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Sound Medicine: Exploring Pharmacology for Hearing Health

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Disclosures

- The speakers have no actual or potential conflict of interest in relation to this presentation.

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Medical Abbreviations

AU – both ears	QD – once daily	PMH – past medical history
AD – right ear	BID – twice daily	NKDA – no known drug allergies
AS – left ear	TID – three times daily	DM – diabetes mellitus
gtts – drops	QID – four times daily	HLD – hyperlipidemia
PO – by mouth	PRN – as needed	HTN – hypertension
SC – subcutaneous	IV- intravenous	FQ- fluoroquinolone

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Objectives

- Identify practitioners with prescribing authority in Kentucky
- Understand the requirements for a prescription in Kentucky
- Recall how to properly administer ear drops
- Explain the significance of antimicrobial stewardship
- Discuss pharmacology of antimicrobials commonly used for conditions of the ear
- Discuss pharmacotherapy for otitis externa

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PRESCRIPTIVE AUTHORITY IN KENTUCKY

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Prescriptive Authority in Kentucky

Practitioners with prescribing authority include:

- Optometrists
- Podiatrists
- Dentists
- Veterinarians
- Physicians
- Physician Assistants
- Advanced Practice Registered Nurses

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Prescriptive Authority in Kentucky

- Optometrists
  - Eye drops
  - Oral medications
    - Only for conditions they are licensed to treat:
      - glaucoma, cataracts, astigmatism, farsightedness/nearsightedness, macular degeneration, diabetes-related retinopathy, color blindness, retinal disorders (blurred vision or vision loss)
    - Must be certified and complete additional training requirements
  - Controlled substances are limited to a 72-hour supply with no refills
    - No C-II controlled substances can be prescribed
      - Exception: 72-hour supply of hydrocodone is allowed

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Prescriptive Authority in Kentucky

- Podiatrists
  - Prescriptions only for the treatment of the ankle or foot
  - No restrictions on prescribing controlled substances
- Dentists
  - Prescriptions only for the treatment of the teeth or mouth
  - No restrictions on prescribing controlled substances

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Kentucky Prescription Requirements

- Prescription must be for legitimate medical purpose
- Can be written or electronic

- Refill requirements:
  - Refills must be authorized by the prescriber
  - C-II prescriptions cannot have refills
  - C-III-V prescriptions can be refilled up to 5 times within 6 months

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Kentucky Prescription Requirements

- Patient full name, address, date of birth
- Medication name, strength, dosage form, quantity, directions for use, number of refills
- Prescriber name, address, telephone number, signature
- Date prescription issued and signed

Additional requirements for controlled substances:

