

Module 2.3

2.3.S.4 Control of Drug Substance**2.3.S.4.1 Specification**

The specifications for KN035 drug substance are listed in [Table 2.7](#).

Table 2.7 Lot Release Specification for KN035 Drug Substance

Category	Test item	Specification	Methods
Identity	Isoelectric point (pI)	Nine peaks in total in the pI range of 7.75-9.55; and five main peaks are in the pI range of 8.50-9.25. Conform to the reference standard.	SOP-QC-227
	Peptide mapping	Conform to the reference standard. RSD of retention time of the characteristic peaks should not be higher than 3.00%	SOP-QC-231
	Western blot	React to Fc specific antibodies	SOP-QC-259
	Relative binding activity	Conform to reference standard	SOP-QC-225
Appearance	Visual inspection	Clear and colorless to orange red liquid, with the faint opalescence.	SOP-QC-010 and SOP-QC-012
Purity	SE-HPLC (%)	Monomer $\geq 95.0\%$ Aggregate $< 3.0\%$ Fragment: report results	SOP-QC-223
	WCX-HPLC (%)	Sum of acid peak 1 $< 20.0\%$, Sum of acidic peak 2: report results Sum of K0, K1 and K2: report results Sum of other basic peaks (1, 2 and 3): report results	SOP-QC-226
Impurities	CE-SDS (Reducing) (%)	Main peak purity $\geq 95.0\%$; Fragment: report results	SOP-QC-228
	Host cell protein (HCP)	< 100 ppm	SOP-QC-229
	Host cell DNA	< 0.33 pg/mg	SOP-QC-030
	Bacterial endotoxin	< 0.2 EU/mg	SOP-QC-028
Potency	Bioburden	< 10 cfu/ml	SOP-QC-049
	Relative binding activity	70-130% of the reference standard	SOP-QC-225
	Relative blocking activity	70-130% of the reference standard	SOP-QC-224
Content	Protein content	13.5~ 16.5mg/ml	SOP-QC-230

2.3.S.4.2 Lot release data

Four GMP DS lots were manufactured up to date. The lot release data are presented in [Table 2.8](#).

Table 2.8 Lot release results

Test item	Acceptance Criteria	141219DS	141230DS	150107DS	151202DS
pI	Nine peaks in total in the pI range of 7.75-9.55; five main peaks are in the pI range of 8.50-9.25. Conform to the reference standard.	Nine peaks in total in the pI range of 7.98-9.44; five main peaks are in the pI range of 8.65-9.20. Conform to the reference standard.	Nine peaks in total in the pI range of 7.98-9.45; five main peaks are in the pI range of 8.66-9.21. Conform to the reference standard.	Nine peaks in total in the pI range of 7.98-9.44; five main peaks are in the pI range of 8.65-9.20. Conform to the reference standard.	Nine peaks in total in the pI range of 7.97-9.47; five main peaks are in the pI range of 8.66-9.24. Conform to the reference standard.
Peptide map	Conform to the reference standard. RSD of retention time of the characteristic peaks should not be higher than 3.00%	Conform to that of the RS. RSD of retention time of the characteristic peak is not higher than 0.13%	Confirm to the RS. RSD of retention time of the characteristic peak is not higher than 0.06%	Conform to the RS. RSD of retention time of the characteristic peak is not higher than 0.28%	Conform to the RS. RSD of retention time of the characteristic peak is not higher than 0.04%
Western blot	React to human Fc specific antibodies	React to human Fc specific antibodies	React to human Fc specific antibodies	React to human Fc specific antibodies	React to human Fc specific antibodies
Relative binding activity	Conform to the RS	Conform to the RS	Conform to the RS	Conform to the RS	Conform to the RS
Appearance	Clear and colorless to orange red liquid, with the faint opalescence.	Clear and colorless liquid, with the faint opalescence.	Clear and colorless liquid, with the faint opalescence.	Clear and colorless liquid, with the faint opalescence.	Clear and colorless liquid, with the faint opalescence.
SE-HPLC (%)	Monomer $\geq 95.0\%$	99.9	99.9	99.6	99.1
	Aggregate $< 3.0\%$	0.1	0.1	0.1	0.9
	Fragment: report results	0.0	0.0	0.3	0.0

3D Medicines (Sichuan) Co., Ltd
Module 2.3

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Test item	Acceptance Criteria	141219DS	141230DS	150107DS	151202DS
WCX-HPLC (%)	Sum of acidic peak 1 < 20.0	3.1	3.5	3.2	3.0
	Sum of acidic peak 2: report results	58.1	57.1	57.3	58.4
	Sum of K0, K1 and K2: report results	35.5	35.5	35.6	35.6
	Sum of basic peaks: report results	3.2	3.9	4.0	3.1
CE-SDS (reducing) (%)	Main peak ≥ 95.0	98.5	98.1	98.4	98.1
	Fragment: report results	1.5	1.9	1.6	1.9
HCP residue (ppm)	< 100	14	13	14	20
Host cell DNA (pg/mg)	< 0.33	< 0.13	0.28	< 0.13	< 0.13
Endotoxin (EU/mg)	< 0.2	< 0.016	< 0.016	< 0.016	< 0.03
Bioburden (cfu/mL)	< 10	< 1	< 1	< 1	< 1
Relative binding activity	70-130 % of RS	89	106	105	115
Relative blocking activity	70-130% of RS	91	91	94	103
Protein content (mg/mL)	13.5~ 16.5	14.8	15.1	14.9	15.2