Vgenfli

Ministry of Food and Drug Safety

APPROVED

PART A - ADMINISTRATIVE INFORMATION		
Entered by:	**Biosimilar Product Information**	
MAH	**Name of the biosimilar medicinal product**	Vgenfli
MAH	**MAH**	SamChunDang Pharm, 71, Jeyakgongdan 2-gil, Hyangnam-eup, Manse-gu, Hwaseong-si, Gyeonggi-do, Republic of Korea
NRA	**Authorisation / Licence number**	SamChunDang Pharm / 1, 2
MAH / NRA	**API manufacturing facilities and batch release site for the finished product** (if applicable)	Confidential
MAH	**Name of the active substance**	Aflibercept (INN)
MAH	**Pharmaco-therapeutic group**	ATC code: S01LA05
MAH	**Substance category**	Recombinant fusion protein
MAH	**Pharmaceutical form**	Solution for injection.
MAH	**Quantitative composition**	2 mg / 0.05 mL
MAH	**Route of administration**	Intravitreal injection
MAH	**Packaging/material**	Vial / Glass Pre-filled syringe / COP
MAH	**Package size(s)**	1 Vial / box 1 Pre-filled Syringe / box
MAH	**Local legal basis**	Article 42 of the Pharmaceutical Affairs Act, and Article 4 of the Regulations on Safety of Pharmaceuticals, etc.
MAH	**Local biosimilar guidelines**	Guidelines on the Evaluation of Biosimilar Products (MFDS 2021)
MAH	**Date of authorisation/licensing**	22 September 2025

	of biosimilar	
	Reference Biotherapeutic Product (RBP) Information	
MAH	**Name of the RBP**	Eylea Injection Eylea Pre-filled Syringe
MAH	**Authorised indications for RBP**	Neovascular (wet) age-related macular degeneration (AMD), Macular edema secondary to retinal vein occlusion (RVO), Diabetic macular edema (DME), Myopic choroidal neovascularization (myopic CNV)
MAH	**Pharmaceutical form**	Solution for injection
MAH	**Quantitative composition**	2 mg / 0.05 mL
MAH	**Route of administration**	Intravitreal injection
MAH	**Packaging/material**	Vial / Glass Pre-filled syringe / glass
MAH	**Package size(s)**	1 vial / pack 1 pre-filled syringe / pack
MAH	**Authorisation (Licence) number (of RBP)**	Bayer Korea / 5013, 5014
MAH	**Date of authorisation (of RBP)**	20 March 2013
MAH	**Authorisation (Licence) Holder (of RBP)**	Bayer Korea
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&itemName=%EC%95%84%EC%9D%BC%EB%A6%AC%EC%95%84&limit=10&totalPages=471&page=1&jdgmnResultInfoSeq=16957
	Summary of outcomes	
MAH	**Comparability exercise to demonstrate similarity to RBP**	Extensive comparability exercise was conducted including physicochemical, biological, *in vitro*, *in vivo*, 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/getItem?searchYn=true&itemName=%EB%B9%84%EC%A0%A0%ED%94%84%EB%A6%AC&limit=10&totalPages=1&page=1&jdgmnResultInfoSeq=20260000038
MAH	**Indications applied for** (if different to RBP)	The indication applied for were all authorized for RBP (see section Authorized indications for RBP)
NRA	**Authorised indications for biosimilar**	Neovascular (wet) age-related macular degeneration (AMD), Macular edema secondary to retinal vein occlusion (RVO), Diabetic macular edema (DME), Myopic choroidal neovascularization (myopic CNV)

