

Bronchitol US Stability Data Summary for First Commercial Batch **Stability Data for Completed Study**

Record reviewed
Signed
Date 04 Apr 24

Product		Bronchitol US									
Batch		21006GUS									
Conditions		25°C/60%RH									
Time Point (Months)		0	3	6	9	12	18	24	36		
Test		Results									
Appearance (Visual)	Capsule	Capsule shell appearance is clear, transparent and almost colorless. The capsules should be clean, undamaged and show no sign of leakage. The content consists of a white or almost white powder, without any visual contamination. The text "PXS 40 mg" is clearly printed on the capsule.									
	Blister	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	
	Inhaler	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	
Mannitol Assay		97.0% – 102.0% Mannitol									
	Maltitol	ND	ND	ND	NR	ND	NR	ND	NR	ND	
Related Substances	Isomalt	0.06	0.06	0.06	NR	0.06	NR	0.06	NR	0.06	
	Sorbitol	0.69	0.70	0.69	NR	0.68	NR	0.69	NR	0.69	
	Individual Unidentified Substances	<0.05	<0.05	<0.05	NR	<0.05	NR	<0.05	NR	<0.05	
	Total Impurities	0.75	0.76	0.75	NR	0.75	NR	0.75	NR	0.75	
Water Content		0.5	0.4	0.4	NR	0.4	NR	0.4	NR	0.4	
Mean Delivered Dose		32.0	30.6	31.8	32.3	33.0	31.6	32.4	32.1		
Delivered Dose Uniformity	Tier 1 Sample 10 capsules 9 of 10 capsules are 80-120% of LC (32.2 mg) 10 of 10 are 75-125% of LC (32.2 mg); if not	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	
		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
	Tier 2 Sample 20 additional capsules 27 of 30 capsules are 80-120% of LC (32.2 mg) 30 of 30 are 75-125% of LC (32.2 mg)	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	

Key: ATP – Adapter, Throat, Pre-separator (of ACI) ND – Not Detected
LC – Label Claim NR – Not Required (as per test protocol)
N/A – Not Applicable (as per specification)

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Aerodynamic Particle Size Distribution (by ACI)	ACI Stage Group	Mannitol Deposition per Capsule	Tier	Mean (mg) Complies / Does Not Comply								
	ATP to Stage -0	5 – 20 mg	Tier 1	11.0	11.5	9.9	10.4	10.8	10.9	11.0	10.3	
			Tier 2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
			Result	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	
	Stage 1 to Stage 3	9 – 20 mg	Tier 1	14.8	14.4	16.3	15.1	15.4	15.1	15.9	16.1	
			Tier 2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
			Result	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	
	Stage 4 to Stage 6	0.5 – 1.9 mg	Tier 1	1.2	1.0	1.3	1.2	1.2	1.2	1.2	1.3	
			Tier 2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	
			Result	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	
Filter	≤ 0.7 mg	Tier 1	0.4	0.4	0.4	0.4	0.4	0.4	0.3	0.4		
		Tier 2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A		
		Result	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies		
Foreign Particulate Matter	Particle Size	Particles per Dose	Tier	Particles per Dose Complies / Does Not Comply								
	2 - 10 µm Particles	≤13,000	Tier 1	5236	3992	4647	NR	4310	NR	5028	4349	
			Tier 2	N/A	N/A	N/A	N/A	N/A	NR	N/A	N/A	
			Result	Complies	Complies	Complies	NR	Complies	NR	Complies	Complies	
	≥10 µm Particles	≤600	Tier 1	9	5	4	NR	4	NR	11	13	
			Tier 2	N/A	N/A	N/A	N/A	NR	N/A	N/A	N/A	
			Result	Complies	Complies	Complies	NR	Complies	NR	Complies	Complies	
	≥25 µm Particles	≤300	Tier 1	0	0	0	NR	2	NR	0	2	
			Tier 2	N/A	N/A	N/A	N/A	NR	N/A	N/A	N/A	
			Result	Complies	Complies	Complies	NR	Complies	NR	Complies	Complies	

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Time Point (Months)		0	3	6	9	12	18	24	36		
Microbial Limits	Total Aerobic Microbial Count NMT 10 ² CFU per gram	<10	NR	NR	NR	<10	NR	<10	<10		
	Total Yeast and Mould Count NMT 10 ¹ CFU per gram	<10	NR	NR	NR	<10	NR	<10	<10		
	Absence of <i>S. Aureus</i> in 1 gram	Complies	NR	NR	NR	Complies	NR	Complies	Complies		
	Absence of <i>P. Aeruginosa</i> in 1 gram	Complies	NR	NR	NR	Complies	NR	Complies	Complies		
Absence of Bile Tolerant Gram Negative Bacteria in 1 gram		Complies	NR	NR	NR	Complies	NR	Complies	Complies		

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