Pharmacologic therapy for Rhinosinusitis

- For mild to moderate acute bacterial or viral sinusitis symptomatic measures should suffice
- Analgesics and antipyretics as needed (AAO-HNSF Option)
- Intranasal corticosteroids
 - <u>Canadian consensus guidelines</u> recommend as sole therapy for mild-to moderate acute viral or bacterial sinusitis (CSO-HNS Moderate Evidence, Strong Recommendation)
 - Recommended as adjunct to antibiotics for bacterial sinusitis, primarily in patients with history of allergic rhinitis (IDSA Weakrecommendation, Moderate-quality evidence; AAO-HNSF Option)
- May reduce symptoms of acute sinusitis (level 2 [mid-level] evidence)

Other treatment options

- consider intranasal saline irrigation with either physiologic or hypertonic saline (IDSA Weak recommendation, Low-moderatequality evidence; AAO-HNSF Option) (CSO-HNS Option, Strong Recommendation)
- Addition of oral corticosteroids to antibiotics may hasten symptom improvement in adults with acute sinusitis (level 2 [mid-level] evidence)
- <u>Pelargonium sidoides</u> liquid solution may reduce sinusitis severity in patients with presumed acute bacterial rhinosinusitis (level 2 [mid-level] evidence)

- Decongestants lack evidence for effectiveness
- Antihistamines not indicated unless allergic component present

Antibiotics for acute bacterial sinusitis

- Antibiotics improve symptoms at 7-15 days in adults with acute maxillary sinusitis but high rate of clinical improvement without antibiotics (level 1 [likely reliable] evidence)
- Only consider treatment with antibiotics if patient meets criteria for acute bacterial sinusitis

- Recommendations for when to initiate antibiotics in adults vary
- ACP/CDC antibiotic recommends for acute rhinosinusitis reserve antibiotics for patients with one of the following
 - 1. > 10 days of persistent symptoms
 - 2. onset of severe symptoms or high fever ([> 39 degrees C] and \geq 3 consecutive days of purulent nasal discharge or facial pain
 - 3. onset of worsening symptoms after typical 5-day viral illness that was initially improving (double sickening)

• Infectious Diseases Society of America (IDSA) recommends starting antibiotics as soon as clinical diagnosis of acute bacterial sinusitis is made (IDSA Strong recommendation, Moderate-quality evidence)

- American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF) suggests considering watchful waiting without antibiotics in patients with uncomplicated mild illness (mild pain and temperature < [38.3 degrees C]) and presumed acute bacterial rhinosinusitis with assurance of follow-up (AAO-HNSF Option)
 - if patient worsens or if patient fails to improve with initial management option by 7 days after diagnosis, reconfirm diagnosis of bacterial rhinosinusitis and if reconfirmed, start antibiotic therapy (AAO-HNSF Recommendation)

- Canadian consensus guidelines recommend intranasal corticosteroids as sole therapy for mild-to-moderate acute viral or bacterial sinusitis (CSO-HNS Moderate Evidence, Strong Recommendation)
- Antibiotics may be prescribed to improve rate of symptom resolution within 14 days or when patient has quality of life or productivity issues or severe sinusitis with comorbidities (CSOHNS Moderate Evidence, Moderate Recommendation)
- Antibiotics should be given if intranasal corticosteroid therapy fails after 72 hours (CSO-HNS Option, Strong Recommendation)

- Amoxicillin or amoxicillin clavulanate is preferred first-line treatment
- IDSA recommends use of amoxicillin-clavulanate rather than amoxicillin alone (IDSA Weak recommendation, Low-quality evidence) based on prevalence data of betalactamase producing Haemophilus influenzae and in vitro susceptibility data in the United States
- If decision made to treat with antibiotics, amoxicillin with or without clavulanate is firstline therapy for most patients (500 mg/125 mg orally 3 times daily or 875 mg/125 mg orally twice daily) (AAO-HNSF Recommendation)

• Amoxicillin is first-line agent and substitute trimethoprimsulfamethoxazole or macrolide antibiotic in beta-lactam allergic patients (CSO-HNS Option, Strong Recommendation)

- Recommendations for treatment duration
- IDSA recommends treat for 5-7 days if uncomplicated bacterial rhinosinusitis (IDSA Weak recommendation, Low-moderatequality evidence)
- Canadian consensus guidelines recommend treating for 5-10 days as recommended by product monograph (CSO-HNS Strong Evidence, Moderate Recommendation)
- AAO-HNSF recommends 10 day course of antibiotics

- Change antibiotic class if antibiotic treatment fails after 72 hours (CSO-HNS Option, Strong Recommendation)
- For chronic or recurrent acute sinusitis:
 - Addition of intranasal steroids to antibiotics accelerates recovery of acute sinusitis in adults with chronic or recurrent sinusitis (level 1 [likely reliable] evidence)
 - Daily hypertonic saline nasal irrigation may improve sinus symptoms and may reduce sinus medication use in adults with frequent sinusitis (level 2 [midlevel] evidence)
 - Surgery reserved for recurrent acute or chronic infective sinusitis refractory to medical treatment

