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### DRIVING EXCELLENCE IN OUTPATIENT UTI CARE

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GREEN FLAG CHOICES: 1 <sup>ST</sup> LINE TREATMENT uUTI		
PREFERRED AGENTS (IDSA 2010; 2025)	TYPICAL DURATION	KEY STEWARDSHIP CAVEATS
Nitrofurantoin 100 mg 2xDay	5 days \$8 to \$20	Avoid if early pyelonephritis suspected (poor tissue levels); minimal collateral damage; <b>NICE Guidelines (2025):</b> bid X 3 days
TMP-SMX 160/800 mg (1 DS) 2xDay	3 days \$4 to \$12	Avoid empirically if local resistance >20% or recent use; consider for men if prostatitis; <b>NICE Guidelines (2025):</b> TMP 200mg bid X 3 days If resistance low
Fosfomycin Trometamol 3 g	Single dose \$100 to \$120	Convenient; may be less effective than some short-course regimens; avoid if early pyelonephritis suspected
Pivmecillinam 400 mg Initial dose, then 200 mg	3xday for 3 days	<b>1<sup>st</sup> line in EAU, 2025; UK (NICE Guide)</b> USA: 2 <sup>nd</sup> line; FDA approved in 2024 ONLY for women 18+ (only comes in 185 mg)

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**1<sup>st</sup> Line Agents for MEN with Localized Cystitis (uUTI)**

**Key Notes**

- Men may be treated as localized uUTI when infection is bladder-confined and prostatic involvement is excluded
- Always consider prostatitis or STI in men with urinary symptoms
- Nitrofurantoin is appropriate only for lower-tract infection (avoid if prostatitis suspected)
- Fluroquinolones avoid if resistance >10%; Last resort.
- Reassess if no improvement at 48–72 hours

Guideline	First-Line Agents	Typical Duration
US: AUA / CUA / SUFU (2025)	Nitrofurantoin; TMP-SMX; Fosfomycin; Pivmecillinam	7 days
US: IDSA (2010; reinforced 2025)	TMP-SMX; Fluoroquinolones*	7 days
EAU (2026)	Nitrofurantoin; Fosfomycin; Pivmecillinam; TMP-SMX	7 days
NICE (UK, 2025/2026)	Nitrofurantoin; Trimethoprim	7 days

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**ALTERED TRACK CONDITIONS: Prophylaxis Agents for rUTI**

Adapted from Nelles & Ermer-Seitun, 2022.

Antibiotic Agent	Daily Prevention	After Sexual Activity	Self-Start*
Nitrofurantoin	50–100 mg daily	50–100 mg once	100 mg BID × 5 d
TMP-SMX	40/200 or 80/400 mg daily	40/200 or 80/400 mg once	160/800 mg BID × 3 d
Trimethoprim	100 mg daily	100 mg once	100 mg BID × 3 d
Cephalexin	125–250 mg daily	125–250 mg once	250 mg q6h × 5–7 d
Cefaclor	250 mg daily	250 mg once	750 mg BID × 5–7 d
Fosfomycin	3 g q10 days	–	3 g once

**NOTE:** Reserve prophylaxis for patients who fail behavioral and non-antibiotic strategies; use shared decision-making and stewardship principles. \*Self-start therapy: F/U in 48 hours if no improvement.



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**PIT STOP: PHARMACOLOGY TERMS**

**Pharmacodynamics**


- The study of what a **drug** does to the body.


**Pharmacokinetics**

- The study of what the **body** does to a drug.

**Clinical Pharmacokinetics Goal**

- Enhance drug efficacy and decrease potential for toxicity.





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## CYTOCHROME P450 Drug Metabolism and Interaction




**CYP 450**

- Superfamily of enzymes present within the body that metabolizes drugs
- Most drugs use these enzymes to break down drugs
- Significant variability & efficiency in people

**Pharmacogenomics**

- Study of how the genetic makeup of an individual affects their response to drugs.



