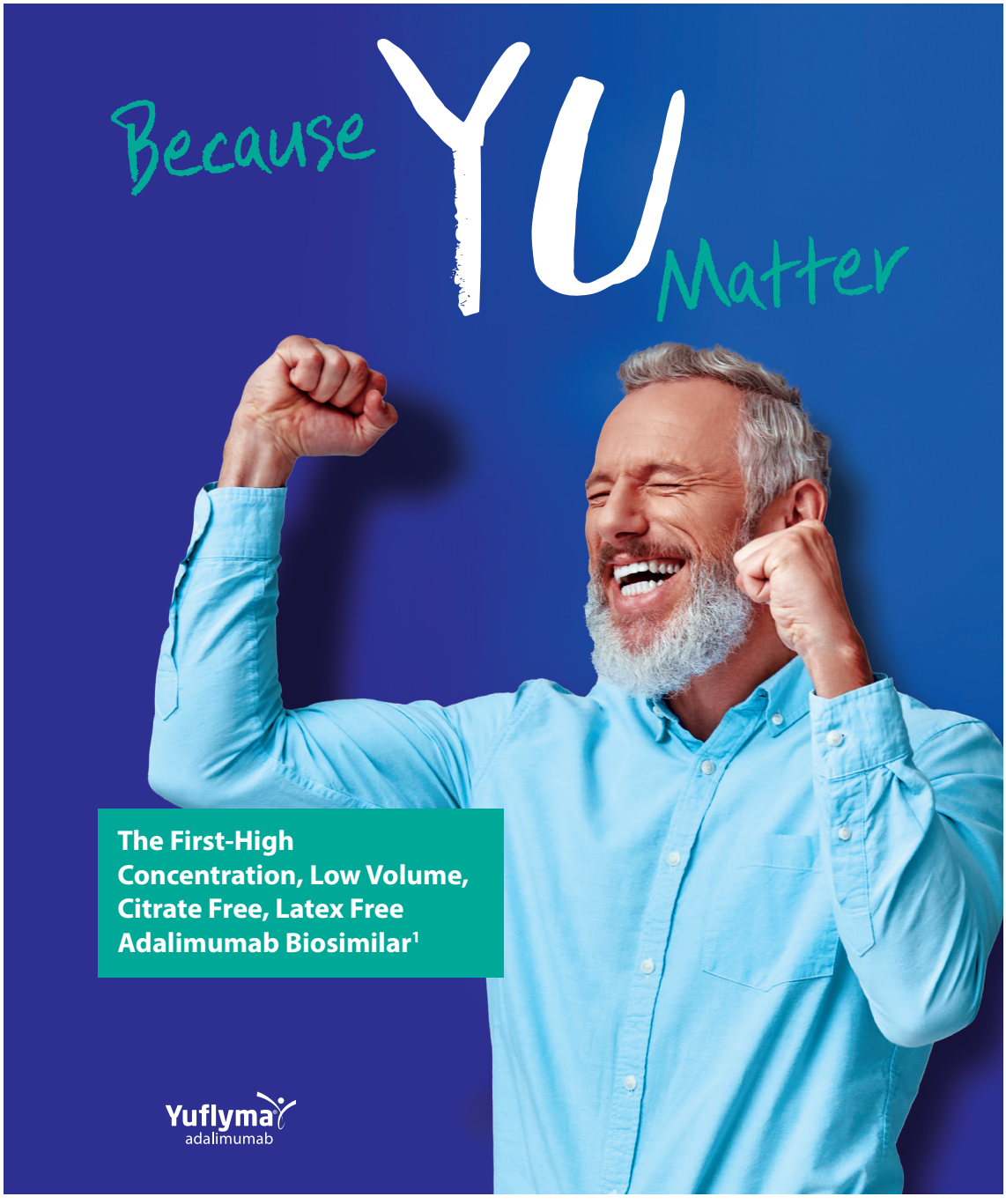
Yuflyma®
adalimumab

What is Your Choice for Patients?

Yuflyma®, for patient-centric treatment

HEALTHCARE
CELLTRION



Yuflyma®, is the first citrate-free, latex-free high concentration, low volume adalimumab biosimilar and is indicated for the treatment of:[1*]

- Rheumatoid arthritis
- Juvenile idiopathic arthritis
- Ankylosing Spondylitis
- Psoriatric arthritis
- Psoriasis
- Paediatric plaque psoriasis
- Hidradentis suppurativa
- Crohn's disease
- Paediatric Crohn's disease
- Ulcerative colitis
- Uveitis

*Please refer to Yuflyma®'s prescribing information for more detailed information on the therapeutic indications of Yuflyma®.

