



*February 25, 2020*

## **Agenda**

- Setting a Framework:  
Prospective Audit & Feedback, Part 2
- Case Discussion



**UW TASP**  
tele-antimicrobial stewardship program

# Setting a Framework: Prospective Audit & Feedback, Part 2

**Zahra Kassamali Escobar, PharmD**

*This presentation is intended for educational use only, and does not in any way constitute medical consultation or advice related to any specific patient.*



# How to take a systematic approach when evaluating a patient's antibiotic therapy?

**I struggle with how to approach evaluating a patient's antibiotic regimen and whether it's the right one.**

**Not the obvious ones like CAP and UTI but different ones like a possible dental abscess or prostatitis.**



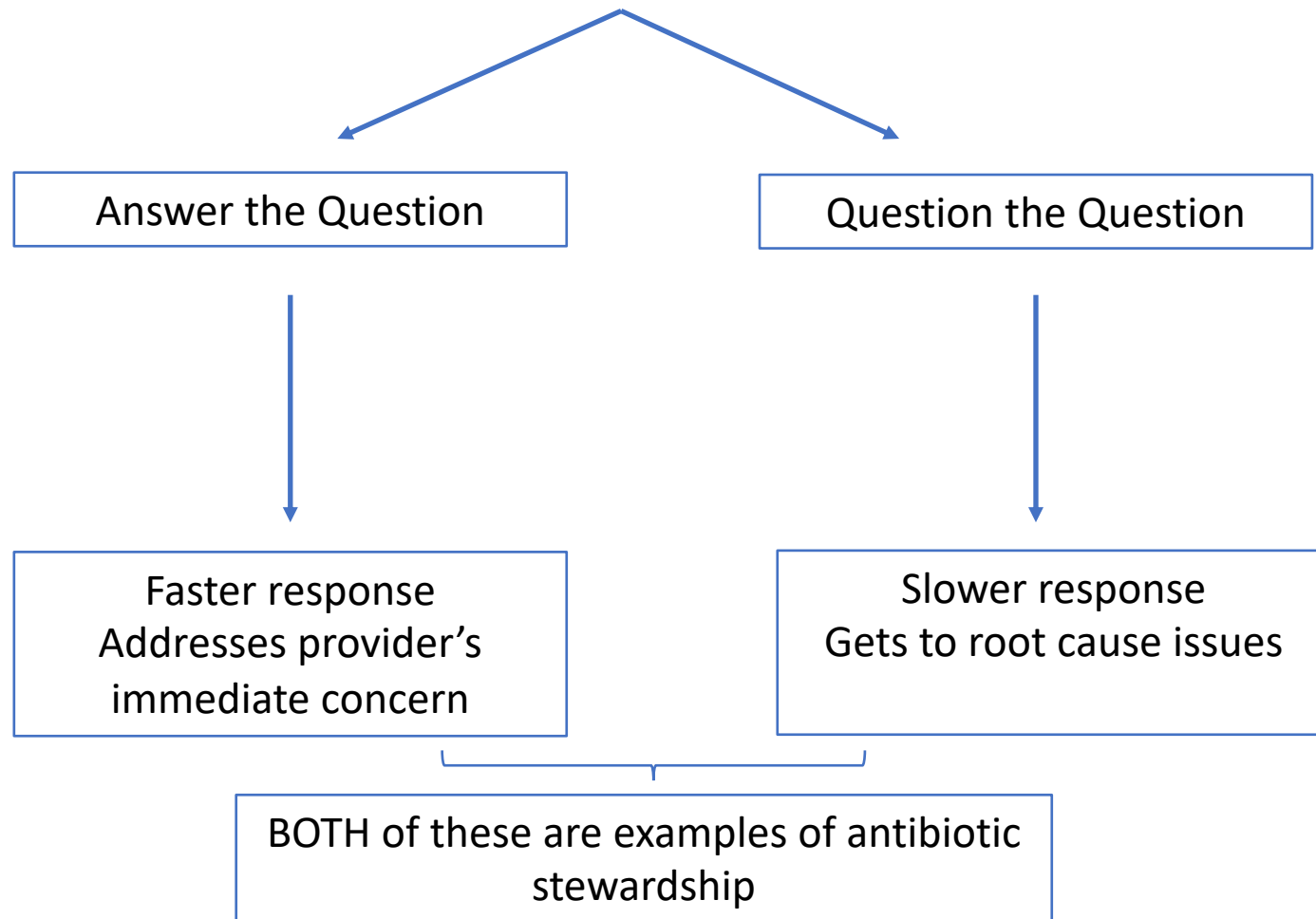
# What do you do when you asked a clinical question that does not have a clear guideline-supported answer?