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## ANTIMICROBIAL AGENT: NITROFURANTOIN



**Goal:** antibacterial

**Dosage**


- 100 mg bid x 5-7 days

**Pharmacokinetics**

- CYP Unknown
- Metabolized by liver
- Excretion- urine/bile
- ½ life 45-60 Minutes
- Pregnancy Cat. B but
  - Avoid 1<sup>st</sup> & 3<sup>rd</sup> Tri

**Pharmacodynamics**

- Active: Broad spectrum with Gram + & Gram -
- inhibits DNA, RNA, protein, and cell wall synthesis
- **Side Effects:** N/V, abd. Pain, anorexia, diarrhea, dizziness, HA, rash, itching, neuropathy\*, anemia\*



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## ANTIMICROBIAL AGENT: NITROFURANTOIN




**Contraindications**

- **CrCl <30:** contraindicated
- Systemic or cUTI
- possible accumulation of toxic metabolite (Pulmonary & liver)
- Caution if pt. neuropathy or anemia, older adults
- G6PD deficiency- hemolysis

**Pearls**

- BUN/Cr at baseline, then if elderly or long-term tx cont. periodically; LFTs
- May reduce OCPs efficacy
- Take with food if less UTI tx needed
- **Probiotic** to prevent antibiotic assoc. diarrhea
- **Beers** List: avoid long-term use for suppression



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**ANTIMICROBIAL AGENT: TMP-SMX**  
 TRIMETHOPRIM – SULFAMETHOXAZOLE

**Goal-** antibacterial

**Dosage-UTI**


- 160/800 mg bid X 3 days
- Peds > 2mo. 8-10 mg/kg/day


**Pharmacokinetics**

- Pregnancy Avoid 1<sup>st</sup> & late 3<sup>rd</sup> trimester
- CYP 2C9 inhibitor (Warfarin, Sulfonylureas, Phenytoin, NSAIDS)
- urine (20-40% unchanged)
- Half-life: 6-12h, 20-50h (R.F.)
- Metabolized by liver

**Pharmacodynamics**

- **Active:** great Gram - but not pseudomonas; & Gram+, MRSA
- **Side Effects:** N/V, anorexia, rash, urticarial, photosensitivity, diarrhea, dizziness, anemia,
- ↑ K+, ↓ Na,
- Thrombocytopenia, Methemoglobinemia
- Stevens -Johnson\* Syndrome, TEN\*





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**ANTIMICROBIAL AGENT: TMP-SMX**  
 TRIMETHOPRIM – SULFAMETHOXAZOLE


**Contraindications**

- **Caution in pregnancy**
- **Avoid in stone-formers**
- CrCl 15-30: decr. dose 50%; CrCl <15: avoid use
- Caution mild/mod. Liver disease; avoid Class C liver disease

**Pearls**

- **R/O Pregnancy if doubt**
- **Stay hydrated** (↓ crystals)
- **Avoid Sun during tx**
- BUN/Cr at baseline, then periodically
- CBC frequently; K+ if renal impairment, concomitant ACE inhibitor, or potassium metab. disorder





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**ANTIMICROBIAL AGENT:**  
 FOSFOMYCIN TROMETAMOL

**Goal-** antibacterial

**Dosage-UTI**


- 3-gram single oral dose
- Peds > 2mo. 8-10 mg/kg/day


**Pharmacokinetics**

- Pregnancy Cat. **B** Hx
- Not metabolized by CYP450
  - Minimal drug to drug interactions
- Excreted in urine (100% unchanged)
- Half-life: 4-8 hrs

**Pharmacodynamics**

- **Active:** E.coli (ESBL strains), Enterococcus faecalis, some Gram - & + uropathogens
- **Side Effects:** Nausea, diarrhea, HA, Dyspepsia, vaginal irritation, Rare hypersensitivity reactions





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**ANTIMICROBIAL AGENT:  
FOSFOMYCIN TROMETAMOL**



<p><b>Contraindications</b></p> <ul style="list-style-type: none"> <li>- Hypersensitivity to</li> <li>- Avoid if CrCl &lt;10-15 mL/min (excreted renal)</li> </ul> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>- PEDs: Not established for &lt;12 yrs.</li> <li>- QT- prolonging drugs (amiodarone, macrolides, antipsychotics)</li> </ul>	<p><b>Pearls</b></p> <ul style="list-style-type: none"> <li>- Great for compliance</li> <li>- Avoid if suspect pyelonephritis or systemic symptoms                             <ul style="list-style-type: none"> <li>• Poor tissue penetration</li> </ul> </li> <li>- Avoid in cUTI</li> <li>- Not ideal for UTI prophylaxis</li> <li>- Hydrate to support urinary clearance</li> <li>- Well tolerated &amp; minimal drug to drug interactions</li> </ul>
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**ANTIMICROBIAL AGENT:  
FLUOROQUINOLONE**