Yuflyma®, matching the originator formulation, with the benefit of streamlined PBS authority, a Patient Support Program and free home delivery.[1,2,3,6,7,8]

01 Proven outcomes [2,4-5]

- Equivalent PK & Efficacy*
- Comparable trough level*
- Comparable ADA level*

* Compared to high-concentration Humira®

02 Same features as originator [1,6]

- High concentration, low volume
- Citrate-free and latex-free
- Two device types

03 Improved convenience [1,3]

- 2 step push-type device (no button)
- Yuflyma® Home Delivery[7]
- 30 days storage period† (still as at February 2023)
- square shape with rounded edges for good grip

† Storage period of up to 30 days at room temperature (25°C with protection from light)

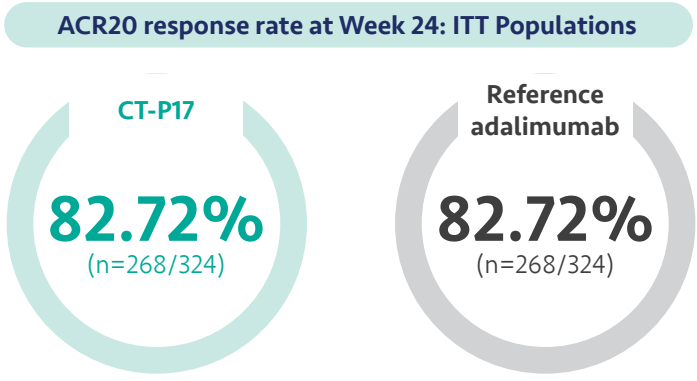
04 Patient Support Program[7]

- F2F or virtual injection trainng by nurses
- Patient Help Hotline 1800-SUBCUT
- Email/SMS injection reminders
- Two cooling boxes: short and long travel

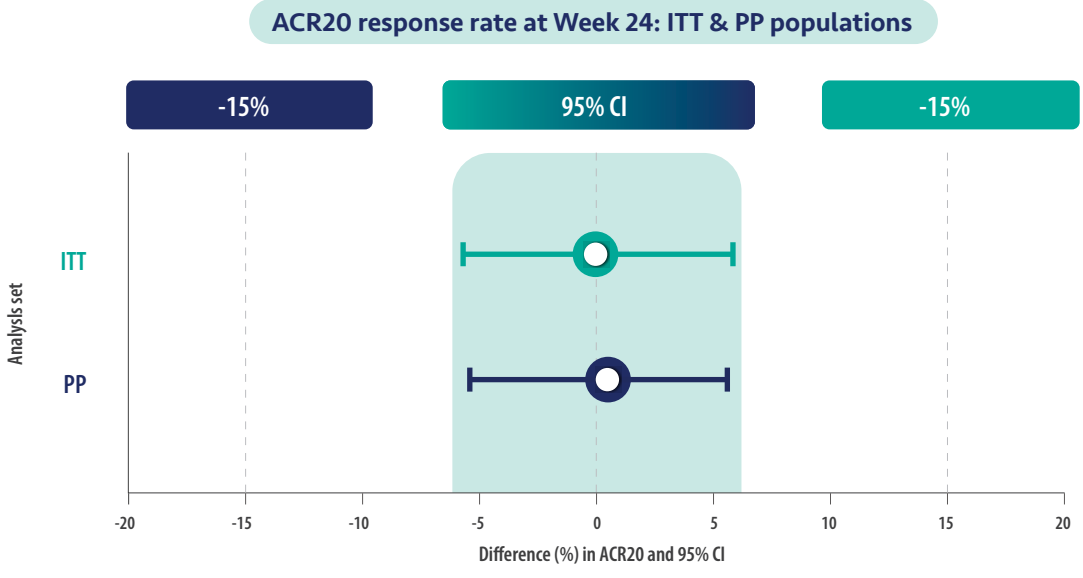
01 PROVEN **OUTCOMES**

Yuflyma® demonstrated equivalence to reference adalimumab in terms of efficacy at Week 24.[4,5]

- The ACR20 response rate at Week 24 in patients with active moderate-to-severe RA was the same in both CT-P17 and reference adalimumab treatment groups, with an estimated treatment difference of 0.