IDSA

- Start empiric antimicrobial therapy as soon as clinical diagnosis of acute bacterial rhinosinusitis established (IDSA Strong recommendation, Moderate-quality evidence)(2)
- Treat uncomplicated acute bacterial rhinosinusitis with 5-7 days of antibiotics (IDSA Weak recommendation, Low-moderate-quality evidence)(2)
- Initial empiric therapy if no risk for antibiotic resistance(2)
- First-line agent is amoxicillin-clavulanate 500 mg/125 mg orally 3 times daily or 875 mg/125 mg orally twice daily amoxicillin-clavulanate preferred over amoxicillin alone (IDSA Weak recommendation, Low-quality evidence)

risk factors for resistance include

- High endemic rates ($\geq 10\%$) of invasive penicillin-nonsusceptible
- Streptococcus pneumoniae
- Severe infection (such as evidence of systemic toxicity with fever of >39 degrees C, and threat of suppurative complications)
- Age > 65 years
- Recent hospitalization
- Antibiotic use within the past month
- Immunocompromised status

if risk of antibiotic resistance or if failed initial therapy, use 1 of the following

- High-dose amoxicillin-clavulanate 2,000 mg/125 mg orally twice daily
- Respiratory fluoroquinolone (IDSA Weak recommendation, Moderate quality evidence)
- Alternative options
- High-dose amoxicillin-clavulanate 2,000 mg/125 mg orally twice daily
- Doxycycline 100 mg orally twice daily or 200 mg orally once daily (IDSA Weak recommendation, Low-quality evidence)

• For severe infection requiring hospitalization, use 1 of the following(2)

- ampicillin-sulbactam 1.5-3 g IV every 6 hours
- levofloxacin 500 mg orally or IV once daily
- moxifloxacin 400 mg orally or IV once daily
- ceftriaxone 1-2 g IV every 12-24 hours
- cefotaxime 2 g IV every 4-6 hours

antibiotics not recommended for initial empiric antimicrobial therapy

- Macrolides (clarithromycin and azithromycin) (IDSA Strong recommendation, Moderatequality evidence)
- Trimethoprim-sulfamethoxazole (IDSA Strong recommendation, Moderatequality evidence)
- Second- and third-generation oral cephalosporin monotherapy (IDSA Weak recommendation, Moderate-quality evidence)
- Routine antimicrobial coverage for Staphylococcus aureus or methicillinresistant S. aureus during initial empiric therapy not recommended (IDSA Strong recommendation, Moderate-quality evidence)

American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF) recommendations for adult sinusitis

- Offer watchful waiting without antibiotics in patients with uncomplicated mild illness (mild pain and temperature < [38.3 degrees C]) with assurance of follow-up (AAO-HNSF Recommendation)
- defer antibiotics for up to 7 days after diagnosis
- limit management to symptomatic relief
- if patient worsens or if patient fails to improve with initial management option by 7 days after diagnosis, reconfirm diagnosis of bacterial rhinosinusitis and if reconfirmed, start antibiotic therapy

- If decision made to treat with antibiotic
- amoxicillin with or without clavulanate is first-line therapy for 5-10 days for most adults (AAO-HNSF Recommendation)
- amoxicillin alone not effective against Moraxella catarrhalis and H. influenzae
- Consider doxycycline or a respiratory fluoroquinolone if patient has penicillin allergy



Drug	Adult Dose	Pediatric Dose ^b	Relative Cost ^c	Comments
Amoxicillin	1.5–4 g/day divided in two to three doses	45–90 mg/kg/day divided in two doses	\$	Lacks coverage against β -lactamase producers
Amoxicillin- clavulanate	1.5–4 g/day divided in two to three doses	45–90 mg/kg/day divided in two doses	\$\$-\$\$\$	Broad coverage particularly with high doses; Augmentin XR (2 g every 12 hours) targeted toward PRSP
Cefdinir	600 mg/day divided in one to two doses	14 mg/kg/day divided in one to two doses	\$\$-\$\$\$	Preferred oral liquid cephalosporin owing to good palatability
Cefixime	200 mg twice daily	8 mg/kg/day divided in two doses	\$\$\$\$	IDSA recommends use only in combination with clindamycin
Cefpodoxime proxetil	200 mg twice daily	10 mg/kg/day divided in two doses	\$\$\$-\$\$\$\$	IDSA recommends use only in combination with clindamycin
Cefuroxime axetil	250-500 mg twice daily	15–30 mg/kg/day divided in two doses	\$\$-\$\$\$	Only included as an option in AAP guideline
Ceftriaxone	1 g IM/IV every 24 hours	50 mg/kg IM/IV every 24 hours	\$\$\$\$	Experts recommend a 5-day treatment course; useful for patients who are vomiting and cannot tolerate oral therapy
Doxycycline	100 mg twice daily	Avoid in children < 8 years	\$-\$\$\$	Can cause photosensitivity, GI problems, tooth staining in young children; many drug–drug interactions (antacids, iron, calcium)
Levofloxacin	500–750 mg once daily (750 mg × 5 days)	10 mg/kg/dose every 12–24 hours	\$-\$\$\$\$	Common fluoroquinolone side effects are nausea, vaginitis, diarrhea, dizziness; many
Moxifloxacin	400 mg once daily	Not available	\$\$\$-\$\$\$\$	drug–drug interactions (antacids, iron, calcium); tendon rupture, photosensitivity, QT prolongation possible
Clindamycin	300–450 mg three times daily	30–40 mg/kg/day divided in three doses	\$-\$\$\$	No Gram-negative coverage; use only in combination with cephalosporin