<p><b>Goal</b>-antibacterial, broad spectrum</p> <p><b>Dosage-UTI</b></p> <ul style="list-style-type: none"> <li>- Cipro 250 mg bid X 3 days</li> <li>- Levofloxacin 250mg daily x 3 days</li> </ul> <p><b>Pharmacokinetics</b></p> <ul style="list-style-type: none"> <li>- Pregnancy Cat. <b>C</b> Hx</li> <li>- Minimal metabolized by CYP450</li> <li>- Notable inhibitor of CYP1A2 (Caffeine, Theophyllin, Tizanidine, Clozapine)</li> <li>- Excreted in urine unchanged (50%)</li> <li>- Half-life: 4- hrs</li> </ul>	<p><b>Pharmacodynamics</b></p> <ul style="list-style-type: none"> <li>- <b>Active: strong Gram – activity</b> (E. coli, Klebsiella, Proteus, Enterobacter, Pseudomonas, serratia, Citrobacter) some gram+ (levofloxacin, moxifloxacin) &amp; atypicals</li> <li>- <b>Side Effects, Black Box warnings:</b> Tendon rupture, peripheral neuropathy, ↑C. Diff, N/V, CNS effects, AA risk, QT prolongation, Dysglycemia, Rash</li> </ul>
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**ANTIMICROBIAL AGENT:  
FLUOROQUINOLONE**



<p><b>Contraindication</b></p> <ul style="list-style-type: none"> <li>- Hx associated tendon disorders</li> <li>- Myasthenia gravis</li> <li>- Using tizanidine (dangerous low B/P &amp; sedation)</li> <li>- CrCl adjustments – lower dosage with 30-50 mL/min; Extend interval if &lt;30 mL</li> </ul> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>- PEDs: ↑ cartilage toxicity risk</li> <li>- Geriatrics: ↑risk of tendon rupture</li> <li>- QT- prolonging drugs (amiodarone, macrolides, antipsychotics)</li> </ul>	<p><b>Pearls</b></p> <ul style="list-style-type: none"> <li>- Last-line for uUTI</li> <li>- Check local resistance                             <ul style="list-style-type: none"> <li>• Consider if &lt;10%</li> </ul> </li> <li>- Reserve for cUTIs and special populations</li> <li>- Black Box warning of collateral damage, educate patients</li> <li>- Avoid antacids (Mg/Al)</li> <li>- Hydrate to support urinary clearance</li> <li>- Probiotic</li> </ul>
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## ANTIMICROBIAL AGENT: PIVMECILLINAM

**Goal**-antibacterial, treatment of localized cystitis (uUTI)

**Dosage-UTI**

- 400mg initial dose, then 200 mg tid X 3-7 days

**Pharmacokinetics**

- Not metabolized by CYP enzymes
- Minimal drug-drug interactions
- Rapid oral absorption
- Renal excretion
- Minimal systemic distribution


**Pharmacodynamics**

**Active:** Narrow Gram-negative activity (*E. coli*, *Proteus*, *Klebsiella*)

- $\beta$ -lactam (amidino-penicillin)
- Targets penicillin-binding protein-2 (PBP-2)
- Low collateral damage

**Side Effects**

- Mild GI upset (nausea, diarrhea)
- Rash (uncommon)
- Vaginal candidiasis (rare)



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## ANTIMICROBIAL AGENT: PIVMECILLINAM

**Contraindications**


- Known  $\beta$ -lactam allergy
- **Systemic Infection** or suspected pyelonephritis
- Poor oral absorption states

**Precautions**

- **Not appropriate for prostatitis** or upper-tract infection
- Use caution in severe renal impairment
- Limited U.S. clinical experience

**Pearls**

- First-line agent in EAU & NICE guidelines
- Excellent for bladder-confined infection
- Low resistance rates
- Preserves microbiome  $\rightarrow$  strong stewardship choice
- FDA approved (U.S., 2024) for adult women with uUTI
- U.S. formulation, \$\$\$
  - 185 mg tablets



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## Class: Transvaginal Estrogen Therapy Estradiol, Conjugated Equine Estrogen, Estrilol

**GOAL**



- Treat Genitourinary Syndrome of Menopause (GSM)
- Reduce uro-genital symptoms (urgency, frequency, dysuria, dyspareunia) in postmenopausal women
- Reduce risk UTI & vaginal symptoms


**Dosage: Vaginally**

- Topical cream: 0.5-2 gms nightly vaginally for 2 weeks then reduce 2-3 Xs week
- Slow-release estradiol ring every 3 months
- 10mcg tablets nightly X 2 wk then 2X wk
- 4 or 10 ug insert daily X 2 wks then 2X wk; Compounded Estrilol 0.05%

**Pharmacodynamics**

- Restores the vaginal epithelium, normalizes pH environment and microflora in the vagina
  - $\uparrow$ s lactobacilli
- Reduces UTI risk
- Reduces dyspareunia



