

**LEUPROLIDE (LEUPRORELIN) EU
DRUG SUBSTANCE SPECIFICATION**



Molecular weight: 1209.4 (free peptide)

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Sequence: p-Glu-His-Trp-Ser-Tyr-D-Leu-Leu-Arg-Pro-NH₂

Last update: 09 JUN 2018

Available registration documents (CTD format): CEP/COS certificate

TEST	ACCEPTANCE CRITERION	ANALYTICAL PROCEDURE																
Appearance	White or almost 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	Ph. Eur.																
Identity, Amino acid analysis	<table border="0"> <tr><td>Ser</td><td>Present</td></tr> <tr><td>Glx</td><td>0.85 to 1.1</td></tr> <tr><td>Pro</td><td>0.85 to 1.1</td></tr> <tr><td>Leu</td><td>1.8 to 2.2</td></tr> <tr><td>Tyr</td><td>0.85 to 1.1</td></tr> <tr><td>His</td><td>0.85 to 1.1</td></tr> <tr><td>Arg</td><td>0.85 to 1.1</td></tr> <tr><td>Trp</td><td>Present</td></tr> </table>	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	Ph. Eur.
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Glx	0.85 to 1.1																	
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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	Ph. Eur.																
Peptide purity, HPLC	≥ 97.5 %	Ph. Eur.																
Total impurities, HPLC	≤ 2.5 %	Ph. Eur.																
Related substances, HPLC																		
Any unspecified impurity	≤ 0.5 %	Ph. Eur.																
Specified impurities		Ph. Eur.																
	[4-D-serine] leuprorelin ≤ 0.5 %																	
	[2-D-histidine] leuprorelin ≤ 0.5 %																	
	[6-L-leucine] leuprorelin ≤ 0.5 %																	
	[4-(<i>O</i> -acetyl-L-serine)] leuprorelin ≤ 1.0 %																	

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TEST	ACCEPTANCE CRITERION	ANALYTICAL PROCEDURE
Acetic acid content, HPLC	4.7 % to 9.0 %	In-house
Water, Karl Fischer	≤ 5.0 %	Ph. Eur.
Leuprorelin content With reference to the anhydrous, acetic acid free substance	97.0 % to 103.0 %	Calculation
Specific optical rotation $[\alpha]_D^{20}$ (c = 1, 1% acetic acid) With reference to the anhydrous, acetic acid free substance	-38 to -42°	Ph. Eur.
Residual solvents, GC		In-house
	Acetonitrile ≤ 410 ppm (w/w)	
	Diisopropylethylamine ≤ 320 ppm (w/w)	
	Dimethylformamide ≤ 880 ppm (w/w)	
	Ethanol ≤ 5000 ppm (w/w)	
	Isopropanol ≤ 1000 ppm (w/w)	
	Methanol ≤ 1000 ppm (w/w)	
	Dichloromethane ≤ 500 ppm (w/w)	
	Triethylamine ≤ 320 ppm (w/w)	
Trifluoroacetic acid, HPLC	≤ 0.1 %	In-house
Phosphate, IC	≤ 0.1 %	In-house
Residue on ignition	≤ 0.3 %	Ph. Eur.
Bacterial endotoxins	< 16.7 IU/mg	Ph. Eur.