- a. Panic
- b. Phone a friend
- c. Search TASP website/Submit case to TASP
- d. Search google
- e. Search UpToDate



# Is nitrofurantoin ok in a 72-year old male with impaired renal function?

Let me look into that!



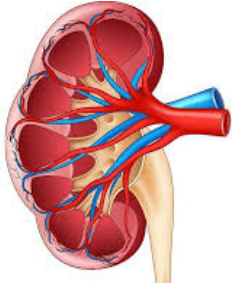
# Answering the Question:

## Is nitrofurantoin ok in a 72-year old male with impaired renal function?

- a. Yes
- b. No
- c. Not sure



# What is the safety of Nitrofurantoin in...



**Renal Impairment**



**Geriatric Patients**



**Men**



# Step 1:

## Reliable Tertiary Resources

**My preferred tertiary antimicrobial resource is:**

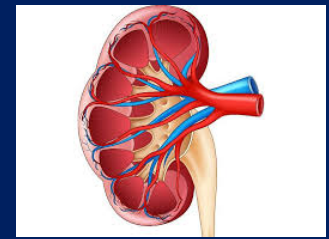
- A. Medication Package insert(s)
- B. Micromedex
- C. Physician's Desk Reference (PDR)
- D. Sanford Guide
- E. UpToDate/Lexi-Comp
- F. Other





# Step 1:

## Reliable Tertiary Resources



### IBM Micromedex®

Home	Drug Interactions	IV Compatibility
------	-------------------	------------------

#### NITROFURANTOIN

Drug Classes: [Antibiotic](#) | [Anti-Infective Agent](#) | [All](#)

Routes: [Oral](#)

#### Dosage in Renal Failure

1.) **CrCl < 60 mL/min:** Use is contraindicated because of increased toxicity.

**Beers Criteria:** Use caution or avoid use as potentially inappropriate in older adults.

### UpToDate®

nitrofurantoin

[Back to Search](#)

Nitrofurantoin: Drug information

#### Dosing: Renal Impairment: Adult

**CrCl < 60 mL/min:** Limited data suggest nitrofurantoin is safe and effective for short-term treatment of uncomplicated cystitis in patients with eGFR or CrCl 30-60 mL/min (Cunha 2017; Oplinger 2013; Santos 2016; Singh 2015).

The Beers Criteria recommends avoiding use in patients  $\geq 65$  years with CrCl < 30 mL/min

*Manufacturer's Labeling:* Dosing is based on product labeling and may not reflect current clinical practice: Use is contraindicated



# Step 2: Snowballing



IBM Micromedex®

Home	Drug Interactions	IV Compatibility
------	-------------------	------------------

## NITROFURANTOIN

Drug Classes: [Antibiotic](#) | [Anti-Infective Agent](#) | [All](#)

Routes: [Oral](#)

UpToDate®

[Back to Search](#)

Nitrofurantoin: Drug information

## Tertiary Resources



## Beers Criteria Updated in 2019



## Primary Literature

(Cunha 2017; Oplinger 2013; Santos 2016; Singh 2015).