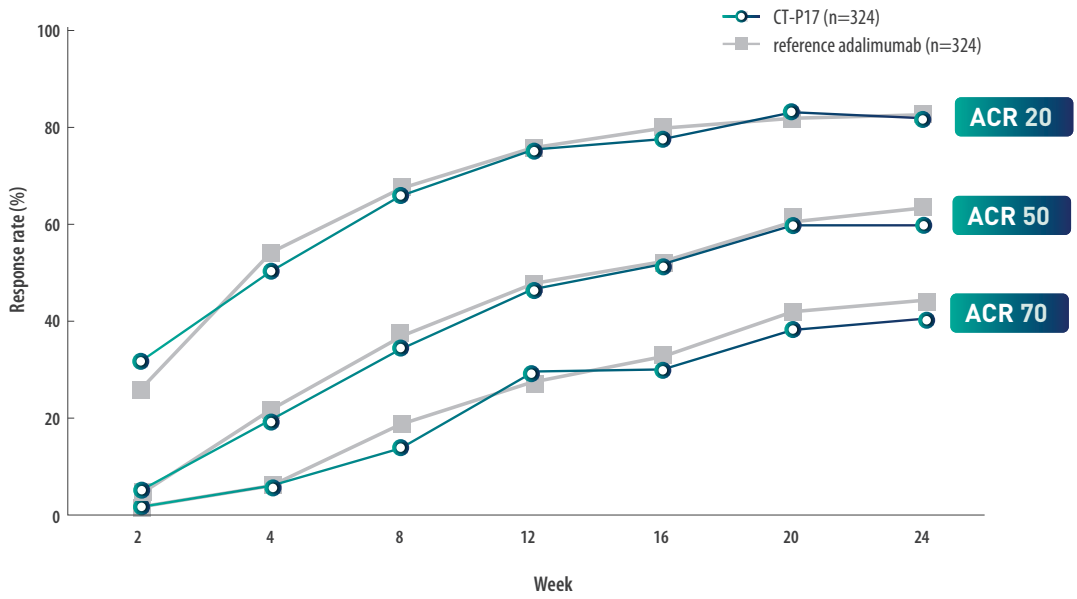
- Corresponding CI was entirely within the predefined symmetric (±15%) equivalence margins, and the per-protocol (PP) analysis also supported biosimilarity of CT-P17 to reference adalimumab.



ACR20/50/70, American College of Rheumatology 20%/50%/70% improvement criteria; **CI,** confidence interval; **ITT,** intent-to-treat; **PP,** per-protocol; **RA,** rheumatoid arthritis

- ACR20/50/70 response rates up to Week 24 showed a similar trend between CT-P17 and reference adalimumab treatment groups.

ACR20/50/70 response rates up to Week 24: ITT populations



[Study Design] A randomized, double-blind phase 3 study in which subjects with active RA at 52 centers were randomized (1:1) to receive CT-P17 or EU-adalimumab 40 mg subcutaneously every 2 weeks until week 52. The primary endpoint was 20% improvement by American College of Rheumatology criteria (ACR20) response rate at week 24. Equivalence was concluded if the corresponding confidence intervals (CIs) for the estimate of treatment difference were within predefined equivalence margins: – 15 to 15% (95% CI; European Medicines Agency assumption); – 12 to 15% (90% CI; Food and Drug Administration assumption). Additional efficacy, pharmacokinetic, usability, safety, and immunogenicity endpoints were evaluated.

01 PROVEN **OUTCOMES**

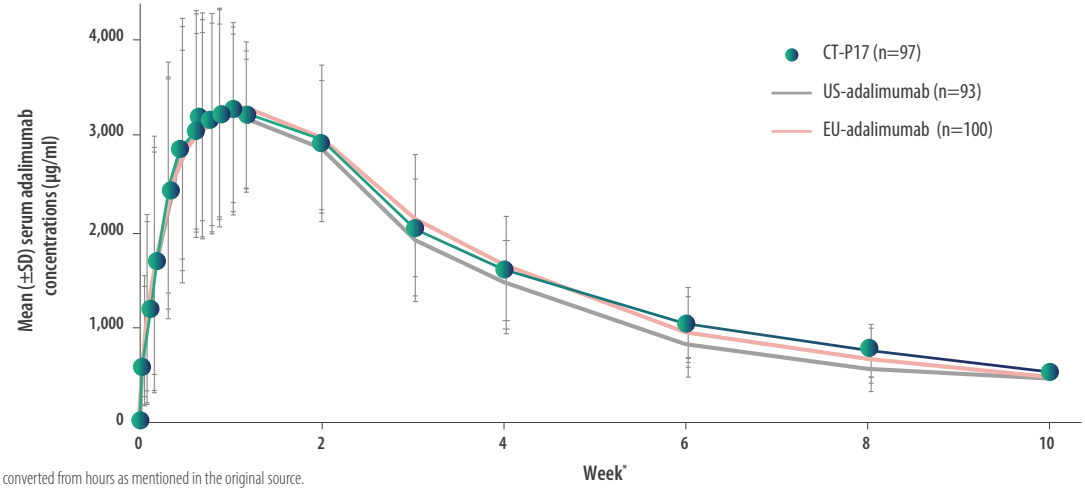
Yuflyma® demonstrated pharmacokinetic equivalence to high-concentration reference adalimumab.[2,4-5]

- The 90% confidence intervals (CI) for the geometric least squares mean ratios of each of the primary PK parameters of CT-P17, US-adalimumab, and EU-adalimumab treatment groups were within the predefined equivalence margin of 80% to 125%.[2]