- Prescribers DEA number
- Quantity check-off box must be marked

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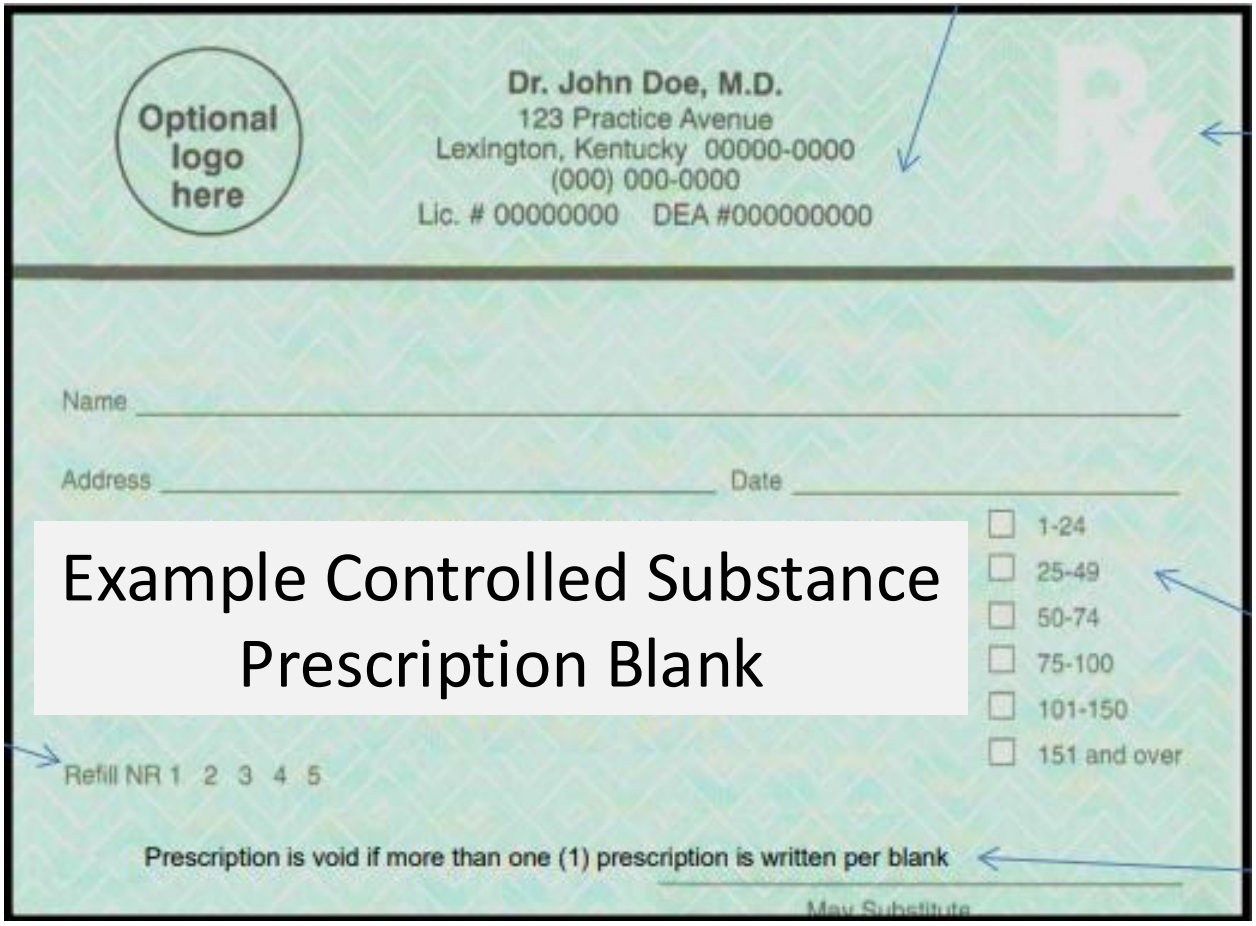
Kentucky Prescription Requirements



Example Controlled Substance Prescription Blank

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Drug Information Resources

- Micromedex® or Lexidrug™ – more credible source
  - Provides information on medication dosing, administration, side effects, IV drug compatibility, pill ID, contraindications, and interactions.
- UpToDate® – more credible source
  - In addition to all the above, also provides treatment guidelines and clinical algorithms.
- Epocrates® or Drugs.com®
  - Provides information on medication use, side effects, and interactions.
- Medscape©
  - Provides information on medical news, clinical trials, and guidelines.

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TREATMENT OVERVIEW

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Ear Hygiene for Otitis Externa

- During bathing or showering, use a cotton ball coated with petroleum jelly in the ear canal to protect from water.
- Refrain from water sports 7-10 days.
- Hearing aids, ear-buds, and other devices should not be worn until pain and discharge have subsided. Devices should be disinfected prior to use.

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Ear Drop Administration

- Wash hands prior to administering ear drops
- Lie down with the affected ear facing up toward the ceiling
  - For adults: gently pull the ear out & up
  - For children: gently pull the ear out & down
- Administer the appropriate number of ear drops
- Continue lying down for a few minutes after ear drop administration

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Ear Drop Administration

Solution vs. Suspension

- A solution is a homogenous mixture, the particles are fully dissolved and equally distributed in the solvent.
- A suspension is a heterogenous mixture, the particles are dispersed throughout the solvent but do not fully dissolve. Because of this, suspensions must be shaken well before use.

Patient Counseling Points

- Shake suspensions well.
- Dizziness may occur with administration of a cold suspension. Patients can roll it in their hands to warm it up prior to administration.
- Patients must avoid touching the ear dropper to the ear to avoid contamination.

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PHARMACOLOGY

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Pharmacologic Classes

- Antibiotics
- Corticosteroids

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Fluoroquinolones

- Ciprofloxacin
- Levofloxacin
- Moxifloxacin
- Ofloxacin

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Fluoroquinolones: MOA

Fluoroquinolones are *bactericidal* antibiotics that directly inhibit DNA synthesis.