# Step 2:

## Snowballing, Beers Criteria

Table 2. 2019 American Geriatrics Society Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults<sup>a</sup>

Organ System, Therapeutic Category, Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
<b>Anticholinergics<sup>b</sup></b>				
First-generation antihistamines Brompheniramine Carbinoxamine Chlorpheniramine	Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity	Avoid	Moderate	Strong

Therapeutic Class	Rationale	Recommendation	Quality of Evidence	Strength of Rec
Anti-infective Nitrofurantoin	Potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy, especially with long-term use	Avoid in CrCl < 30 mL/min or for long-term suppression	Low	Strong

Dicyclomine Homatropine  
(excludes ophthalmic)  
Hyoscyamine  
Methscopolamine  
Propantheline  
Scopolamine

<b>Antithrombotics</b>				
Dipyridamole, oral short acting (does not apply to the extended-release combination with aspirin)	May cause orthostatic hypotension; more effective alternatives available; IV form acceptable for use in cardiac stress testing	Avoid	Moderate	Strong
<b>Anti-infective</b>				
Nitrofurantoin	Potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy, especially with long-term use; safer alternatives available	Avoid in individuals with creatinine clearance <30 mL/min or for long-term suppression	Low	Strong

<b>Cardiovascular</b>				
-----------------------	--	--	--	--



# Step 2:

## Snowballing, Primary Literature



Google

Oplinger 2013



Effectiveness and safety of nitrofurantoin in outpatient male veterans

[Ther Adv Urol. 2015 Aug; 7\(4\): 186-193.](#)



Alt

PDF



Therapeutic Advances in  
Urology

SAGE

### Effectiveness and safety of nitrofurantoin in outpatient male veterans

Michelle L. Ingalsbe, Amy L. Wojciechowski, [...], and Kari A. Mergenhagen

[Additional article information](#)

#### Abstract

#### Objectives:

The aim of the study was to assess both the safety and the effectiveness of nitrofurantoin in male veterans treated for urinary tract infections (UTIs) with varying degrees of renal impairment in the outpatient setting. Nitrofurantoin is an important oral option for treating UTIs given increasing resistance to commonly used agents. Nitrofurantoin is currently contraindicated in patients with a creatinine clearance (CrCl) of < 60 ml/min, but the reason for this threshold has not been well documented.

#### Methods:

Data were collected through a retrospective chart review from January 2004 to July 2013 of men who had received nitrofurantoin. Bivariate analyses followed by multivariate analyses were performed between patients experiencing clinical cure and those who did not, to determine factors significantly impacting effectiveness.

#### Results:

The Gram stain of the organism causing the UTI and CrCl were significant factors impacting effectiveness. For every 1 ml/min increase in CrCl, the odds of clinical cure increased by 1.3%. Patients with Gram-negative UTIs predictably had 80% cure rates with CrCl around 60 ml/min. Patients with Gram-positive UTIs required higher CrCl, nearing 100 ml/min, to establish an 80% cure rate. Adverse effects did not vary with CrCl.

#### Conclusions:

The odds of clinical cure varied with CrCl and with the type of organism causing the UTI, while adverse events did not differ based on renal function. A

minimum CrCl of 60 ml/min is suggested for men to achieve an 80% cure rate for UTIs with the most common urinary pathogens.

**Keywords:** effectiveness, nitrofurantoin, safety, urinary tract infection

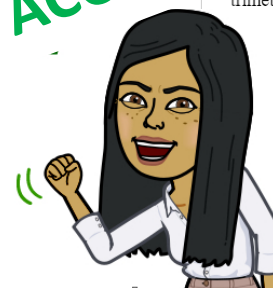
#### Introduction

Urinary tract infections (UTIs) are amongst the most common types of infections in older men [Gupta et al. 2001]. They appear to be more common in healthy women than in men and in older adults age 65 and older [Gupta et al. 2001]. There is a difference in rates between men and women [Gupta and Prince, 2008]. These abnormalities can be associated with factors including the use of antibiotics for the bladder, and prostate [Gupta et al. 2001]. This study focuses on the effectiveness and safety of nitrofurantoin treatment of complicated UTIs in older men. Treatment of uncomplicated UTIs and pyelonephritis in men is a pressing topic, however guidelines, such as those published by the Infectious Disease Society of America, are exclusive to women.