Treatment and comparison	Geometric least squares mean (n)		
	C_{max} (µg/mL)	$AUC_{0\text{-}inf}$ (h·µg/mL	$AUC_{0\text{-}last}$, (h·µg/mL)
CT-P17	3.008 (96)	2,165.0 (80)	1,949.2 (96)
US - adalimumab	2.952 (93)	2,046.5 (86)	1,816.6 (93)
EU - adalimumab	3.006 (98)	2,209.3 (89)	1,933.9 (98)
	Ratio of geometric least squares mean (90% CI)		
CT-P17 vs US-adalimumab	101.89 (95.33-108.89)	105.79 (97.19-115.16)	107.30 (98.29-117.13)
CT-P17 vs EU-adalimumab	100.05 (93.69-106.85)	98.00 (90.06-106.63)	100.79 (92.42-109.92)
US-adalimumab vs EU-adalimumab	98.20 (91.91-104.92)	92.63 (85.29-100.61)	93.93 (86.08-102.50)

- Mean serum concentrations of adalimumab up to Day 71 were comparable among the CT-P17, US-adalimumab, and EU-adalimumab treatment groups.[2]

Mean (±SD) serum concentrations of adalimumab: PK population



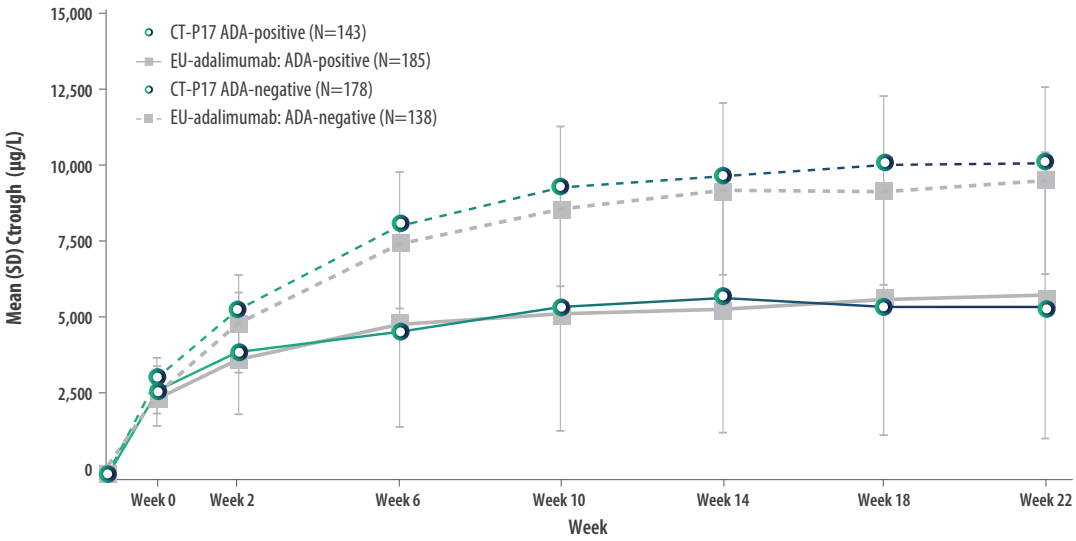
* Time converted from hours as mentioned in the original source.

ADA, anti-drug antibody; **AUC0-inf,** area under the concentration-time curve from time zero to infinity; **AUC0-last**, area under the concentration-time curve from time zero to last quantifiable concentration; **CI,** confidence intervals; **Cmax**, maximum serum concentration; **Ctrough,** trough serum concentration; **PK,** pharmacokinetics; ref-adalimumab, reference adalimumab; **SD,** standard deviation

[Study Design] Adouble-blind, parallel-group, phase I trial conducted at 10 hospitals (Republic of Korea) to demonstrate pharmacokinetic (PK) equivalence of a single dose of the proposed adalimumab biosimilar CT-P17 to United States-licensed adalimumab (US-adalimumab)and European Union-approved adalimumab (EU-adalimumab) in which healthy subjects (1:1:1) were randomized to receive a single 40 mg (100 mg/ mL) subcutaneous injection of CT-P17, US-adalimumab, or EU-adalimumab. Primary endpoints were PK equivalence in terms of: area under the concentration–time curve from time zero to infinity (AUC0–inf); area under the concentration–time curve from time zero to the last quantifiable concentration (AUC0–last); and maximum serum concentration (Cmax). PK equivalence was concluded if 90% confidence intervals (CIs) for percent ratios of geometric least squares means (gLSMs) for pairwise comparisons were within the equivalence margin of 80–125%. Additional PK endpoints, safety, and immunogenicity were evaluated.