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)**
	Aflibercept Sodium acetate trihydrate Acetic acid Sodium chloride Sucrose Polysorbate 20 Acetic acid Sodium hydroxide Water for injection
MAH	**Quality data. State-of-the-art methods**
	(1) Physicochemical properties - Primary Structure: Peptide mapping, N-terminal sequence analysis, Amino acid variations, Amino acid composition and disulfide bond analysis - Higher-order structure: UV/Vis absorbance spectra, Secondary and tertiary structure, Helix and β sheet content, Conformational stability, Intact/Apparent molecular weight - Glycan structure: Sites and occupancy of N-linked glycan chains, N-linked oligosaccharide profile, O-linked oligosaccharide profile, and Quantitative sialic acid content - Purity: Charge variant profile, Monomer purity (2) General properties - Protein content: Protein concentration analysis, Extinction coefficient (3) Biological & Functional Activity - Inhibition of VEGF induced cell proliferation, Inhibition of VEGF induced cell migration, Inhibition of VEGFR2 phosphorylation, Binding to VEGF-A165, Binding affinity to the VEGF family, Selectivity for the VEGF family, Binding affinity to the PlGF subclass, Binding affinity to Fc receptors, Binding affinity to C1q, Absence of ADCC, Absence of CDC
NRA	**Quality data assessment outcome**
	Comprehensive head-to-head comparability studies performed using state-of-the art analytical procedures demonstrated that all major quality attributes of Vgenfli were comparable to those of Eylea® with respect to physiochemical, biological and immunochemical properties. The similarity range were defined using sufficient EU Eylea®, and the bridging data demonstrated the equivalence of EU Eylea® and KR Eylea®.

	There were slight differences in DSC and N-linked glycan profiles. The differences were appropriately justified with comparability on the biological activity of Vgenfli. Under heat, basic, acidic, oxidative and photostress conditions, comparative stability studies demonstrated similar degradation profiles for Vgenfli and Eylea®. Overall, based on the totality of evidence with respect to all quality characteristics and global clinical studies, the biosimilarity of Vgenfli to Eylea® was concluded.
MAH	**Mechanism of action**
	Aflibercept acts as a soluble decoy receptor that binds VEGF-A and PIGF, and thereby can inhibit the binding and activation of their cognate VEGF receptors
MAH	**Nonclinical data. *In vitro* studies**
	Nonclinical *in vtitro* PD studies were performed between Vgenfli and Eylea® (Refer to quality data section)
MAH	**Nonclinical data. *In vivo* studies**
	Toxicity Study (including TK) 13-week Intravitreal Injection Toxicity Study using Vgenfli and Eylea® in Cynomolgus Monkeys was performed. The comparative toxicokinetic (TK) studies were performed as part of repeat-dose toxicity study. **Pharmacokinetics(ADME)** Single Intravitreal Injection ADME Study in Pigmented Rabbits was performed.
NRA	**Nonclinical data assessment outcome**
	1. *In vitro* studies In vitro PD studies demonstrated the similarity between Vgenfli and Eylea®. **2. *In vivo* studies** In a 13-weekrepeat-dose toxicity study using cynomolgus monkeys, treatment with Vgenfli and Eylea® were well tolerated in all animals and there were no differences in toxicity profile between two groups. PK and ocular distribution profiles were similar between Vigenfli and Elyea® groups at a dose level of 2 mg.

	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 studies**
	PK studies were collected from clinical study: SCD411-CP101 **Study Number: SCD411-CP101** ● Summary of design: A Phase III Randomized, Double-Masked, Parallel-Group, Multicenter Study to Compare the Efficacy, Safety, Tolerability, Pharmacokinetics, and Immunogenicity between Vgenfli and Eylea in Subjects with Neovascular Age-related Macular Degeneration. ● Randomized subject (N=576): 288 for Vgenfli 288 for Eylea® ● PK endpoints: AUC_{0-t}: area under the concentration-time curve from time zero to the last measurable observed concentration AUC_{0-tau}: area under the concentration-time curve within a dosing interval AUC_{0-inf}: area under the concentration-time curve from time zero to an infinite time C_{max}: maximum plasma concentration t_{max}: time to reach the maximum plasma concentration $t_{1/2}$: elimination half-life ● Dose used: 2 mg/0.05 mL by intravitreal injection
NRA	**Clinical data. PK data assessment outcome**
	Systemic exposure of Vigenfli and Eylea® evaluated in a subset of subjects with AMD in Study SCD411-CP101 were comparable based on descriptive analysis.
MAH	**Clinical data. PD studies**
	No specific PD study was conducted.
NRA	**Clinical data. PD data assessment outcome**
	Not applicable
MAH	**Clinical data. Efficacy studies**
	Study Number: SCD411-CP101 ● Summary of design: A Phase III Randomized, Double-Masked, Parallel-Group, Multicenter Study to Compare the Efficacy, Safety, Tolerability, Pharmacokinetics, and Immunogenicity between Vgenfli and Eylea in Subjects with Neovascular Age-related Macular Degeneration. ● Randomized subject (N=576): 288 for Vgenfli, 288 for Eylea® ● Objective and primary endpoints: To prove the equivalence of Vgenfil as compared. with Eylea® in BCVA after 8 weeks of treatment among subjects with wet AMD. - Primary endpoint : change from baseline in BCVA as measured by ETDRS letters score or 2702 charts at Week 8. ● Secondary objective: - To compare the efficacy of Vgefli and Eylea® after 8 weeks and 52 weeks of treatment demonstrated by BCVA, CRT and CNV. - To compare the safety and tolerability of Vgenfli and Eylea® ● Dose used: 2 mg/0.05 mL by intravitreal injection