Nitrofurantoin is recommended as first-line treatment for uncomplicated UTIs in women, however efficacy data in men are lacking [Gupta et al. 2011]. Antibiotic resistance is forcing clinicians to use nitrofurantoin in the male population, despite lack of randomized controlled trials and guidelines to support its use in this population.

Antibiotic resistance among Gram-negative urinary pathogens is increasing. Agents commonly used to treat UTIs in the USA include quinolones, trimethoprim/sulfamethoxazole, and nitrofurantoin. The most prevalent pathogen implicated in UTIs is *Escherichia coli* [Hooton et al. 2010; Gupta et al. 2011]. A recent study measured the change in antibiotic resistance to outpatient urinary isolates in the USA between 2000 and 2010. Steady increases in resistance were seen for most of the agents tested. Trimethoprim/sulfamethoxazole resistance increased from 17.9% to 24.2%, and nitrofurantoin resistance increased from 3.0% to 17.1%. Resistance to nitrofurantoin rose from 0.8% in 2000 to 1.6% in 2010, but remained low relative to other agents [Sanchez et al. 2012]. Given the relative stability of *E. coli* susceptibilities to nitrofurantoin, and low rates of resistance, nitrofurantoin is becoming

OPEN ACCESS!



# Step 2:

## Snowballing, Primary Literature

### Effectiveness and safety of nitrofurantoin in outpatient male veterans

Michelle L. Ingalsbe, Amy L. Wojciechowski, Kelly A. Smith and Kari A. Mergenhagen

#### My Goals: SAFETY FIRST

Quick skim:

Study Design – Retrospective study of **men who received NTF**

Time Period – Jan 2004 – Jul 2013, **10 years**

Sample Size – **N = 801**

Does the Population Include my Patient (Table 1)?

Age  $73 \pm 11$ , ClCr  $66 \pm 27$

ADR Paragraph– GI distress (N = 7), Peripheral neuropathy (N = 4), Acute pulmonary reaction (N = 3), Hepatotoxicity (N = 4). **Renal function did not affect the incidence of ADEs**

Correspondence to:  
**Kari A. Mergenhagen,**  
PharmD, BCPS AQ-ID  
Infectious Diseases  
Clinical Pharmacist,  
Department of Pharmacy –  
119, VA Western New York  
Healthcare System, 3495  
Bailey Avenue, Buffalo,  
NY 14215, USA

[kari.mergenhagen@va.gov](mailto:kari.mergenhagen@va.gov)

**Michelle L. Ingalsbe,**  
PharmD  
**Kelly A. Smith, PharmD,**  
BCPS, CACP  
Department of Pharmacy,  
VA Western New York  
Healthcare System,  
Buffalo, NY, USA

**Amy L. Wojciechowski,**  
PharmD, BCPS  
Department of Pharmacy  
Practice, D'Youville  
College School of  
Pharmacy, Buffalo, NY,  
USA



# Step 2:

## Snowballing, Primary Literature



### Effectiveness and safety of nitrofurantoin in outpatient male veterans

Michelle L. Ingalsbe, Amy L. Wojciechowski, Kelly A. Smith and Kari A. Mergenhagen

My Goals: SAFETY FIRST

In a 10-year review including 801 men treated with NTF for cystitis/uncomplicated UTI at the VA, 77% experienced clinical cure. Adverse events were rare and not necessarily correlated with renal function.

