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Literature Scan: Inhaled Medications for Cystic Fibrosis

Date of Review: January 2016

Date of Last Review: May 2015
Literature Search: April 2015-December 2015

Current Status of PDL Class:
See **Appendix 1**.

Conclusions:
- There is no new clinical evidence that can further inform PDL decisions for inhaled agents for Cystic Fibrosis.

Recommendations:
- Make tobramycin inhaled solution (Kitabis®) the sole preferred inhaled tobramycin product. No other changes to the PDL recommended.

Previous Conclusions:
- There is insufficient new evidence of inhaled agents for management of Cystic Fibrosis (CF) complication that would change current PDL class management.
- There remains insufficient comparative evidence to directly compare inhaled tobramycin (TIS) to inhaled aztreonam (AZLI) for the treatment of P. aerugonisa in patients with CF and there is no evidence that continuous use is superior to the recommended 28-day cycle (on 28 days, off 28 days).
- There remains insufficient evidence to recommend for or against the chronic use of other inhaled antibiotics (ceftazidime, colistin, gentamicin) to improve lung function and quality of life or reduce exacerbations in patients with CF.
- For the early eradication of P. aeruginosa, there is evidence that treatment with inhaled antibiotics is better than no treatment in eradication; but there is no strong evidence of a superior regimen over another. There is also moderate quality evidence that there is no significant difference between 28 days of TIS and 56 days of therapy.
- There is low quality evidence that TIS administered by the PARI LC PLUS Nebulizer is effective in improving lung function in patients with CF.

Previous Recommendations:
- Evaluate comparative costs in executive session; maintain at least one formulation of either inhaled tobramycin or aztreonam as preferred on the PDL for the treatment of chronic infection with *P. aerugonisa*.

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Date: January 2016

Methods:
A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. A summary of the clinical trials is available in **Appendix 2**. The Medline search strategy used for this literature scan is available in **Appendix 3**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), Cochrane Collection, National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, BMJ Clinical Evidence, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts. Finally, the AHRQ National Guideline Clearinghouse (NGC) was searched for updated and recent evidence-based guidelines.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:

Timing of hypertonic saline inhalation for cystic fibrosis [Cochrane Review]
Researchers sought to determine whether the timing of hypertonic saline inhalation (in relation to airway clearance techniques or in relation to time of day) had an impact on its clinical efficacy in patients with cystic fibrosis.[1] However, researchers were unable to identify any studies that adequately compared the timing of treatment in relation to airway clearance physiotherapy.[1]

New Guidelines:
None identified.

New FDA Drug Approvals:
None identified.

New Formulations/Indications:
None identified.

New FDA Safety Alerts:
None identified.

Reference:

1. Elkins M, Dentice R. Timing of hypertonic saline inhalation for cystic fibrosis. *Cochrane Database of Systematic Reviews*. 2012, Issue 2. Art. No.: CD008816. DOI: 10.1002/14651858.CD008816.pub2.

Appendix 1: Current Status on Preferred Drug List

ROUTE	FORMULATION	BRAND	GENERIC	PDL
INHALATION	VIAL-NEB	SODIUM CHLORIDE	SODIUM CHLORIDE FOR INHALATION	Y
INHALATION	VIAL-NEB	SODIUM CHLORIDE	SODIUM CHLORIDE FOR INHALATION	Y
INHALATION	VIAL-NEB	SODIUM CHLORIDE	SODIUM CHLORIDE FOR INHALATION	Y
INHALATION	VIAL-NEB	SODIUM CHLORIDE	SODIUM CHLORIDE FOR INHALATION	Y
INHALATION	SOLUTION	PULMOZYME	DORNASE ALFA	Y
INHALATION	AMPUL-NEB	TOBI	TOBRAMYCIN IN 0.225% NACL	Y
INHALATION	AMPUL-NEB	BETHKIS	TOBRAMYCIN	Y
INHALATION	CAP W/DEV	TOBI PODHALER	TOBRAMYCIN	Y
INHALATION	CAPSULE	TOBI PODHALER	TOBRAMYCIN	Y
INHALATION	AMPUL-NEB	KITABIS PAK	TOBRAMYCIN/NEBULIZER	Y
INHALATION	AMPUL-NEB	TOBRAMYCIN	TOBRAMYCIN IN 0.225% NACL	N
INHALATION	VIAL-NEB	CAYSTON	AZTREONAM LYSINE	N

Appendix 2: New Clinical Trials

A total of 6 citations were manually reviewed from the literature search. After further review, all trials were excluded because of wrong study design (observational), comparator (placebo), or outcome studied (non-clinical).

Appendix 3: Medline Search Strategy

Ovid MEDLINE(R) without Revisions 1996 to November Week 3 2015

1 exp Cystic Fibrosis/ 16588
2 dornase alfa.mp. 123
3 exp Tobramycin/ 1513
4 exp Aztreonam/ 332
5 inhal*.mp. 78918
6 2 or 3 or 4 1939
7 1 and 5 and 6 251
8 limit 7 to (english language and yr="2015 -Current") 6