Omlyclo

Ministry of Food and Drug Safety

APPROVED

PART A - ADMINISTRATIVE INFORMATION		
Entered by:	**Biosimilar Product Information**	
MAH	**Name of the biosimilar medicinal product**	Omlyclo
MAH	**MAH**	Celltrion Inc. 20, Academy-ro 51 beon-gil, Yeonsu-gu, Incheon, Republic of Korea
NRA	**Authorisation / Licence number**	Celltrion / 34
MAH / NRA	**API manufacturing facilities and batch release site for the finished product** (if applicable)	Confidential
MAH	**Name of the active substance**	Omalizumab (INN)
MAH	**Pharmaco-therapeutic group**	ATC code: R03DX05
MAH	**Substance category**	Monoclonal antibodies
MAH	**Pharmaceutical form**	Solution for injection
MAH	**Quantitative composition**	150 mg/1.0 mL 75 mg/0.5 mL
MAH	**Route of administration**	Subcutaneous administration
MAH	**Packaging/material**	Pre-filled pen (PFP) / glass
MAH	**Package size(s)**	1 PFP /pack
MAH	**Local legal basis**	Pharmaceutical Affairs Act article 42 and Enforcement for drug safety article 4
MAH	**Local biosimilar guidelines**	Guidelines on the Evaluation of Biosimilar Products (MFDS 2021)

MAH	**Date of authorisation/licensing of biosimilar**	19 December 2025
	Reference Biotherapeutic Product (RBP) Information	
MAH	**Name of the RBP**	Xolair
MAH	**Authorised indications for RBP**	Allergic Asthma Chronic rhinosinusitis with nasal polyps Chronic Spontaneous Urticaria
MAH	**Pharmaceutical form**	Colorless to light yellow-yellow, transparent to opalescent solution
MAH	**Quantitative composition**	150 mg/1.0 mL 75 mg/0.5 mL 300 mg/2.0 mL
MAH	**Route of administration**	Subcutaneous administration
MAH	**Packaging/material**	Pre-filled syringe / glass
MAH	**Package size(s)**	1 PFS-S/pack
MAH	**Authorisation (Licence) number (of RBP)**	Novartis Korea Ltd. / 5076, 5085, 5140
MAH	**Date of authorisation (of RBP)**	150 mg: 27 May 2016 75 mg: 26 June 2017 300 mg: 07 March 2024
MAH	**Authorisation (Licence) Holder (of RBP)**	Novartis Korea Ltd.
MAH	**Source of RBP (or other comparator) for comparability exercise**	Republic of Korea European Union
MAH / NRA	**Availability of the RBP assessment report** (korean)/**link**	NeDrug – Public Assessment Report (Korean): https://nedrug.mfds.go.kr/pbp/CCBAC02/getItem?searchYn=true&title=%EC%A1%B8%EB%A0%88%EC%96%B4&totalPages=0&limit=10&page=1&jdgmnResultInfoSeq=32446
	Summary of outcomes	
MAH	**Comparability exercise to demonstrate similarity to RBP**	Extensive comparability exercise including data from : physicochemical, biological characterization, *in vitro, in vivo* non-clinical studies, PK, efficacy, safety and immunogenicity studies
NRA	**Availability of full assessment report** (korean)/**link**	NeDrug – Public Assessment Report (Korean): https://nedrug.mfds.go.kr/pbp/CCBAC02/getList?totalPages=448&page=1&limit=10&sort=&sortOrder=&sear

		chYn=true&targetGb=&title=%EC%98%B4%EB%A6%AC%ED%81%B4%EB%A1%9C&entpName=&itemName=&mainIngrName=&mainIngrEngName=&btnSearch=
MAH	**Indications applied for** (if different to RBP)	The indications applied for were all authorized for RBP except for the treatment of Chronic rhinosinusitis with nasal polyps (see section Authorized indications for RBP).
NRA	**Authorised indications for biosimilar**	Allergic Asthma Chronic Spontaneous Urticaria