Correspondence to:  
**Kari A. Mergenhagen,**  
PharmD, BCPS AQ-ID  
Infectious Diseases  
Clinical Pharmacist,  
Department of Pharmacy –  
119, VA Western New York  
Healthcare System, 3495  
Bailey Avenue, Buffalo,  
NY 14215, USA

[kari.mergenhagen@va.gov](mailto:kari.mergenhagen@va.gov)

Michelle L. Ingalsbe,  
PharmD

Smith, PharmD,  
P  
t of Pharmacy,  
New York  
System,  
USA

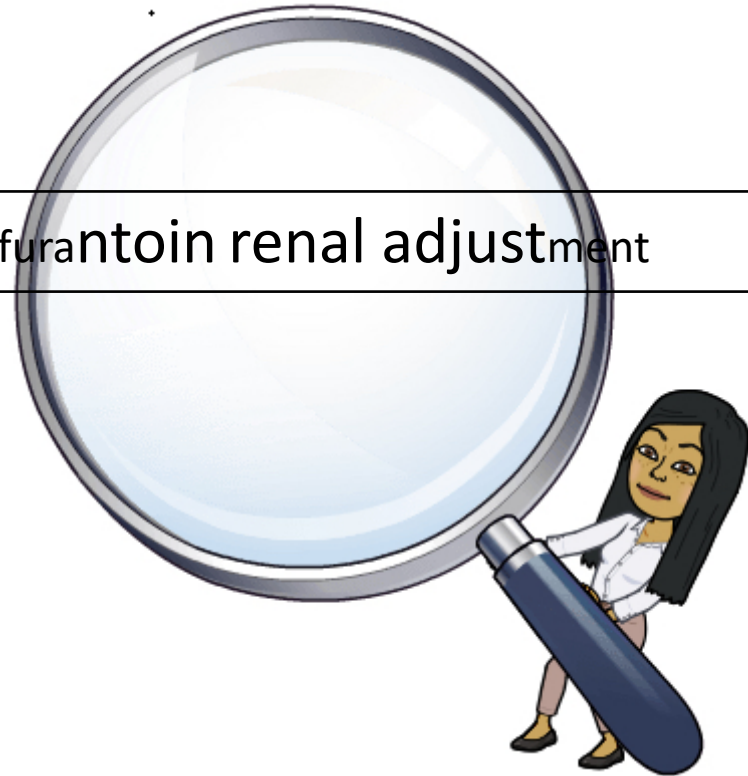
Wojciechowski,  
BCPS  
t of Pharmacy  
Youville  
School of  
Buffalo, NY,



# Step 3: Repeat steps 1&2

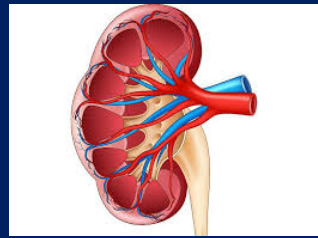


Nitrofurantoin renal adjustment





# Step 3: Repeat steps 1&2



Google

Nitrofurantoin renal adjustment



Pharmacy  
Times

Clinical Focus

Clinical Role

Videos

Publications

## Nitrofurantoin and CrCl: How Low Can You Go?

2016-02-03 02:38:11

Published relatively recently

### References

1. The American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatric Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. 2015 Nov;63(11):2227-46. doi: 10.1111/jgs.13702. Epub 2015 Oct 27.
2. Gupta K, Hooten TM, et al. Nitrofurantoin for urinary tract infections: a systematic review. *Antimicrob Res*. 2011 Mar 1;52:103-112. doi: 10.1016/j.amr.2010.12.001. Epub 2011 Mar 1.
3. Oplinger M, Andrews CO. Nitrofurantoin contraindication in patients with a creatinine clearance below 60 mL/min: looking for evidence. *Ann Pharmacother*. 2013;47:106-111.
4. Bains A, Buna D, Hoag NA. A retrospective review assessing the efficacy and safety of nitrofurantoin in renal impairment. *Can Pharm J*. 2009;142:248-252.
5. Geerts AFJ, Eppenga WL, Heerdink R, et al. Ineffectiveness and adverse events of nitrofurantoin in women with urinary tract infection and renal impairment in primary care. *Eur J Clin Pharmacol*. 2013;69:1701-1707.
6. Singh N, Gandhi S, McArthur E, et al. Kidney function and the use of nitrofurantoin to treat urinary tract infections in older women. *CMAJ*. 2015 Jun 16;187(9):648-56. doi: 10.1503/cmaj.150067. Epub 2015 Apr 27.