- The mean C_{trough} for both CT-P17 and reference adalimumab treatment groups in the PK population gradually increased from baseline up to Week 24. The mean Ctrough was generally lower in the ADA-positive subgroup compared to the ADA-negative subgroup in both treatment groups.[4,5]

Mean C_{trough} up to Week 22 by ADA status: PK population



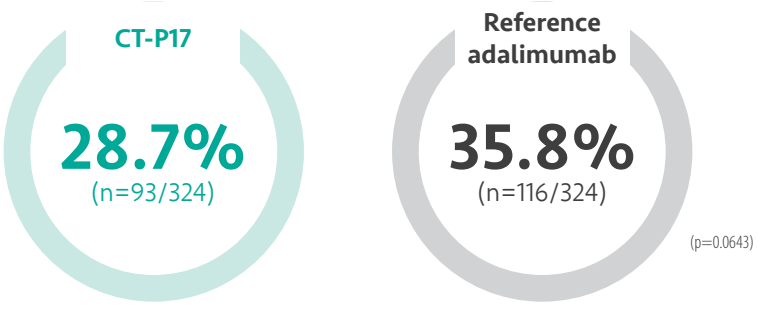
[Study Design] A randomized, double-blind phase 3 study in which subjects with active RA at 52 centers were randomized (1:1) to receive CT-P17 or EU-adalimumab 40 mg subcutaneously every 2 weeks until week 52. The primary endpoint was 20% improvement by American College of Rheumatology criteria (ACR20) response rate at week 24. Equivalence was concluded if the corresponding confidence intervals (CIs) for the estimate of treatment difference were within predefined equivalence margins: – 15 to 15% (95% CI; European Medicines Agency assumption); – 12 to 15% (90% CI; Food and Drug Administration assumption). Additional efficacy, pharmacokinetic, usability, safety, and immunogenicity endpoints were evaluated.

01 PROVEN **OUTCOMES**

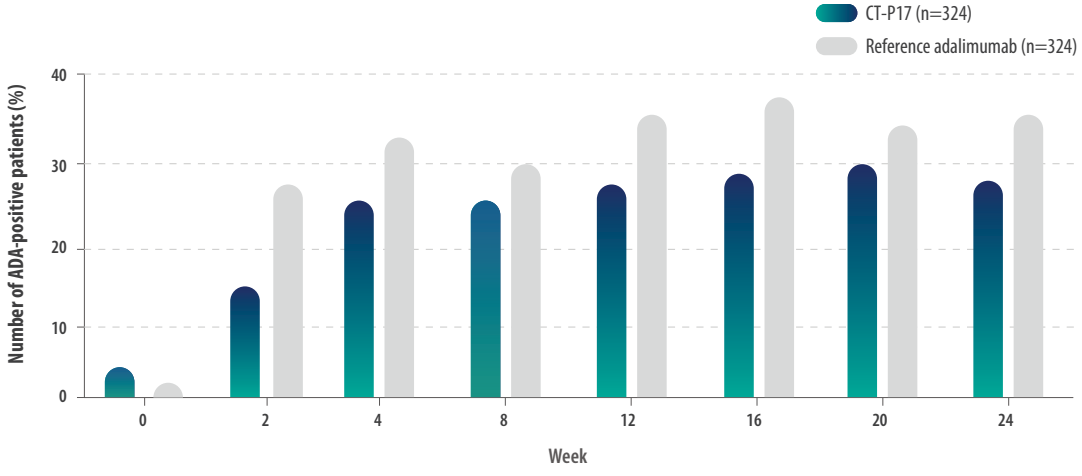
Yuflyma® demonstrated a slightly lower proportion of patients with ADA than reference adalimumab.[4,5]

- CT-P17 demonstrated a slightly lower proportion of patients who had ADA compared to reference adalimumab at Week 24.

Proportion of patients with ADA at Week 24



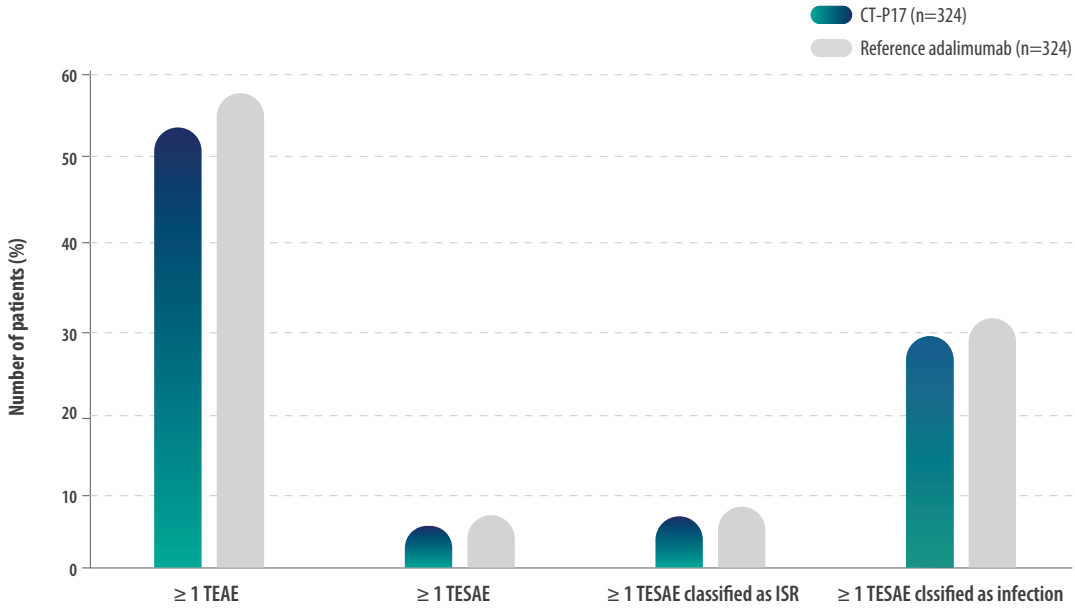
Immunogenicity results from Week 0-24: safety populations



Yuflyma® demonstrated a comparable safety profile to reference adalimumab.[4,5]

- The safety profile of CT-P17 was similar to that of reference adalimumab, with majority of events being grade 1 or grade 2 in intensity.