- Bind DNA gyrase and DNA topoisomerase IV which generates DNA cleavage.
- This results in cessation of DNA replication, DNA damage, and cell death.

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Fluoroquinolones: Spectrum

- Ciprofloxacin
  - Aerobic, gram-negative bacilli
  - Pseudomonas coverage
  - **No** activity against gram-positive organisms
- Levofloxacin
  - Gram-positive organisms
  - Aerobic, gram-negative organisms
  - Pseudomonas coverage
- Moxifloxacin
  - Gram-positive coverage
  - Gram-negative coverage
  - Some activity against pseudomonas, but not preferred
  - Anaerobe coverage
  - Most active FQ against mycobacteria
- Ofloxacin
  - **No** pseudomonas coverage
  - Enteric gram-negative organisms
  - Respiratory gram-positive organisms

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Fluoroquinolone Clinical Pearls

- PO/IV FQs should be reserved for more severe infections
- PO/IV FQs should not be used in pregnancy or in children due to cartilage and bone toxicity
- PO/IV FQs can prolong the QTc interval which can cause fatal arrythmias.

Aminoglycosides

- Gentamicin
- Tobramycin
- Amikacin
- Neomycin
- Streptomycin

Aminoglycosides: MOA

- Aminoglycosides act by binding the aminoacyl site of the 16S ribosomal RNA, leading to misreading of the genetic code and inhibition of translocation.
- Activity is usually bactericidal

Aminoglycosides: Spectrum

- No anaerobic coverage
- Gram-negative organisms, including pseudomonas coverage
- Some Gram-positive organisms
  - Monotherapy not adequate for *S.aureus* coverage

Aminoglycoside Clinical Pearls

- Require drug concentration monitoring
- Typically used with another antimicrobial agent
- Not absorbed after oral administration
- Ototoxic
  - May result in vestibular or cochlear damage.
  - Damage may be irreversible

Beta Lactams

- Penicillins
- Cephalosporins
- Cephamycins
- Carbapenems
- Monobactams
- Beta-lactamase inhibitors

Beta Lactams: MOA

- Beta Lactams are a very broad category of antibiotics & spectrum of activity varies widely
- Their mechanism of action is to inhibit enzymes located in the bacterial cell membrane, which are involved in cell wall synthesis.
- Generally bactericidal

Corticosteroids

- Prednisone
- Dexamethasone
- Hydrocortisone

Corticosteroids

Mechanism of Action: Once entered in the cell, topical corticosteroids bind to the cytoplasmic glucocorticoid receptor and are transported to the nucleus.

This complex then binds to the glucocorticoid response element in the promoter region of a number of genes and modulate the transcription by inducing or inhibiting the transcription of specific mRNA and protein synthesis.

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Corticosteroids

- Suppress the synthesis and release of prostaglandins and other inflammatory mediators
- Release of *anti*-inflammatory proteins
- Reduce release of inflammatory cytokines
- Inhibit of T cell activation
- Change the function of endothelial cells, granulocytes, mast cells, and Langerhans cells

Corticosteroids

- Glucocorticoids (corticosteroids) are very efficacious in managing inflammatory and autoimmune disorders due to their inhibitory effects on a broad range of immune responses.
- Locally acting preparations (i.e. topical otic preparations) minimize infection risk as well as the systemic adverse effects of glucocorticoid therapy

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PHARMACOTHERAPY

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Medications known to cause ototoxicity

- Aminoglycosides
- Aspirin
- Vancomycin
- Loop Diuretics
- Cisplatin

Auralgan

- Combination ear drop consisting of antipyrine, benzocaine, and glycerin
- It was used to relieve ear *pain* in patients caused by infections of the ear
- It was removed from the market by the FDA

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Topical Otic Preparations

Single Therapy Products

- Acetic Acid
- Ofloxacin
- Ciprofloxacin

Combination Products

- Ciprofloxacin/Dexamethasone
- Ciprofloxacin/Hydrocortisone
- Tobramycin/Dexamethasone
- Neomycin/Polymyxin B/Hydrocortisone
- Neomycin/Colistin/Hydrocortisone/Thonzonium (Cortisporin TC)

Contraindications to Ear Drops

- Hypersensitivity to the medication or any of the components
- Perforated tympanic membrane
  - If unsure if tympanic membrane has ruptured, avoid aminoglycosides, products with alcohol, or acidifying agents

