

2.3.P.5 Control of Drug Product**Table 2.13 Specifications for KN035 Drug Product**

Category	Test item	Acceptance criteria	Methods
Identity	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
	Relative binding activity (%)	Conform to the reference standard	SOP-QC-225
General	Appearance	Clear and colorless to orange red liquid, with the faint opalescence	SOP-QC-010 and SOP-QC-012
	pH	6.0~7.0	SOP-QC-009
	Filling volume (ml)	No less than 1.5ml	SOP-QC-014
	Subvisible particles	≥10 μm: no more than 6000; ≥25μm: no more than 600	SOP-QC-013
	Visible particles	Practically free from visible particles	SOP-QC-011
	Osmolality (mOsmol/kg)	300~450	SOP-QC-281
Purity	SE-HPLC (%)	Monomer ≥95.0	SOP-QC-223
		Aggregate <3.0%	
		Fragment : report results	
	WCX-HPLC(%)	Sum of acidic peak 1 <20.0	SOP-QC-226
		Sum of acidic peak 2: report results	
		Sum ofK0, K1 and K2: report results	
		Sum of other basic peaks: report results	
Safety	Bacterial endotoxin (EU/mg)	<0.5	SOP-QC-028
	Sterility test	Sterile	SOP-QC-027
Potency	Relative blocking activity (%)	70-130 of RS	SOP-QC-224
	Relative binding activity (%)	70-130 of RS	SOP-QC-225
Content	Protein content (mg/mL)	180.0~220.0	SOP-QC-230

2.3.P.5.4 Lot Analysis

Four DP GMP lots were manufactured up to date (Table 2.14). The DS lots used to manufacture the DP lots are also provided in the Table 2.14. The release results are presented in Table 2.15.

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Table 2.14 DP lot manufactured

DP lots	20150501	20150502	20150503	20160501
DS lots used	141219DS	141230DS	150107DS	151202DS
Manufacturing date	May 20, 2015	May 27, 2015	May 28, 2015	May 05, 2016
Disposition	Stability	Nonclinical, stability and clinical studies	Stability	Clinical studies
Lot size (vials)	1027	961	1265	1417

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Table 2.15 Lot release results

Test item	Acceptance criteria	20150501	20150502	20150503	20160501
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.	Nine peaks in total in the pI range of 7.97-9.44; and five main peaks are in the pI range of 8.66-9.20. Conform to the reference standard.	Nine peaks in total in the pI range of 7.97-9.43; and five main peaks are in the pI range of 8.66-9.20. Conform to the reference standard.	Nine peaks in total in the pI range of 7.97-9.43; and five main peaks are in the pI range of 8.66-9.19. Conform to the reference standard.	Nine peaks in total in the pI range of 7.99-9.48; and five main peaks are in the pI range of 8.67-9.24. Conform to the reference standard.
Relative binding activity (%)	Conform to the reference standard.	Conform to the reference standard.	Conform to the reference standard.	Conform to the reference standard.	Conform to the reference standard
Appearance	Clear, and colorless to orange red color, with the faint opalescence	Clear and orange red color, with the faint opalescence	Clear and orange red color, with the faint opalescence	Clear and orange red color, with the faint opalescence	Clear and orange red color, with the faint opalescence
pH	6.0~7.0	6.5	6.5	6.5	6.5
Filling volume (mL)	No less than 1.5mL	1.724	1.704	1.59	1.690
Subvisible particles	≥10 μm: no more than 6000;	60	131	71	908
	≥25μm: no more than 600	5	0	3	3
Visible particles	Practically free from visible particles	Practically free from visible particles	Practically free from visible particles	Practically free from visible particles	Practically free from visible particles
Osmolality (mOsmol/kg)	300~450	330	341	373	374
SE-HPLC (%)	Monomer ≥ 95.0	99.9	99.8	99.1	98.8
	Aggregate < 3%	0.1	0.1	0.1	1.2
	Fragment : report results	0.02	0.02	0.8	0.05

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WCX-HPLC (%)	Sum of acidic peak 1 <20.0	3.0	3.1	3.1	3.4
	Sum of acidic peak 2: report results	58.1	58.0	56.3	57.9
	Sum of K0, K1 and K2: report results	35.0	35.2	35.2	36.1
	Sum of basic peaks: report results	3.9	3.7	5.4	2.7
Bacterial endotoxin* (EU/mg)	< 0.5	<0.05	<0.05	<0.05	<0.05
Sterility test (USP <71>)	Sterile	Sterile	Sterile	Sterile	Sterile
Relative blocking activity (%)	70-130 of RS	90	86	99	104
Relative binding activity (%)	70-130 of RS	95	96	96	99
Protein content (mg/mL)	180.0~220.0	194.3	196.3	199.5	197.7