Summary of adverse events: safety populations



*There were no significant differences between the CT-P17 and EU-adalimumab groups for any parameter ($p > 0.05$)

ADA, anti-drug antibody; **ISR,** injection site reaction; **TEAE**, treatment-emergent adverse event; **TESAE,** treatment-emergent serious adverse event

[Study Design] A randomized, double-blind phase 3 study in which subjects with active RA at 52 centers were randomized (1:1) to receive CT-P17 or EU-adalimumab 40 mg subcutaneously every 2 weeks until week 52. The primary endpoint was 20% improvement by American College of Rheumatology criteria (ACR20) response rate at week 24. Equivalence was concluded if the corresponding confidence intervals (CIs) for the estimate of treatment difference were within predefined equivalence margins: – 15 to 15% (95% CI; European Medicines Agency assumption); – 12 to 15% (90% CI; Food and Drug Administration assumption).Additional efficacy, pharmacokinetic, usability, safety, and immunogenicity endpoints were evaluated.[4]

02 SAME FEATURES **AS ORIGINATOR**

Yuflyma®'s features and benefits

Yuflyma®'s features including its high concentration, low volume formulation, removal of citrate buffers, and a thin* 29-gauge needle.[1]

* compared to adalimumab biosimilar devices with 27- gauge needles

High concentration, low volume

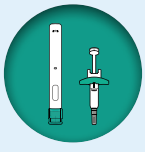
With a high concentration (100 mg/mL) of adalimumab, Yuflyma® allows patients to inject only half the amount of liquid compared to other currently available adalimumab biosimilars[1]

Citrate-free

Citrate buffers were removed in Yuflyma®.[1]

Latex-free

There is no latex any Yuflyma® device [1]



Two device types[1]

Pre-filled pen (autoinjector)

Pre-filled syringe with needle guard to choose from

Thin needle[3]

Yuflyma's pre-filled pen and pre-filled syringe with needle guard have a thin* 29-gauge needle.

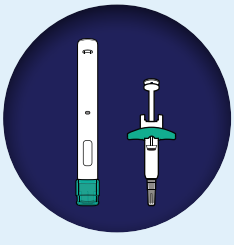
03 IMPROVED **CONVENIENCE**

Yuflyma®'s distinct features improve convenience during self-administration.[1,3]

Yuflyma®'s features including extension of stability period, latex-free devices, and two administration options allow for improved convenience for patients.

Storage period for up to 30 days
Yuflyma® has a stability period of up to 30 days at room temperature (25˚C) with protection from light.[1]

Latex-free
There is no latex in the Yuflyma® injection devices.[1]



Administration options
Yuflyma® is available in two user-friendly administration options that are designed to meet the needs of the patient.[1,3]

Pre-filled pen in square shape with rounded edges allowing effortless injections.

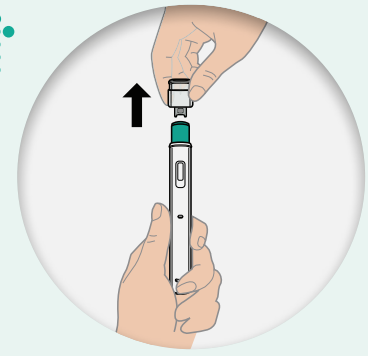
Pre-filled syringe with needle guard for added patient safety.

2-STEP
PUSH-TYPE PEN

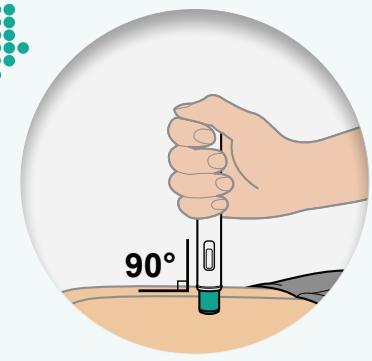
Yuflyma®
adalimumab

Yuflyma®'s 2-step push-type pen allows for convenient and effortless injection in 2 steps.[1,3]

STEP 1 **PULL**



STEP 2 **PUSH**



With proven outcomes*[2,4-5], and improved convenience [1,3], Yuflyma® offers **patient-centric treatment** for your patients.