MAH (Marketing Authorisation Holder) or Sponsor
NRA (National Regulatory Authority) i.e. CA (Competent Authority)

PART B - SUBMITTED DATA AND REVIEWER SUMMARY	
Procedure: < Initial Application >	
MAH	**Quality data. Composition of the biosimilar product(s)**
	Omalizumab 150 mg, Omalizumab 75 mg L-Histidine L-Histidine HCl Monohydrate L-Arginine HCl Polysorbate 20 Water for Injection
MAH	**Quality data. State-of-the-art methods**
	Structural Chracteristics - Primary Structure: Peptide mapping, N-, C-terminal Sequence analysis, Intact mass - High Order Structure analysis: Disulfide bonds, Free thiol analysis, CD, FTIR, DSC **Physicochemical Test** - Purity/Impurity, Charge variants, Glycation/Glycosylation, Protein concentration **Biological properties** - IgE Binding Assay, IgE Binding Inhibition Assay, Cell-based IgE Binding Inhibition Assay, Beta-hexosaminidase Release Inhibition Assay **Immunochemial properties** - IgE-FcεRII Binding Inhibition Assay, C1q Binding Assay, Fcγ Receptor (FcγRIIIa (V type), FcγRIIIa (F-type), FcγRIIIb, FcγRIIa, FcγRIIb, FcγRI) Binding Assay, FcRn Binding Assay
NRA	**Quality data assessment outcome**
	Comprehensive head-to-head quality comparability study, utilizing various sensitive and orthogonal analytical methods, was conducted to evaluate the similarity between Omlyclo PFP and Xolair PFS. Since Omlyclo PFP is manufactured using the same omalizumab drug product solution as the previously approved Omlyclo PFS, the extensive quality comparability data generated during the original biosimilarity assessment against EU Xolair PFS were considered supportive. These assessments demonstrated that omalizumab is highly similar to Xolair PFS with respect to primary and higher-order structures, post-translational modifications, physicochemical and biophysical properties, and biological activities, thereby establishing quality equivalence. Due to the inherent structural heterogeneity of omalizumab, slight differences were identified in certain post-translational modification-related attributes, including charge variants and N-glycan profiles, when compared with Xolair PFS. However, these differences were not considered clinically meaningful, as they did not impact biological activities associated with the primary mechanism of action, including Fab-binding-related activities. Furthermore, the

	observed differences were not considered significant enough to produce a physiological effect, as demonstrated by the pharmacokinetic equivalence observed in global clinical studies. Furthermore, a comprehensive quality comparison study using the final assembled Omlyclo PFP and EU Xolair PFS demonstrated similarity across all major quality attributes. Although minor differences were observed in certain analytical parameters, these findings were consistent with those previously identified in the comparison between the Omlyclo PFS and Xolair PFS and could be adequately explained based on the known structural heterogeneity of omalizumab. Importantly, these differences were not considered to affect the quality, safety, or efficacy of the product. In conclusion, the totality of evidence, encompassing analytical comparability data, all relevant quality attributes, and clinical study data, supports the biosimilarity of Omlyclo PFP to Xolair PFS and demonstrates that the change in presentation from the PFS to the PFP does not adversely impact product quality, safety, or efficacy.
MAH	**Mechanism of action**
	Omalizumab is a recombinant DNA-derived humanised monoclonal antibody that selectively binds to human immunoglobulin E (IgE) and prevents binding of IgE to FcεRI (high-affinity IgE receptor) on basophils and mast cells, thereby reducing the amount of free IgE that is available to trigger the allergic cascade.
MAH	**Nonclinical data. *In vitro* studies**
	No new non-clinical *in vitro* studies were submitted. As comparability between Omlyclo PFP and Omlyclo PFS has been established~~,~~ the previously accepted *in vitro* functional comparability data are considered applicable to the present application.
MAH	**Nonclinical data. *In vivo* studies**
	Pharmacology No new Pharmacology studies were submitted. As comparability between Omlyclo PFP and Omlyclo PFS has been established, the pharmacology data accepted for the initial approval of Omlyclo are considered applicable to the present application. **Toxicity Study (including TK)** No new Toxicity studies were submitted. As comparability between Omlyclo PFP and Omlyclo PFS has been established, the pharmacology data accepted for the initial approval of Omlyclo are considered applicable to the present application.
NRA	**Nonclinical data assessment outcome**
	1. *In vitro* studies No new *in vitro* studies were submitted. As comparability between Omlyclo PFP and Omlyclo PFS has been established, the previously accepted in vitro functional comparability data are considered applicable to the present application. **2. *In vivo* studies**

