

**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: 15 MAR 2010

Available registration documents (CTD format): US DMF

TEST	ACCEPTANCE CRITERIA	ANALYTICAL PROCEDURE
CHARACTERISTICS		
Appearance	White or almost white powder	Visual inspection
	Freely soluble in water	USP
IDENTIFICATION		
Identification, HPLC	Retention time of the principle peak in the sample is similar to the retention time of the principle peak in the reference	USP
Amino acid analysis	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	

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TEST	ACCEPTANCE CRITERIA	ANALYTICAL PROCEDURE
Bioidentity	The potency levels determined from all three performances of the test are homogeneous, and the confidence limits for all three determinations are between 64% and 156% of the calculated potency	USP
PURITY		
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%	

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PURITY		
Peptide related impurities, HPLC:		USP
Any unspecified impurities/degradation products	≤ 0.2%	
Sum of impurities/degradation products	≤ 3.0%	
ASSAY		
Peptide content	Report result (%)	USP
Mass balance	90.0 to 105.0%	USP
Biological activity	Report result, IU/mg	USP
Calculated as: $\frac{\text{peptide content} \times 6000 \text{ IU/mg}}{100}$		
OTHER TESTS		
Chloride	≤ 0.2% (w/w)	In-house
Water	≤ 10% (w/w)	USP
Acetic acid	4.0 to 15.0% (w/w)	USP
Heavy metals	≤ 20 ppm (w/w)	In-house

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TEST	ACCEPTANCE CRITERIA	ANALYTICAL PROCEDURE
RESIDUAL SOLVENTS		
Trifluoroacetic acid	≤ 100 ppm	In-house
Ethanol	≤ 2000 ppm	In-house
Acetonitrile	≤ 410 ppm	In-house
MICROBIOLOGICAL TESTS		
Microbial enumeration tests:		USP
TAMC	≤ 100 CFU/g	
TYMC	≤ 100 CFU/g	
Bacterial endotoxins	≤ 1000 EU/mg	USP