* compared to high- concentration Humira

04 PATIENT SUPPORT PROGRAM **CELLTRIONCARE**

WELCOME KIT AND TRAVEL BAG

delivered to newly enrolled patients

1800 SUB CUT [782 288]
Weekdays
(excluding public holidays)
9:00 am – 5:00 pm AEST

SELF-INJECTION TRAINING

Including how-to videos, downloadable instructions, self-injection training (virtual or home visit) with a nurse

MEDICATION REMINDERS

Email or SMS reminders to help patients keep track of their injections

Please scan this QR code to access www.celltrioncare.com

WEB-PORTAL

Access to disease and product information, injection training support materials and resources available to you at all times

MEDICATION HOME DELIVERY

Delivery of the patient's medication directly to their home

CelltrionCare ensures that your patients receive support and advice about accessing services that are relevant to their individual needs and situation

Patients can opt-in or out of any of these services at any time by contacting the CelltrionCare Clinical Liaison on **1800 SUB CUT (782 288) or support@celltrioncare.com**

FOR HEALTHCARE PROFESSIONALS ONLY

PBS Information: For Rheumatoid Arthritis & Ankylosing Spondilitis: Authority required (telephone/immediate online assessment) for initial treatment. Authority required (STREAMLINED) for first and subsequent continuing treatment courses. This product is not PBS listed for the treatment of Uveitis. **All other indications:** Authority required for initial and first continuing treatment courses. Authority required (STREAMLINED) for subsequent continuing courses. Refer to PBS schedule for full authority information.

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

MINIMUM PRODUCT INFORMATION. YUFLYMA containing 40 mg adalimumab for subcutaneous (SC) injection in a single dose pre-filled pen or syringe. **INDICATIONS:** Rheumatoid arthritis (RA), Yuflyma is indicated for reducing signs and symptoms, as well as inhibiting the progression of structural damage in adult patients with moderate to severely active RA. This includes the treatment of patients with recently diagnosed moderate to severely active disease who have not received methotrexate (MTX). Yuflyma can be used alone or in combination with methotrexate.; Juvenile Idiopathic Arthritis, in combination with MTX in patients (≥ 2 years of age) with active polyarticular juvenile idiopathic arthritis who have had an inadequate response to disease-modifying anti-rheumatic drugs (DMARDs). YUFLYMA can be given as monotherapy in case of intolerance to MTX or when continued MTX treatment is inappropriate; YUFLYMA is indicated for the treatment of active enthesitis-related arthritis in patients ≥ 6 years of age, who have had an inadequate response to, or who are intolerant of, conventional therapy; Ankylosing spondylitis (AS): YUFLYMA is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis. Psoriatic arthritis (PsA), YUFLYMA is indicated for the treatment of signs and symptoms, as well as inhibiting the progression of structural damage, of moderate to severely active psoriatic arthritis in adult patients where response to previous DMARDs has been inadequate; Psoriasis (PsO), for the treatment of moderate to severe chronic plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. YUFLYMA is indicated for the treatment of severe chronic plaque psoriasis in children and adolescent patients ≥ 4 years of age who have had an inadequate response to or are inappropriate candidates for topical therapy and phototherapy. Hidradenitis suppurativa (HS), in adults and adolescents ≥ 12 years of age with moderate to severe HS (acne inversa) with an inadequate response to conventional systemic HS therapy. Crohn's disease (CD): in adults and children ≥ 6 years of age to reduce the signs and symptoms of the disease and to induce and maintain clinical remission in patients; (1) who have had an inadequate response to conventional therapies or, (2) who have lost response to or are intolerant to infliximab. Ulcerative Colitis (UC): in adult patients who have had an inadequate response to conventional therapy or who are intolerant to or have medical contraindications for such therapies. Patients should show a clinical response within 8 weeks of treatment to continue treatment beyond that time; Uveitis, in adults for the treatment of non-infectious intermediate, posterior and pan-uveitis who have had an inadequate response to corticosteroids, in patients in need of corticosteroid sparing, or in whom corticosteroid treatment is inappropriate. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any excipients listed in the Product Information (PI); active tuberculosis or other severe infections such as sepsis, and opportunistic infections; moderate to severe heart failure (NYHA class III/IV). **PRECAUTIONS:** Infections: monitor closely for infections including TB before, during and after treatment. YUFLYMA should not be initiated in patients with active infections including chronic or localised until they are controlled. Caution with a history of recurrent infection, underlying conditions and new infection while undergoing treatment with YUFLYMA. Hepatitis B (HBV) reactivation: reactivation of HBV has occurred in chronic carriers when receiving adalimumab. Test for HBV infection before initiating treatment and closely monitor for symptoms of active HBV. Neurological events: anti-TNF agents are associated with new onset or exacerbation of clinical symptoms and/or radiographic evidence of CNS demyelinating disease, including multiple sclerosis and optic neuritis, and peripheral demyelinating disease, including Guillain-Barré syndrome. Malignancies and lymphoproliferative disorders: risk of development of lymphomas/leukaemia/other malignancies cannot be excluded. Caution with history of malignancy, with increased risk for malignancy, and treating patients who develop a malignancy. Haematologic reactions: consider discontinuation when significant haematologic abnormalities, including pancytopenia and cytopenia. Vaccinations: prior to therapy vaccinations should be up to date. Patients on YUFLYMA may receive concurrent vaccinations, except for live vaccines. Administration of live vaccines to infants exposed to adalimumab in utero is not recommended for 5 months following the mother's last adalimumab injection during pregnancy. Congestive Heart failure: caution with mild heart failure (NYHA class I/II) and discontinue when new or worsening symptoms of heart failure develop. Autoimmune processes: discontinue treatment if symptoms suggestive of a lupus-like syndrome and positive for antibodies against double-stranded DNA. Use in the elderly: particular attention regarding the risk for infection should be paid. Fertility, pregnancy and lactation: women of childbearing potential should consider adequate contraception to prevent pregnancy and continue use for ≥5 months after treatment. Due to its inhibition of TNFα, adalimumab administered during pregnancy could affect normal immune responses in the newborn. Adalimumab should only be used during pregnancy if clearly needed. YUFLYMA can be used during breastfeeding. **INTERACTIONS:** Combination with anakinra or abatacept is contraindicated, and not recommended due to increased risk of serious infection. YUFLYMA can be taken together with: methotrexate, certain dMARDs, steroids or pain medications including NSAIDs. **ADVERSE EFFECTS (AEs):** The most commonly reported adverse reactions are infections (such as nasopharyngitis, upper respiratory tract infection and sinusitis), injection site reactions (erythema, itching, haemorrhage, pain or swelling), headache and musculoskeletal pain. For more information on reported AEs see full PI. **DOSAGE AND ADMINISTRATION:** YUFLYMA is available as 40 mg presentations in pre-filled syringe and/or pre-filled pen. RA, PsA, AS: 40mg every other week (EOW). In RA, methotrexate, glucocorticoids, salicylates, nonsteroidal anti-inflammatory drugs or analgesics may be continued while using YUFLYMA. Polyarticular Juvenile Idiopathic Arthritis: patients ≥2 years of age (≥30kg) can use 40mg EOW. Active Enthesitis-Related Arthritis: patients ≥6 years of age (≥30kg) can use 40mg EOW. PsO: for adult patients – 1st dose of 80mg (2 x 40 mg injections in 1 day), followed by 40mg EOW starting 1 week after 1st dose. Paediatric Plaque PsO: See PI. Hidradenitis Suppurativa: see PI. CD (adult and paediatric patients ≥ 40kg) & UC (adult patients) - induction of 160mg (4 x 40 mg in 1 day or 2 x 40mg per day for 2 consecutive days), followed by 80mg (2 x 40mg in 1 day) 2 weeks later. Thereafter, 40mg EOW. Uveitis: see PI