^aRefer to Table 72–2 for more information on antibiotics. Other FDA-approved antibiotics for ABRS not included in the Infectious Diseases Society of America, American Academy of Pediatrics, or American Academy of Otolaryngology-Head and Neck Surgery Foundation guidelines: azithromycin, cefaclor, cefprozil, clarithromycin, ciprofloxacin, erythromycin, and trimethoprim-sulfamethoxazole.

^bMaximum dose not to exceed adult dose.

^cApproximate cost per course: \$ (under \$25), \$\$ (\$25-\$50), \$\$\$ (\$50-\$100), \$\$\$\$ (over \$100).

AAP, American Academy of Pediatrics; ABRS, acute bacterial rhinosinusitis; IDSA, Infectious Diseases Society of America; IM, intramuscular; PRSP, penicillin-resistant *S. pneumoniae*.

Table 4. Antibiotic Therapy for Acute Rhinosinusitis						
Drug	Dose	Cost*				
A. First Line Antibiotic						
Amoxicillin-clavulanate	875/125 mg every 12 hours for 5-7 days	gen \$8-10				
Amoxicillin-clavulanate, high dose	2000/125 mg every 12 hours for 5-7 days	gen \$121-170				
D. Alternative First Line Antibiotic (if allergie to an intelement of amovicillin elevalenets)						
Doxycycline hyclate	100 mg every 12 hours for 5-7 days	gen \$8-10				
If allergic to or intolerant of doxycycline						
Levofloxacin	500 mg daily for 5-7 days	gen \$5-6				
Moxifloxacin	400 mg daily for 5-7 days	gen \$18-24				
C. If Treatment Failure Amoxicillin-clavulanate, high dose Levofloxacin Moxifloxacin	2000/125 mg every 12 hours for 7-10 days 500 mg daily for 7-10 days 400 mg daily for 7-10 days	gen \$168-240 gen \$9-11 gen \$24-33				

^{*} For cost presented as range, low=5 days, high=7 days. Cost=Maximum Allowable Cost (MAC) + \$3 for generics on 30-day supply or less, *Michigan Department of Community Health M.A.C. Manager, 12/18*

Drug therapy monitoring

- If symptoms persist or worsen after 48 to 72 hours of appropriate antibiotic therapy, then the patient should be reevaluated and alternative antibiotics should be considered.
- Patients who do not respond to first- or second-line therapies should be referred to a specialist and worked up more aggressively, potentially with direct sinus aspiration or contrast-enhanced computed tomography

Beta-lactam

- Allergy
- Clavulanic acid related hepatitis

Fluoroquinolones The Tramadol of Antimicrobials: Fluoroquinolones

Warnings

Commonly Known Adverse Effects	Lesser Known Adverse Effects	
QT prolongation	GI perforation	
Clostridium difficile infection	Aortic aneurysm/dissection	
Tendinopathy	Retinal detachment	
Peripheral neuropathy	Hypo/hyperglycemia	
Black box warnings	Seizures/Psychiatric AEs	

FDA recommends that:

- Serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections (UTI) who have other treatment options.
- For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.
- Providers should instruct patients to contact their health care professional immediately if they experience any serious side effects while taking fluoroquinolone medicine such as tendon, joint and muscle pain; a "pins and needles" tingling or pricking sensation; confusion; and hallucinations.
- Providers should stop systemic fluoroquinolone treatment immediately if a patient reports serious side effects, and switch to a non-fluoroquinolone antibacterial drug to complete the patient's treatment course.

- Fatal hypoglycemia Report of at least 67 cases of life-threatening hypoglycemic coma- including 13 deaths, 9 with permanent and disabling injuries
- Occurred more frequently in the elderly and those with diabetes taking an oral hypoglycemic medicine or insulin.
- Others had renal insufficiency as a risk factor (? Was dose renally adjusted)
- Four of these antibiotics have labeled drug interaction already with sulfonylurea
- Seen mostly with levofloxacin (44), cipro (12)

New neuropsychiatric side-effects 2018