Topical (otic) preparations for external otitis*

Topical preparation	Brand name (United States)	Usual dosage (adult)*	Corticosteroid	pH	Preservative	Notes
Acidifying/antiseptic solution						
Acetic acid 2% otic solution	Generic (formerly Acetasol)	3 to 5 drops four to six times daily	None	3.5 to 5	No additional	• Avoid if TM is known or suspected to be nonintact (acidic preparation)¶ • Combination with corticosteroid (refer to next row) generally preferred by UpToDate • Contains boric acid
Acidifying/antiseptic and corticosteroid combination						
Acetic acid 2% and hydrocortisone 1% otic solution	Acetasol HC	4 to 6 drops three or four times daily	Hydrocortisone	2 to 4	No additional	• Avoid if TM is known or suspected to be nonintact (acidic preparation)¶ • Often used for treatment of mild disease • Contains 3% propylene glycol (drying agent) and benzethonium for promoting tissue penetration
Antibiotic and corticosteroid combinations						
Ciprofloxacin 0.3% and dexamethasone 0.1% otic suspension	Ciprodex	4 drops twice daily	Dexamethasone	Buffered	Benzalkonium chloride	• Non-ototoxic; may use if TM is known or suspected to be nonintact • Often used for treatment of mild to moderate disease • Contains boric acid
Ciprofloxacin 0.2% and hydrocortisone 1% otic suspension	Cipro HC	3 drops twice daily	Hydrocortisone	Buffered	Benzyl alcohol	• Avoid if TM is known or suspected to be nonintact (nonsterile preparation)¶ • Often used for treatment of mild to moderate disease
Neomycin, polymyxin B, and hydrocortisone otic suspension (each mL contains 3.5 mg neomycin, 10,000 units polymyxin B, and 10 mg hydrocortisone)	Generic (formerly Cortisporin otic)	4 drops three or four times daily	Hydrocortisone	Acidic	Potassium metabisulfite	• Avoid if TM is known or suspected to be nonintact (aminoglycoside-containing formulation)¶ • Suspension is less irritating than solution
Neomycin 0.33%, colistin 0.3%, and hydrocortisone 1% otic suspension	Cortisporin-TC	5 drops three or four times daily	Hydrocortisone	5	Thimerosal	• Avoid if TM is known or suspected to be nonintact (aminoglycoside-containing formulation)¶ • Contains thonzonium for promoting tissue penetration
Tobramycin 0.3% and dexamethasone 0.1% ophthalmic suspension△	TobraDex	4 drops three or four times daily	Dexamethasone	Buffered	Benzalkonium chloride	• Avoid if TM is known or suspected to be nonintact (aminoglycoside-containing formulation)¶
Antibiotic						
Solutions						
Ciprofloxacin 0.2% otic solution	Cetraxal	0.25 mL twice daily	None	Buffered	None; single-use container	• Non-ototoxic; may use if TM is known or suspected to be nonintact • Supplied as 0.5 mg per 0.25 mL sterile individual use containers; contains povidone
Ofloxacin 0.3% otic solution	Generic (formerly Floxin otic)	10 drops once daily	None	6.5	Benzalkonium chloride	• Non-ototoxic; may use if TM is known or suspected to be nonintact

Otitis Externa

- Otitis externa is the inflammation auditory canal
- It is imperative that the ear is properly cleaned before ear drops are used
- Otitis externa treatment is separated into three categories: mild, moderate, and severe

