## **FMOLHS Respiratory Agent Review**

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<b>Respiratory Agent</b>	Dose/Frequency	Indication	Evidence	Approved on	Administration/
				Respiratory	Special Considerations
				Agent List?	
Amikacin	Pneumonia: 400mg q12h	Gram-	The INHALE 1 and 2 trials (n=712)	Yes	-Vial size is 1000mg/4mL
(injectable solution)	for 10 days	negative	evaluated the use of inhaled		
		pneumonia	amikacin in patients with gram-		-Draw 1.6mL (400mg) from vial
			negative lung pneumonia and an		and dilute with 3.2mL saline;
			APACHE II score of at least 10.		
			However, there was no observed		-synchronized innalation system
			difference in survival compared to		(for intubated patients) and
					chamber (for extubated
					nationts): Non-humidified
					nebulization increases particle
					deposition in the lungs
	NTM-LD: 250mg once	*NTM-LD as	A retrospective chart review (n=20)		NTM-LD:
	daily and titrated every 2	an alternative	with treatment refractory NTM-LD		-Draw 1mL (250mg) from vial
	weeks up to 500mg BID	to Amikacin	found that 40% of patients had at		and dilute with 3mL of saline
		liposomal	least one negative culture and smear		
		inhalation	at follow up and symptom scores		
		solution (ALIS)	improved in 45%. <sup>2</sup>		
Ampicillin/Sulbactam	3 g every 8 h	Gram-	In a small case series (n=20)	No	-3 g in 3 mL of sterile water
		negative	conducted in patients with A.		administered via nebulizer
		pneumonia	baumannii pneumonia. Ten patients		
			received IV ampicillin-sulbactam		
			alone, compared to 10 who received		
			subsetam After 2 to 2 days of		
			therapy, patients who received both		
			IV and inhaled therapy had		
			reductions in viable counts of		
			bacteria to <102 CFU/ml. compared		
			to no reduction in CFU/mL for those		
			who received IV monotherapy. <sup>4</sup>		

Ciprodex	4-5 drops BID for 1 week,	Tracheal	One study (n=4) patients with TCS	No	-Typically administered in about
	repeated every other	cartilaginous	evaluated the efficacy of nebulized		5mL of solution
	week	sleave,	<i>Ciprodex</i> . The study found that the	(An inhaled	
		Tracheal	number of hospitalizations and	corticosteroid,	
		stenosis	number of infections decreased for	such as	
			each patient upon follow up in an	budesonide,	
			ENT clinic. <sup>5</sup> However, the actual dose	should be	
			of ciprofloxacin with each	used instead)	
			nebulization is negligible and the		
			perceived benefit is likely due to the		
			more substantial doses of		
			dexamethasone (the steroid		
			component).		
			Yokoi and colleagues evaluated the		
			efficacy of inhaled <u>budesonide</u> in		
			patients with CTS for the treatment		
			of postoperative granulation tissue.		
			Patients that received inhaled		
			budesonide showed significant		
			improvement on bronchoscopy in		
			the development of postoperative		
			granulation tissue. In addition to this,		
			no patients in the budesonide group		
			required subsequent stenting. <sup>6</sup>		
Colistin	150mg q8h for 14 days	VAP	A prospective, observational,	Yes	-Vial size is 150mg/4mL
			comparative study in VAP patients	(EPIC build	
MRN: 403527			(n=122) with <i>P. aeruginosa</i> and <i>A.</i>	already	-Draw 4mL from vial and
			<i>baumannii</i> (susceptible to β-lactams,	available)	administer via nebulization (may
			aminoglycosides, or quinolones and		add normal saline based on
			treated with intravenous antibiotics		nebulizer volume limits)
			for 14 days) found that nebulized		
			colistin was noninferior to		Consider use of a bronchodilator
			intravenous antibiotic therapy. 28		prior to administration
			patients received nebulized colistin		
			as monotherapy; whereas the		
			remaining patients received it in		
			conjunction with a 3-day intravenous		
			aminoglycoside course.'		

