

**CALCITONIN (SALMON) US
DRUG SUBSTANCE SPECIFICATION**



Molecular weight: 3432 (as free base)

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Sequence: H-Cys-Ser-Asn-Leu-Ser-Thr-Cys-Val-Leu-Gly-Lys-Leu-Ser-Gln-Glu-Leu-His-Lys-Leu-Gln-Thr-Tyr-Pro-Arg-Thr-Asn-Thr-Gly-Ser-Gly-Thr-Pro-NH₂ Acetate salt

Last update: 09 JUN 2018

Available registration documents (CTD format): DMF

TEST	ACCEPTANCE CRITERION	ANALYTICAL PROCEDURE																										
Appearance	White or almost white powder	Visual inspection																										
Solubility	Freely soluble in water	USP																										
Identity, HPLC	Retention time of the principle peak in the sample is similar to the retention time of the principle peak in the reference	USP																										
Identity, Amino acid analysis	<table border="0"> <tr><td>Asp</td><td>1.8 to 2.2</td></tr> <tr><td>Glu</td><td>2.7 to 3.3</td></tr> <tr><td>Pro</td><td>1.7 to 2.3</td></tr> <tr><td>Gly</td><td>2.7 to 3.3</td></tr> <tr><td>Val</td><td>0.9 to 1.1</td></tr> <tr><td>Leu</td><td>4.5 to 5.3</td></tr> <tr><td>His</td><td>0.9 to 1.1</td></tr> <tr><td>Arg</td><td>0.9 to 1.1</td></tr> <tr><td>Lys</td><td>1.8 to 2.2</td></tr> <tr><td>Ser</td><td>3.2 to 4.2</td></tr> <tr><td>Thr</td><td>4.2 to 5.2</td></tr> <tr><td>Tyr</td><td>0.7 to 1.1</td></tr> <tr><td>Half-cystine</td><td>1.4 to 2.1</td></tr> </table>	Asp	1.8 to 2.2	Glu	2.7 to 3.3	Pro	1.7 to 2.3	Gly	2.7 to 3.3	Val	0.9 to 1.1	Leu	4.5 to 5.3	His	0.9 to 1.1	Arg	0.9 to 1.1	Lys	1.8 to 2.2	Ser	3.2 to 4.2	Thr	4.2 to 5.2	Tyr	0.7 to 1.1	Half-cystine	1.4 to 2.1	USP
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Bioidentity	<p>The potency levels determined from at least three performances of the test are homogeneous, and the confidence limits for all determinations are between 64% and 156% of the calculated potency</p> <p>Geometric mean 80% to 125% of assay value</p>	USP																										

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TEST	ACCEPTANCE CRITERION	ANALYTICAL PROCEDURE
Peptide purity, HPLC	≥ 97.0%	USP
Peptide related impurities, HPLC		USP
RRt approx. 0.84 (molecular weight 3473.7 and 3431.7)	≤ 0.3%	
RRt approx. 0.92 (molecular weight 3431.7)	≤ 0.3%	
RRt approx. 0.95 (molecular weight 3463.7)	≤ 0.3%	
Sum of identified related peptides with RRt approx. 1.05 to 1.07	≤ 1.0%	
[Glu ¹⁴]-Calcitonin	≤ 1.0%	
Sum of [Glu ²⁰]-Calcitonin and N-Acetyl-Cys(1)-Calcitonin	≤ 1.0%	
[Glu ²⁰]-Calcitonin	≤ 1.0%	
N-Acetyl-Cys(1)-Calcitonin	≤ 1.0%	
Any unspecified impurities/degradation products	≤ 0.2%	
Sum of impurities/degradation products	≤ 3.0%	

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TEST	ACCEPTANCE CRITERION	ANALYTICAL PROCEDURE
Chloride, IC	≤ 0.2% (w/w)	In-house
Water, Karl Fischer	≤ 10% (w/w)	USP
Acetic acid, HPLC	4.0 to 15.0% (w/w)	USP
Heavy metals, ICP	≤ 20 ppm	In-house
Mass balance	90.0 to 105.0%	USP
Peptide content, HPLC	Report result %(w/w)	USP
Biological activity Calculated as: $\frac{\text{peptide content} \times 6000 \text{ IU/mg}}{100}$	Report result, IU/mg	USP
Trifluoroacetic acid, IC	≤ 100 ppm	In-house
Ethanol, GC-HS	≤ 2000 ppm	In-house
Acetonitrile, GC-HS	≤ 410 ppm	In-house
Microbial enumeration tests:		USP
TAMC	≤ 100 CFU/g	
TYMC	≤ 100 CFU/g	
Bacterial endotoxins	≤ 1000 EU/mg	USP