NRA

Clinical data. Efficacy data assessment outcome

At Week 8, the LS mean difference between the treatment groups (Vgenfli-Eylea®) for estimated mean change from baseline in BCVA score was -0.4 letters with 90% CI = -1.6 to 0.9 and 95% CI = -1.8 to 1.1. The 90% CI was within the limit required for US FDA and MFDS (-3.0 and 3.0 letters) and the 95% CI was within the limit required for EMA and PMDA (-3.8 and 3.8 letters) for claiming equivalence between the treatment groups.

Multiple Imputation[a] Results Using Rubin's Method[b]	SCD411 (N=287)	Eylea (N=286)
Estimated mean change from baseline, MMRM[d]		
LS mean (SE)[e]	5.5 (0.53)	5.9 (0.52)
95% CI	4.5, 6.5	4.8, 6.9
Estimated mean difference (SCD411 – Eylea), MMRM[d]		
LS means difference (SE)[e]	-0.4 (0.74)	
90% CI	-1.6, 0.9	
95% CI	-1.8, 1.1	
Estimated mean change from baseline, ANCOVA[f]		
LS mean (SE)[g]	5.5 (0.53)	5.9 (0.52)
95% CI	4.5, 6.5	4.8, 6.9
Estimated mean difference (SCD411 – Eylea), ANCOVA[f]		
LS means difference (SE)[g]	-0.4 (0.74)	
90% CI	-1.6, 0.8	
95% CI	-1.8, 1.1	

MAH

Clinical data. Safety/ Immunogenicity studies

Safety and immunogenicity data were collected from all clinical studies: SCD411-CP101.

NRA

Clinical data. Safety/ Immunogenicity data assessment outcome

Safety.
The overall safety profiles were similar between Vgenfli and Eylea® treatment groups.

Immunogenicity.
The overall immunogenicity profiles were similar between the Vgenfli and Eylea® treatment groups.

MAH

Interchangeability data

No additional data were provided

MAH

Additional information about | Not applicable

	the comparability exercise	
MAH	**Post-authorization measures**	
	Post-authorization study in Korea: Observational, prospective cohort study to evaluate safety and efficacy of Vigenfli Period: 2025.09.22 ~ 2029.09.22	
NRA	**Post-authorization risk measures: assessment outcome.**	
	Post-marketing surveillance 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

The biosimilar manufacturer has developed and validated a process capable of consistently manufacturing a product of appropriate quality, with satisfactory control of impurities. Manufacturing operations are carried out according to GMP requirements.

The quality attributes of high relevance for clinical safety and efficacy, e.g. physicochemical characteristics and biological activities of Vgenfli were comparable to those of the reference biotherapeutic product Eylea®.

Nonclinical

No major differences in nonclinical data were observed for Vigenfli compared to the reference biotherapeutic product Eylea®.

Clinical Studies

The Phase III study to demonstrate biosimilarity conducted in neovascular AMD patients provided robust evidence that there are no clinically meaningful differences between Vigenfli and the reference biotherapeutic product Eylea®.

Safety: The Serious adverse event (SAE) and Adeverse drug reactions (ADRs) observed with Vigenfli were in the similar range as observed with the reference biotherapeutic product Eylea®.

Immunogenicity: The proportion of patients who developed ADA and nAB with Vigenfli was generally similar to the reference biotherapeutic product Eylea®.

Extrapolation of indications: Based on the totality of evidence, all indications applied for Eylea® (see Part A, summary of outcomes) were considered to be extrapolated to Vigenfli.

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 Vgenfli was considered approvable.