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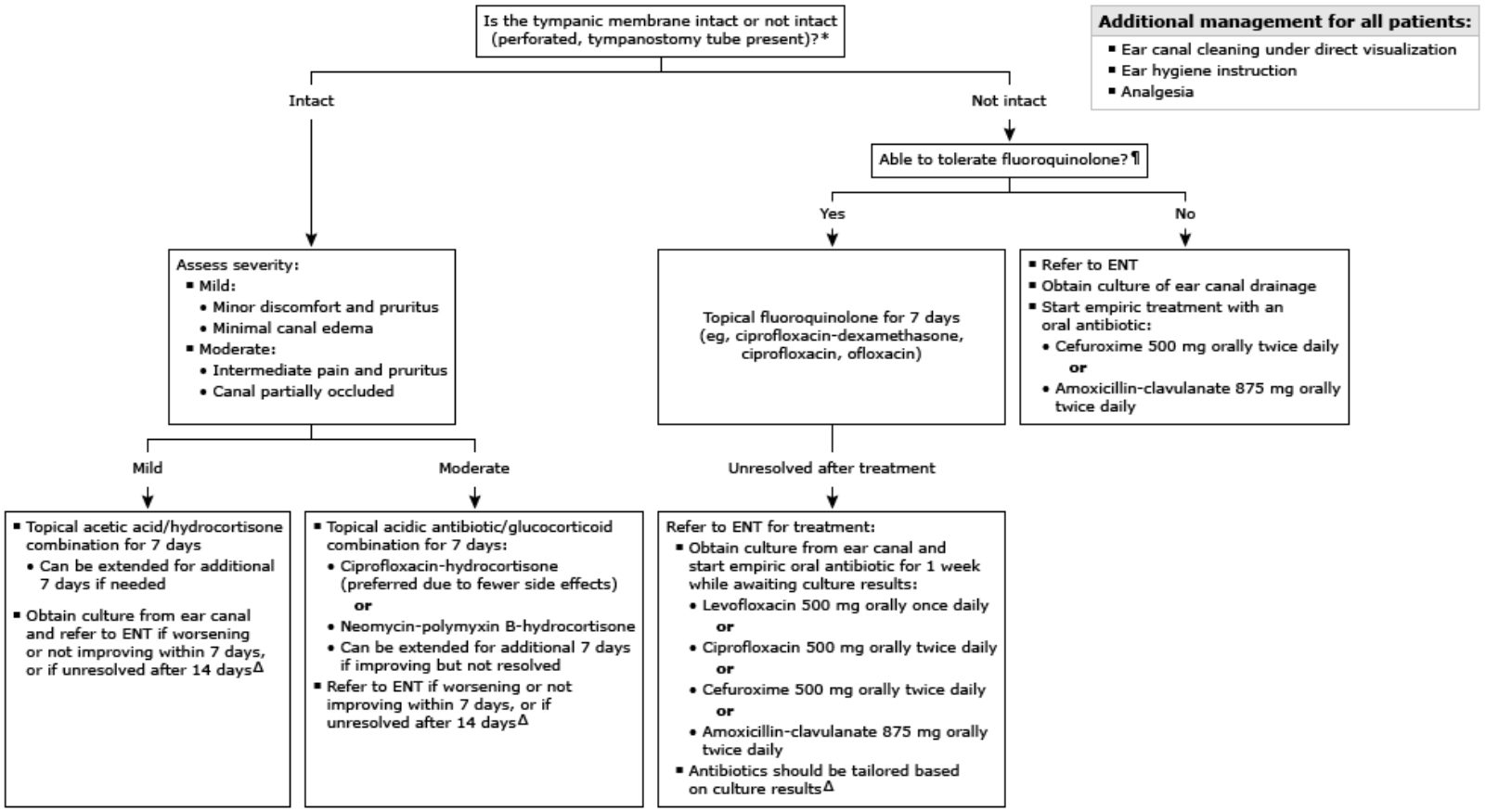
Otitis Externa-Treatment Algorithm



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Management of Otitis Externa

Common Pathogens

- Staphylococcus aureus
- Pseudomonas aeruginosa

Pharmacological Treatment

- Ciprofloxacin-hydrocortisone
- Neomycin-polymyxin B-hydrocortisone

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Antimicrobial Stewardship

- The primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing the exposure to unnecessary antibiotics
- Where healthcare professionals play a role?
  - Educating patients on the importance of using antibiotics appropriately

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PATIENT CASES

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Case #1

Patient SW is a 35 yo female with a PMH significant for anxiety.

Today's Vital Signs: Height: 66” Weight: 175lbs BP: 120/80 HR: 70 RR: 20 Temp: 98.1°F

Allergies: Levofloxacin (anaphylaxis)

Medications: sertraline 50mg daily & ethinyl estradiol/drospirenone 1 tab daily

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Case #1

She comes to clinic today with a primary complaint of pain and pruritus of her right ear.

You examine her ear and notice that the canal is partially occluded. The tympanic membrane is intact.

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Case #1

Diagnosis: Moderate External Otitis.