	No new non-clinical *in vitro studies* were submitted. As comparability between Omlyclo PFP and Omlyclo PFS has been established, the previously accepted *in vitro* functional comparability data are considered applicable to the present application.

	CLINICAL STUDIES **- include relevant study data from the following (not all may be required) which have been included to demonstrate biosimilarity.** • **Pharmacokinetic (PK)** • **Pharmacodynamic (PD)** • **Efficacy** • **Safety** • **Immunogenicity**
MAH	**Clinical data. PK study between PFP and PFS**
	Study Number: CT-P39 1.2 ● Summary of design: Phase 1, randomized, openlabel, two-arm, parallel group, single-dose study to compare the PK and safety of two formulations of omalizumab (Omlyclo PFP and EU approved Xolair PFS) ● Healthy Japanese subjects. Randomized: 129 (Omlyclo PFP: 65, EU-approved Xolair PFS:64) Objective and primary endpoints: PK similarity in terms of $AUC_{0\text{-}inf}$ and C_{max} of Omlyclo via PFP versus EU-approved Xolair PFS administration in healthy Japanese subjects ● Dose used: 150 mg (150 mg/1.0 mL), SC injection to the upper arm via PFP as a single administration ● Length of the study: 127 days
NRA	**Clinical data. PK study between PFP and PFS, PK studies assessment outcome**
	Study Number: CT-P39 1.2 The 90% Confidence Interval (CI) of the geometric least squares means (LSMeans) ratios of Omlyclo PFP to EU-Xolair PFS for $AUC_{0\text{-}inf}$ and C_{max} were contained within the predefined bioequivalence margin of 80-125%.

PK parameter (units)	CT-P39 AI / EU-approved Xolair PFS	
	Geometric Least-Square Mean Ratio	90% CI
$AUC_{0\text{-}inf}$ (day·µg/mL)	101.66	[95.31 – 108.45]
C_{max} (µg/mL)	93.91	[87.20 – 101.14]

* CT-P39 AI refers to Omlyclo PFP

MAH	**Clinical data. PK study between Omlyclo PFS and Xolair PFS**
	Study Number: CT-P39 1.1 (Identical to those previously approved) ● Summary of design: Phase 1, randomized, double-blind, three-arm, parallel group, single-dose study to compare the PK and safety of three formulations of omalizumab (Omlyclo PFS, EU Xolair PFS, and US Xolair PFS) in Healthy Subjects

- Randomized subject: 176
- Objective and primary endpoints: Demonstration of Pharmacokinetic (PK) similarity in terms of $AUC_{0\text{-inf}}$, $AUC_{0\text{-last}}$, C_{max} of Omlyclo PFS, EU-Xolair PFS, and US- Xolair PFS in healthy subjects
- Dose used: 150 mg (150 mg/1.0 mL), a single PFS SC injection of study drug
- Length of the study: 127 days

NRA

Clinical data. PK study between Omlyclo PFS and Xolair PFS assessment outcome

Study Number: CT-P39 1.1 (Identical to those previously approved)

The 90% Confidence Interval (CI) of the geometric least squares means (LSMeans) ratios of Omlyclo PFS to EU-Xolair PFS/US- Xolair PFS for $AUC_{0\text{-last}}$, $AUC_{0\text{-inf}}$ and C_{max} were contained within the predefined bioequivalence margin of 80-125%.