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**Class: Transvaginal Estrogen Therapy**  
**Estradiol, Conjugated Equine Estrogen, Estriol**

**Side Effects**

- **Local (most common):** vaginal irritation, burning, itching
- **Others:** breast tenderness, vaginal spotting, abdominal cramps or distention, nausea, headache, **rare:** ↑ blood pressure, mood changes, libido changes
- **Infection:** vaginal candidiasis (rare)

**Pharmacokinetics**

- Pregnancy: d/c use
- Local absorption; minimal systemic exposure
- No first-pass hepatic metabolism
- Estradiol levels remain postmenopausal

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**Class: Transvaginal Estrogen Therapy**  
**Estradiol, Conjugated Equine Estrogen, Estriol**

**Hx: Contraindications/ Caution**

- FDA initiated removal of **broad boxed warnings** (including VTE and breast cancer) from **topical low-dose vaginal estrogen**
- Labeling is being revised to reflect **route-specific risk**
- Endometrial cancer warnings remain for **systemic estrogen only**
- Low-dose vaginal estrogen results in minimal systemic absorption and has **NOT** been shown to increase **thromboembolic or breast cancer risk or recurrences.**

**Pearls**

- Creams provide faster relief of symptoms
- Ring provides lowest, non-systemic dose
- Switch to a vaginal tablet if experiencing burning with the cream
- Can be very \$\$\$; consider compounded pharmacy
- Can use if Breast Ca or hx of. See ACOG, 2021.
- **Shared Decision Making**

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**CLASS: Urinary Antiseptic**  
**Methenamine Hippurate**

**Goal:** Prevent *rUTI*, **NOT Treatment**

**Dosage:** 1 g 2 x day; Take with 500mg Vit. C


**Pharmacokinetics**

- Rapid GI absorption
- Excreted renally
- **Hydrolyzed in acidic urine → formaldehyde (active)**
- Minimal systemic distribution
- No CYP450 metabolism

**Pharmacodynamics**

- **Active:** Gram + & - uropathogens;
- Formaldehyde released in acidic urine → nonspecific bactericidal activity
- Resistance-independent activity

**Side Effects:** GI upset, rash (uncommon), Dysuria (rare)

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**CLASS: Urinary Antiseptic  
Methenamine Hippurate**

**Contraindications**


- Severe renal impairment
- Severe hepatic disease
- Dehydration
- **Concomitant sulfonamides**
  - ↑ crystalluria risk

**Caution**

- **Ineffective if urine not acidic**
- Avoid in suspected cUTI
- Use caution in patients with gout or metabolic acidosis risk

**Pearls**

- Prevention only
- Co-administer with Vit C 500 mg
- Safe for long-term use; No resistance
- Pause if prescribed any antibiotic, then resume
- Great alternative to avoid ABX prophylaxis
- Supported by Guidelines

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**CLASS: CRANBERRY  
Proanthocyanidin-containing (PAC) Non-antibiotic Prophylaxis  
Vaccinium Macrocarpon**

**Goal:** ↓ risk of recurrent UTI; Prevention only

**Dosage:**


- Juice 1-2 c. daily
- Tablets- 3600-6000mg/d
- PAC ≥36mg daily

**Pharmacodynamics**

- Proanthocyanidin (PAC) compounds cause P fimbriated-E.coli to exhibit anti-adhesion properties

**Side Effects**

- GI upset or diarrhea in large doses
- rash

AUI/CAU/SUFU; EAU; NICE 

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**CLASS: CRANBERRY  
Proanthocyanidin-containing (PAC) Non-antibiotic Prophylaxis  
Vaccinium Macrocarpon**

**Pharmacokinetics**

- Metabolized-liver
- CYP 2C9 substrate
- CYP 2C9 inhibitor
- Excretion-renal
- Pregnancy Cat. A

**Caution or Contraindications**

- May ↑ warfarin effects?
- Contains salicylic acid so avoid if allergic to ASA
- Caution use in patients with kidney stones (oxalate) unless type of stones known
  - High levels of oxalate in cranberry



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**CLASS: CRANBERRY**  
**Proanthocyanidin-containing (PAC) Non-antibiotic Prophylaxis**  
***Vaccinium Macrocarpon***

**Pearls**

- Counsel patients: Used for prevention not tx of UTI's
- Advise patients S&S of UTI
- Investigate a product line you are comfortable with for recommendation
- DM: Watch sugar content of juices



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**“TOOK THE CHECKER”**  
**DRIVING EXCELLENCE IN OUTPATIENT UTI CARE!**




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