### References Listed

acute uncomplicated  
and the European

Author looks legitimate



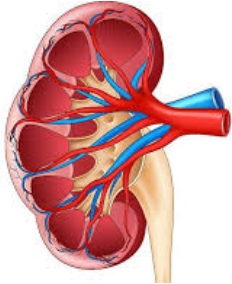
### Monica V. Golik Mahoney, PharmD, BCPS-AQ ID

Monica V. Mahoney, PharmD, BCPS-AQ ID, is a graduate of the Massachusetts College of Pharmacy and Health Sciences (Boston) and has completed specialized residency training as an infectious diseases pharmacist. She currently practices as a clinical coordinator of infectious diseases at Beth Israel Deaconess Medical Center in Boston, MA. She precepts pharmacy students and PGY1 and PGY2 residents on their ID rotations.





# What is the safety of Nitrofurantoin in...



## Renal Impairment



Ok as long as  $\text{ClCr} > 30 \text{ mL/min}$   
[UpToDate + Primary Lit + Beers Criteria]



## Geriatric Patients



Ok as long as short course +  $\text{ClCr} > 30 \text{ mL/min}$   
[Beers Criteria/Primary Literature]



## Men



Ok as long as uncomplicated UTI  
[Primary Literature]



# Question the Question:

## Is nitrofurantoin ok in a 72-year old male with impaired renal function?

Why is this patient getting nitrofurantoin in the first place?

Step 1: Open the chart: review objective data and notes

Symptomatic

Asymptomatic



### Renal Impairment

Ok as long as  $CrCl > 30$  mL/min  
[UpToDate + Primary Lit + Beers Criteria]



### Geriatric Patients

Ok as long as short course +  $CrCl > 30$  mL/min  
[Beers Criteria/Primary Literature]



### Men

Ok as long as uncomplicated UTI  
[Primary Literature]



UW Medicine

Log out

Home Resources

Resources / Documents

Documents

Types

UTI

Title

Title	Date	Type
Management of Urinary Tract Infections	Jul 9, 2019	pdf
Diagnosis of urinary tract infections: need for a reflective rather than reflexive approach	Jul 9, 2019	pdf
Mind the Gap on UTI's and Delirium	Jun 25, 2019	pdf
Point-Counterpoint: Reflex Cultures Reduce Laboratory Workload and Improve Antimicrobial Stewardship in Patients Suspected of Having Urinary Tract Infections	Apr 2, 2019	pdf
A Statewide Antibiotic Stewardship Collaborative to Improve the Diagnosis and Treatment of Urinary Tract and Skin and Soft Tissue Infections	Dec 20, 2018	pdf
Urinary Tract Infections in Older Women A Clinical Review	Sep 13, 2018	pdf
Coveler Medical Center - UTI management for LTC/Swing Bed	Sep 13, 2018	pdf

# Growing your Database

## Professional Organizations:

- SHEA
- SIDP
- ACCP ID PRN
- Vizient
- Emerging infections diseases

## Subscribe to Journal Alerts

- Clinical Infectious Diseases
- NEJM
- JAMA

## PubMed / Open Access Articles

- If you precept students, request library access from their schools
- Open Forum Infectious Diseases
- Contagion Live

## Social Media

- Twitter #IDTwitter
- AntibioticStewardship (blog)
- @SIDP
- @BradSpellberg
- @uwtaskp

**UWTASP**



# Become Your Institution's Database

*In a 10-year review including 801 men treated with NTF for cystitis/uncomplicated UTI at the VA, 77% experienced clinical cure. Adverse events were rare and not necessarily correlated with renal function.*



And maintain  
**Build  $\Delta$  Credibility**