PK parameter (units)	CT-P39 / EU-approved Xolair		CT-P39 / US-licensed Xolair		EU-approved Xolair / US-licensed Xolair	
	Ratio	90% CI	Ratio	90% CI	Ratio	90% CI
$AUC_{0\text{-last}}$ (day·µg/mL)	104.00	[94.96 - 113.89]	99.30	[90.79 - 108.61]	95.48	[87.36 - 104.37]
$AUC_{0\text{-inf}}$ (day·µg/mL)	105.62	[95.91 - 116.31]	98.72	[89.76 - 108.58]	93.47	[85.09 - 102.68]
C_{max} (µg/mL)	113.14	[103.15 - 124.11]	103.88	[94.83 - 113.80]	91.82	[83.87 - 100.52]

* CT-P39 refers to Omlyclo PFS

MAH

Clinical data. PD studies

No specific PD study was conducted.
Pharmacodynamic endpoints were assessed as part of study CT-P39 1.1.

NRA

Clinical data. PD data assessment outcome

The mean total and free serum IgE was generally comparable between the Omlyclo PFS, EU-Xolair PFS and US-Xolair PFS groups. All groups showed an increase in mean total IgE and a suppression of free IgE.

MAH

Clinical data. Efficacy studies

Study Number: CT-P39 3.1 (Identical to those previously approved)

- Summary of design: Double-blind, randomized, active-controlled, parallel group, Phase 3 study to compare efficacy and safety of Omlyclo PFS and Xolair PFS in patients with CSU
- Randomized subject: 634
- Primary objective: To demonstrate the equivalence of Omlyclo PFS to Xolair PFS at a dose of 300 mg in terms of efficacy in patients with CSU as determined by change from baseline in ISS7 at Week 12
- Secondary objective:
  - To evaluate relative potency and dose response in terms of efficacy between 300 mg and 150 mg for Omlyclo PFS and Xolair PFS
  - To evaluate additional efficacy of CT-P39 and Xolair at each dose level of 300 mg and 150 mg
  - To evaluate the PK, QoL, safety, and immunogenicity of Omlyclo PFS and Xolair PFS
- Dose used:
  - Treatment Period I: Arm 1, 2: 300 mg (2 injections of 150 mg/1.0 mL) / Arm 3, 4: 150 mg (1 injection of 150 mg/1.0 mL) of study drug by SC injection via PFS

- Treatment Period II: 300 mg (2 injections of 150 mg/1.0 mL) of study drug by SC injection via PFS
- Length of the study: 40 weeks

NRA

Clinical data. Efficacy data assessment outcome

Study Number: CT-P39 3.1 (Identical to those previously approved)
The LS mean (SE) change from baseline in weekly Itch Severity Score (ISS7) at Week 12 was -9.21 (0.796) points in Omlyclo PFS 300 mg treatment arm (Arm 1) and -9.98 (0.798) points in Xolair PFS 300 mg treatment arm (Arm 2) for the mITT Set (estimate of treatment difference: 0.77). The 95% CI of treatment difference in the mean change from baseline in ISS7 at Week 12 between 300 mg of CT-P39 and 300 mg of Xolair treatment arms was [-0.37, 1.90] for the mITT Set and entirely within the equivalence margin of [-2.0, 2.0] which demonstrated the therapeutic equivalence between Omlyclo PFS and Xolair PFS.
In the PP set, the 95% CI of treatment difference in the mean change from baseline in ISS7 at Week 12 between 300 mg of Omlyclo PFS and 300 mg of Xolair PFS was [-0.45, 1.84]. The result of multiple imputation and tipping point analysis showed that missing data had no major impact on the result for the primary efficacy endpoint.

Treatment	n	LS Mean (SE)	Estimate of Treatment Difference	95% CI of Treatment Difference
mITT Set				
CT-P39 300 mg (Arm 1)	186	-9.21 (0.796)	0.77	[-0.37, 1.90]
Xolair 300 mg (Arm 2)	192	-9.98 (0.798)		
PP Set				
CT-P39 300 mg (Arm 1)	179	-9.48 (0.790)	0.69	[-0.45, 1.84]
Xolair 300 mg (Arm 2)	183	-10.17 (0.792)		

* CT-P39 refers to Omlyclo PFS

The therapeutic equivalence was reaffirmed by the sensitivity analysis results using multiple imputation. Additional scenarios for the impact of missing data on the treatment difference were explored via the tipping point analysis and the results generally supported the therapeutic equivalence between Omlyclo PFS and Xolair PFS.