In addition to ear hygiene instruction, what treatment would you recommend?

a. ciprofloxacin/dexamethasone otic solution: 4 gtts AD BID x 7 days
b. neomycin-polymyxin B-hydrocortisone otic suspension: 4 gtts AD TID-QID x 7 days
c. amoxicillin/clavulanate tablets: 875mg PO BID x 7 days
d. ofloxacin otic solution: 10 drops AD QD x 7 days

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Case #1

Diagnosis: Moderate External Otitis.

In addition to ear hygiene instruction, what treatment would you recommend?

a. ciprofloxacin/dexamethasone otic solution: 4 gtts AD BID x 7 days
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d. ofloxacin otic solution: 10 drops AD QD x 7 days

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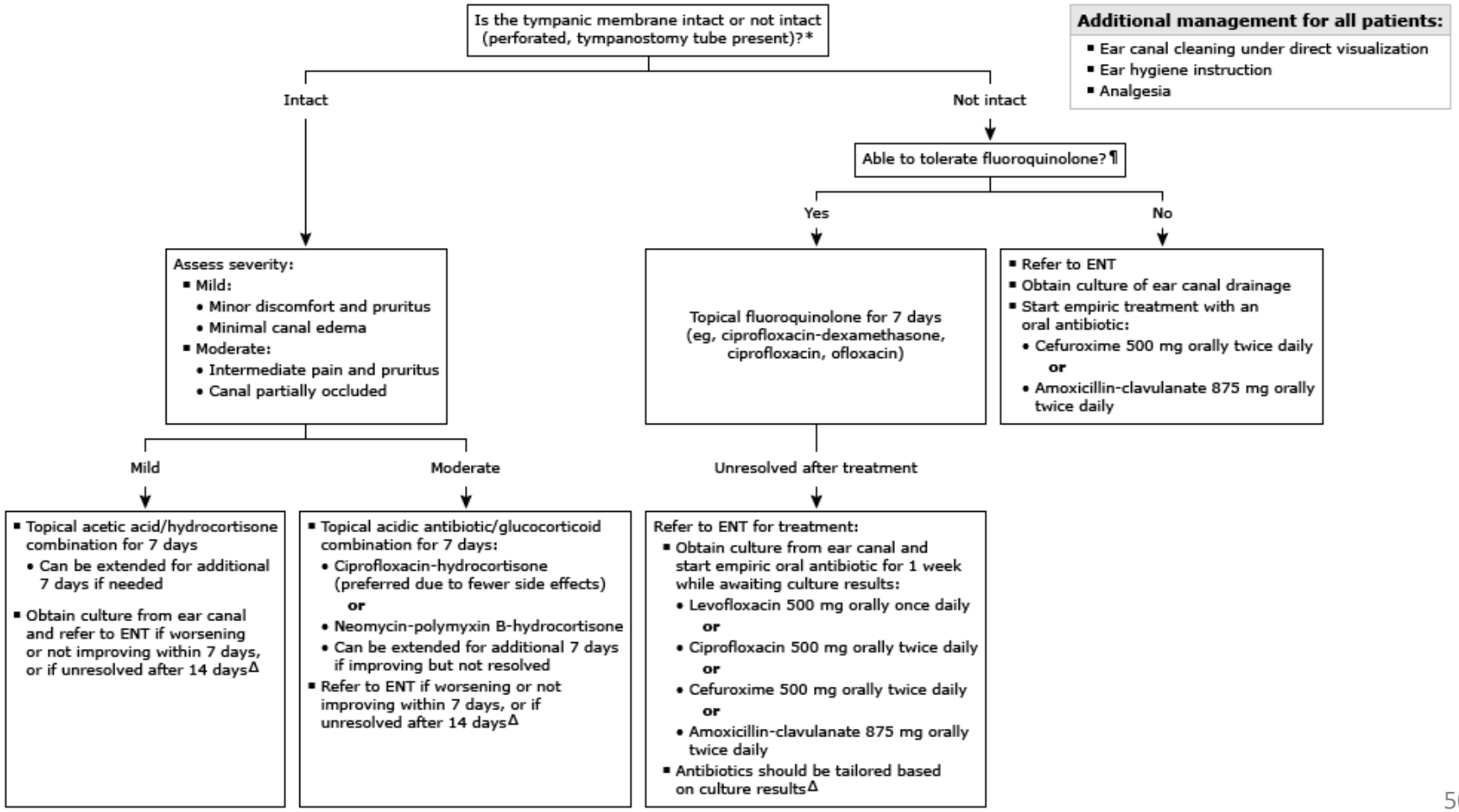
Algorithm for the management of mild or moderate external otitis in immunocompetent adults



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Case #2

CJ is a 55 yo Male with a PMH including DM, HTN, COPD, and HLD.

