LEUPROLIDE (LEUPRORELIN) US DRUG SUBSTANCE SPECIFICATION

Molecular weight: 1209.4 (free peptide)

Sequence: p-Glu-His-Trp-Ser-Tyr-D-Leu-Leu-Arg-Pro-NHEt

Last update: 14 SEP 2020

Available registration documents (CTD format): DMF

TEST	ACCEPTANCE CRITERION	ANALYTICAL PROCEDURE
Appearance	White to off-white powder	Visual inspection
Solubility	Soluble in water and 1% (v/v) aqueous acetic acid at a concentration of ≥ 10 mg/mL to give a clear, colorless solution	Visual inspection
Identity, MS	Monoisotopic mass 1208.7 ± 1 u	USP
Identity, Amino acid analysis		USP
	Ser: Present Glx: 0.85 to 1.1 Pro: 0.85 to 1.1 Leu: 1.8 to 2.2 Tyr: 0.85 to 1.1 His: 0.85 to 1.1 Arg: 0.85 to 1.1 Trp: Present	
Identity, HPLC	Co-elutes with reference standard	USP
Peptide purity, HPLC	≥ 98.5%	USP/Ph. Eur.
Total impurities, HPLC	≤ 1.5%	USP/Ph. Eur.
Related substances, HPLC		USP/Ph. Eur.
Peptide related impurities[1]		
Any other impurity	≤ 0.10%	

[1] Detailed impurity specification not provided

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TEST	ACCEPTANCE CRITERION		ANALYTICAL PROCEDURE
Acetic acid, HPLC	4.7% to 9.0%		In-house
Water, Karl Fischer	≤ 8.0%		USP
Assay Leuprolide content, HPLC	≥ 82%		USP/Ph. Eur.
Leuprolide content (With reference to the anhydrous, acetic acid free substance)	97.0% to 103.0%		Calculation
Residual solvents, GC			In-house
	Acetonitrile	≤ 410 ppm (w/w)	
	Ethanol	≤ 1000 ppm (w/w)	
	Methanol	≤ 1000 ppm (w/w)	
	Triethylamine	≤ 320 ppm (w/w)	
Trifluoroacetic acid, HPLC	≤ 0.25%		In-house
Phosphate, IC	≤ 0.1%		In-house
Microbial enumeration tests			
TAMC	≤ 100 CFU/g		USP
TYMC	≤ 100 CFU/g		USP
Bacterial endotoxins	≤ 166.7 IU/mg		USP