The mean ISS7, UAS7, and HSS7 decreased from baseline in all treatment arms throughout Treatment Period I. The mean changes from baseline in ISS7, UAS7, and HSS7 at each week were similar between 300 mg of Omlyclo PFS and 300 mg of Xolair PFS treatment arms despite the slight fluctuations by timepoints.
During Treatment Period 2, efficacy after a single transition from Xolair PFS to Omlyclo PFS was not different from those of patients maintained on Omlyclo PFS or Xolair PFS up to Week 24.

MAH

Clinical data. Safety/ Immunogenicity studies

The overall safety and immunogenicity profiles of Omlyclo PFS, including CT-P39 PFP, were comparable to those of the reference product, with no clinically meaningful differences observed.

NRA

Clinical data. Safety/ Immunogenicity data assessment outcome

Safety.

	Across Studies CT-P39 1.1, CT-P39 1.2, and CT-P39 3.1, the overall safety profile of Omlyclo was comparable to that of the reference product, with no new or unexpected safety findings, safety signals, or clinically meaningful differences observed. Immunogenicity. Across Studies CT-P39 1.1, CT-P39 1.2, and CT-P39 3.1, the immunogenicity profile of CT-P39 was comparable to that of the reference product. No clinically meaningful differences in ADA or NAb responses were observed between Omlyclo and the reference product.	
MAH	**Interchangeability data**	
	No additional data were provided	
MAH	**Additional information about the comparability exercise**	Not applicable
MAH	**Post-authorization measures**	
	Re-examination study in Study: Observational, prospective cohort study to evaluate safety and efficacy of Omlyclo PFP (The product is subject to the same re-examination period as the previously approved presentation.) Period: 2025.12.19 – 2028.06.23	
NRA	**Post-authorization risk measures: assessment outcome.**	
	Post-marketing surveillance study (re-examination study) plan was considered to be acceptable.	
MAH	**Availability of additional relevant information in the local language/ link**	Not applicable

PART C - REVIEWER CONCLUSIONS	
NRA	**Conclusions on biosimilarity, approval**

The data provided by the Applicant were in line with the local legislation and guidelines.

Quality
Comprehensive head-to-head characterization studies, utilizing sensitive and orthogonal analytical methods, demonstrated that all major quality attributes of Omlyco PFP were comparable to those of Xolair PFS. In conclusion, the totality of evidence, encompassing analytical comparability data, all relevant quality attributes, and clinical study data, supports the biosimilarity of Omlyco PFP to Xolair PFS.

Nonclinical
No new non-clinical *in vitro studies* were submitted. Previously accepted in vitro functional comparability data are considered applicable to the present application.

Clinical Studies
The Phase I study (CT-P39 1.2) demonstrated pharmacokinetic equivalence between Omlyco PFP and EU-approved Xolair PFS based on the primary PK endpoints, AUC_{0-inf} and C_{max}.

Safety: The Adeverse drug reactions (ADRs) observed with Omlyclo were in the similar range as the ADRs observed with the reference biotherapeutic product EU-approved Xolair PFS.

Immunogenicity: The proportion of patients who developed ADA with Omlyclo was generally similar to the reference biotherapeutic product EU-approved Xolair PFS.

Extrapolation of indications: Based on the totality of evidence, all indications applied for Xolair PFS (see Part A, summary of outcomes) were considered to be extrapolated to Omlyclo PFP except for chronic rhinosinusitis with nasal polyps (under re-examination).

Risk Management
The risk management plan was considered to be acceptable.

Overall Conclusion
Satisfactory assurance of biosimilarity was demonstrated using an appropriate comparability exercise. The biosimilar product Omlyco PFP was considered approvable.