Today's Vital Signs: Height: 68” Weight: 240lbs BP: 138/80 HR: 62 RR: 20 Temp: 100.2°F

Allergies: NKDA

Medications: Mounjaro 5mg SC weekly, metformin 500mg PO BID, lisinopril 20mg QD, albuterol inhaler 2 puffs Q 4-6 H PRN, Breztri 2 puffs BID, atorvastatin 40mg QD, & prednisone 20mg PO QD

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Case #2

He comes to clinic today with a primary complaint of severe pain in both ears.

You examine his ear and notice the external auditory canal appears swollen and inflamed.

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Case #2

Diagnosis: Severe Otitis Externa (Immunocompromised Patient)

In addition to obtaining cultures of the ear canal, what treatment would you recommend?

a. Ciprofloxacin/dexamethasone otic solution: 4 gtts AU BID x 7 days
b. Levofloxacin 500mg PO daily x 7 days
c. Ciprofloxacin/hydrocortisone otic solution: 3 gtts AU BID x 7 days + levofloxacin 500mg PO QD x 7 days

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Case #2

Diagnosis: Severe Otitis Externa (Immunocompromised)

In addition to obtaining cultures of the ear canal, what treatment would you recommend?

a. Ciprofloxacin/dexamethasone otic solution: 4 gtts AU BID x 7 days
b. Levofloxacin 500mg PO daily x 7 days
c. **Ciprofloxacin/hydrocortisone otic solution: 3 gtts AU BID x 7 days + levofloxacin 500mg PO QD x 7 days**

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Case #2 Continued

CJ returns to your clinic after 4 days of therapy. Symptoms have not improved, and he complains his ear pain is worse than ever.

Today's Vital Signs: Height: 68” Weight: 240lbs BP: 146/86 HR: 102 RR: 18 Temp: 103°F

Allergies: NKDA

Medications: Mounjaro 5mg SC weekly, metformin 500mg PO BID, lisinopril 20mg QD, albuterol inhaler 2 puffs Q 4-6 H PRN, Breztri 2 puffs BID, atorvastatin 40mg QD, prednisone 20mg PO QD, levofloxacin 500mg QD & ciprofloxacin/hydrocortisone gtts

Upon examination, the external auditory canal is still swollen and inflamed but also has a purulent discharge.

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Case #2 Continued

What do you recommend for CJ?

a. Continue Ciprofloxacin/hydrocortisone otic solution: 3 gtts AU BID x 7 days + levofloxacin 500mg PO QD x 7 days
b. Extend the length of therapy, ciprofloxacin/hydrocortisone otic solution: 3 gtts AU BID x 14 days + levofloxacin 500mg PO QD x 14 days
c. STAT referral to ENT

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Case #2 Continued

What do you recommend for CJ?

a. Continue Ciprofloxacin/hydrocortisone otic solution: 3 gtts AU BID x 7 days + levofloxacin 500mg PO QD x 7 days
b. Extend the length of therapy, ciprofloxacin/hydrocortisone otic solution: 3 gtts AU BID x 14 days + levofloxacin 500mg PO QD x 14 days
c. **STAT referral to ENT**

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Case #3

Patient JD is a 24 yo male with no significant PMH

Today's Vital Signs: Height: 70” Weight: 205lbs BP: 120/80 HR: 65 RR: 18 Temp: 98.1°F

Allergies: erythromycin (hives) & sulfa (rash)

Medications: None

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Case #3 Continued

He comes to clinic today with a primary complaint of mild pain & pruritus in his right ear.

You examine his ear and notice the canal is partially occluded. The tympanic membrane is intact.