Furosemide	4 ml of furosemide as a	Dyspnea	A double-blind, randomized,	No	-Administered via jet nebulizer
	10 mg/ml solution		crossover study compared the effect		and nebulized to dryness
			of inhaled furosemide on dyspneic	Standard	
			sensation in COPD patient during	inhaled	
			exercise vs placebo. There was	therapy for	
			significant improvement in mean	the treatment	
			FEV1 and FVC after inhalation of	of dyspnea in	
			furosemide (p = 0.038 and 0.005,	COPD should	
			respectively) but not after placebo.	be used (i.e.,	
			The mean dyspneic visual analog	Duoneb)	
			scale score was lower after		
			inhalation of furosemide compared		
			with placebo (33.7 $\pm$ 25.2 vs. 42.4 $\pm$		
			24.0 mm, respectively, p = 0.014). <sup>9</sup>		
Milrinone	50 mcg/kg	Pulmonary	Singh et al. (n=40) performed a	No	-The milrinone dose was
		hypertension	three-way comparison of nebulized		dissolved with normal saline to a
			NTG, nebulized milrinone, and 100%		volume of 3mL and they were
			inspired oxygen in children with left-		nebulized with a jet
			to-right intracardiac shunt and		nebulizer using 8 L/min of 50%
			elevated mPAP (>30 mmHg)		air-oxygen mixture
			undergoing right heart		
			catheterization. Both nebulized NTG		
			and nebulized milrinone lowered		
			mPAP (–15%) while keeping other		
			hemodynamic variables stable and it		
			was concluded that the three		
			treatments had comparable effect. <sup>10</sup>		
Tranexamic Acid	500mg q8h (up to 5 days)	Hemoptysis	In one small case series (n=4) and	Yes	-Vial size is 1000mg/10mL
(TXA)			one randomized control trial (n=47),		
			tranexamic acid inhalation reduced		-Draw 5mL from syringe and
			expectorated blood volume in		administer undiluted
			patients receiving treatment.		
			Additionally, fewer procedures were		
			pertormed (bronchoscopies,		
			embolization) and hospital length of		
			stay was reduced. <sup>11,12</sup>		

## **FMOLHS Approved Respiratory Agent List**

- 1. Amikacin injectable solution
- 2. Colistin injectable solution
- 3. Tranexamic acid injectable solution

## **References:**

- Niederman MS, et al. J. Inhaled amikacin adjunctive to intravenous standard-of-care antibiotics in mechanically ventilated patients with Gram-negative pneumonia (INHALE): a double-blind, randomised, placebo-controlled, phase 3, superiority trial. Lancet Infect Dis. 2020 Mar;20(3):330-340. doi: 10.1016/S1473-3099(19)30574-2. Epub 2019 Dec 19. PMID: 31866328.
- 2. Olivier KN, et al. Inhaled amikacin for treatment of refractory pulmonary nontuberculous mycobacterial disease. *Ann Am Thorac Soc.* 2014 Jan;11(1):30-5. doi: 10.1513/AnnalsATS.201307-2310C.
- 3. Yagi K, Ishii M, Namkoong H, et al. The efficacy, safety, and feasibility of inhaled amikacin for the treatment of difficult-to-treat non-tuberculous mycobacterial lung diseases. *BMC Infect Dis*. 2017;17(1):558. Published 2017 Aug 9. doi:10.1186/s12879-017-2665-5
- 4. Horianopoulou, M et al. Use of inhaled ampicillin–sulbactam against multiresistant Acinetobacter baumannii in bronchial secretions of intensive care unit patients. Clinical Microbiology and Infection. DOI:https://doi.org/10.1111/j.1469-0691.2004.00806
- 5. Regone R, et al. *Airway Management in Patients with Tracheal Cartilaginous Sleeve*. Department of Pediatric Otolaryngology, Texas Children's Hospital and Baylor College of Medicine.
- 6. Yokoi A, et al. *Treatment of postoperative tracheal granulation tissue with inhaled budesonide in congenital tracheal stenosis*. J Pediatr Surg. 2014 Feb;49(2):293-5; discussion 295. doi: 10.1016/j.jpedsurg.2013.11.041. Epub 2013 Nov 16. PMID: 24528970.
- 7. Lu Q, Luo R, Bodin L, et al, "Efficacy of High-Dose Nebulized Colistin In Ventilator-Associated Pneumonia Caused By Multidrug-Resistant Pseudomonas aeruginosa and Acinetobacter baumannii," Anesthesiology, 2012, 117(6):1335-47.
- 8. Wenzler E, Fraidenburg DR, Scardina T, Danziger LH. Inhaled Antibiotics for Gram-Negative Respiratory Infections. Clin Microbiol Rev. 2016;29(3):581-632. doi:10.1128/CMR.00101-15
- 9. Kian-Chung Ong, et al. Effects of Inhaled Furosemide on Exertional Dyspnea in Chronic Obstructive Pulmonary Disease. American Journal of Respiratory and Critical Care Medicine. https://doi.org/10.1164/rccm.200308-11710C
- 10. Singh, R et al. Inhaled Nitroglycerin Versus Inhaled Milrinone in Children with Congenital Heart Disease Suffering from Pulmonary Artery Hypertension. Journal of Cardiothoracic and Vascular Anesthesia, Vol 24, No 5 (October), 2010: pp 797-801. doi:https://doi.org/10.1053/j.jvca.2009.10.024
- 11. Segrelles Calvo G, De Granda-Orive I, López Padilla D. Inhaled tranexamic acid as an alternative for hemoptysis treatment. Chest. 2016;149(2):604. doi: 10.1016/j.chest.2015.10.016[PubMed 26867844]
- 12. Wand O, Guber E, Guber A, Epstein Shochet G, Israeli-Shani L, Shitrit D. Inhaled tranexamic acid for hemoptysis treatment: a randomized controlled trial. Chest. 2018;154(6):1379-1384. doi: 10.1016/j.chest.2018.09.026.