

**EXENDIN-4 ACETATE (EXENATIDE)
DRUG SUBSTANCE SPECIFICATION**



Molecular weight: 4186.6 u (free base)

Page 1 of 2

Sequence: H-His-Gly-Glu-Gly-Thr⁵-Phe-Thr-Ser-Asp-Leu¹⁰-Ser-Lys-Gln-Met-Glu¹⁵-Glu-Glu-Ala-Val-Arg²⁰-Leu-Phe-Ile-Glu-Trp²⁵-Leu-Lys-Asn- Gly-Gly³⁰-Pro-Ser-Ser-Gly-Ala³⁵-Pro-Pro-Pro-Ser-NH₂

Last update: 09 JUN 2018

Available registration documents (CTD format): DMF

TEST	ACCEPTANCE CRITERION	ANALYTICAL PROCEDURE																																
Appearance	White to off-white powder	Visual inspection																																
Identity, MS	Monoisotopic mass 4184.0 ± 2 u	USP																																
Identity, AAA	<table border="0"> <tr><td>Asx</td><td>1.8 - 2.2</td></tr> <tr><td>Thr</td><td>1.8 - 2.2</td></tr> <tr><td>Ser</td><td>4.2 - 5.5</td></tr> <tr><td>Glx</td><td>5.4 - 6.6</td></tr> <tr><td>Pro</td><td>3.6 - 4.4</td></tr> <tr><td>Gly</td><td>4.5 - 5.5</td></tr> <tr><td>Ala</td><td>1.8 - 2.2</td></tr> <tr><td>Val</td><td>0.8 - 1.2</td></tr> <tr><td>Met</td><td>0.9 - 1.1</td></tr> <tr><td>Ile</td><td>0.9 - 1.1</td></tr> <tr><td>Leu</td><td>2.7 - 3.3</td></tr> <tr><td>Phe</td><td>1.8 - 2.2</td></tr> <tr><td>His</td><td>0.9 - 1.1</td></tr> <tr><td>Lys</td><td>1.8 - 2.2</td></tr> <tr><td>Trp</td><td>0.4 - 1.1</td></tr> <tr><td>Arg</td><td>0.9 - 1.1</td></tr> </table>	Asx	1.8 - 2.2	Thr	1.8 - 2.2	Ser	4.2 - 5.5	Glx	5.4 - 6.6	Pro	3.6 - 4.4	Gly	4.5 - 5.5	Ala	1.8 - 2.2	Val	0.8 - 1.2	Met	0.9 - 1.1	Ile	0.9 - 1.1	Leu	2.7 - 3.3	Phe	1.8 - 2.2	His	0.9 - 1.1	Lys	1.8 - 2.2	Trp	0.4 - 1.1	Arg	0.9 - 1.1	USP
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Identity, HPLC	Conforms to reference standard	USP																																
Assay of exenatide, HPLC	≥ 80 % (w/w)	USP																																
Exenatide content (anhydrous and acetic acid-free substance)	95 - 105 % (w/w)	USP																																
Peptide purity, HPLC	≥ 97.0 %	USP																																

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TEST	ACCEPTANCE CRITERION	ANALYTICAL PROCEDURE
Peptide related impurities,		USP
[Glu ¹³]exenatide, HPLC	≤ 0.5 %	
Sum of [Asp ²⁸]exenatide and [Met(O) ¹⁴]exenatide, HPLC	≤ 0.5 %	
[N-Acetyl-His ¹]exenatide, HPLC	≤ 0.5%	
Impurity A, HPLC	≤ 0.5%	
[D-His ¹]exenatide, GC-MS	≤ 1.0%	
Any unspecified impurity, HPLC	≤ 0.5%	
Total sum of impurities	≤ 4.0%	
Acetic acid content, HPLC	≤ 5.0 % (w/w)	In-house
Water, Karl Fischer	≤ 7.0 % (w/w)	USP
Trifluoroacetic acid, HPLC	≤ 0.25 % (w/w)	In-house
Residual solvents, GC		In-house
Acetonitrile	≤ 410 ppm (w/w)	
Triethylamine	≤ 320 ppm (w/w)	
Phosphate, IC	≤ 0.1 % (w/w)	USP
Microbiological tests		USP
TAMC	≤ 200 CFU/g	
TYMC	≤ 200 CFU/g	
Bacterial endotoxins	≤ 10 EU/mg	