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Case #3

Diagnosis: Moderate Otitis Externa

What topical otic preparation would ***not*** be appropriate for JD?

a. ciprofloxacin-hydrocortisone otic susp 3 gtts AD BID x 7 days
b. neomycin-polymyxin B-hydrocortisone otic susp 4 drops AD TID-QID x 7 days
c. Either of the choices would be appropriate
d. Neither choice would be appropriate

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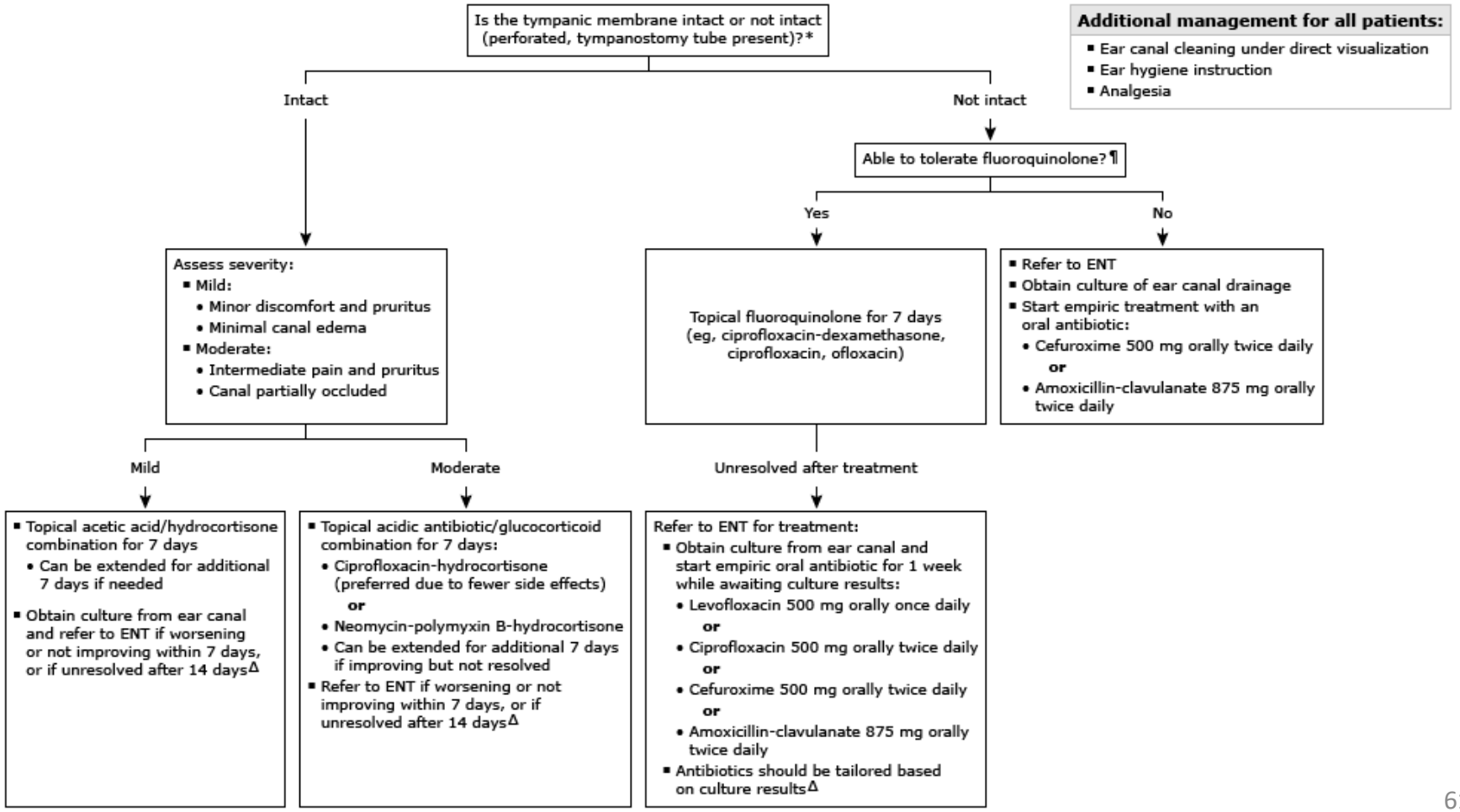
Algorithm for the management of mild or moderate external otitis in immunocompetent adults



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Case #3

Diagnosis: Moderate Otitis Externa

What topical otic preparation would ***not*** be appropriate for JD?

a. ciprofloxacin-hydrocortisone otic susp 3 gtts AD BID x 7 days
b. neomycin-polymyxin B-hydrocortisone otic susp 4 drops AD TID-QID x 7 days
c. Either of the choices would be appropriate
d. Neither choice would be appropriate

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QUESTIONS?