References: 1. Yuflyma® pre-filled pen Approved Australian Product Information available at https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2022-PI-02304-1&d=20230530172310101 Yuflyma pre-filled syringe Approved Australian Product information available at https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2022-PI-02306-1 Both Last accessed: 05.03.2024. **2.** Yu KS , et al. Clin Transl Sci. 2021 Jan 27. doi:10.1111/cts.12967. Epub ahead of print. **3.** Celltrion Healthcare. Data on File. 2020. **4.** Kay J, et al. Arthritis Res Ther. 2021;23:51. **5.** Kay J, et al. (Nov, 2020). A Randomized, Double-Blind, Phase 3 Study to Compare the Efficacy and Safety of a Proposed High Concentration (100 mg/mL) Adalimumab Biosimilar (CT-P17) with Reference Adalimumab in Patients with Moderate-to-Severe Active Rheumatoid Arthritis. [Poster presentation]. ACR Convergence 2020. **6.** Humira and Yuflyma PBS listing available at https://www.pbs.gov.au/medicine/item/12335F-12340L-12341M-12342N-12345R-12347W-12358K-12362P-12363Q-12373F-12375H-12376J-12377K-12381P-12383R-12389C-12390D-12411F-12412G-12414J-12425Y-12428D-12429E-12432H-12433J-12444Y-12446C-12454L-13211H-13212J-13214L-13215M-13221W-13223Y-13224B-13225C-13226D-13227E-13229G-13230H-13691N-13703F-13764K last accessed on 16.02.2024. **7.** CelltrionCare Patient Support Program available at www.celltrioncare.com last accessed 12.03.2024. **8.** Free Home Delivery available via JustMeds https:// www.justmeds.com.au/ last accessed 12.03.2024.

Celltrion Healthcare Australia Pty Ltd. ABN 66 625 407 105
Suite 13.03, 31 Market Street, Sydney NSW 2000, Australia
Medical Information Phone 1800 325 228
Email: info-anz@celltrionhc.com
www.celltrionhealthcare.com.au

HEALTHCARE CELLTRION