REVIEW ARTICLE

Fosfomycin Tromethamine: A Urinary Antibiotic

Abhijit A Trailokya[1*], Mangesh Tiwaskar[2]

Received: 02 September 2024; *Accepted:* 28 March 2025

Abstract

Urinary tract infection (UTI) is the second most common type of infection in the human body. It is one of the most prevalent conditions in medical practice, with approximately 150 million cases occurring globally each year. Approximately 50% of women will experience at least one episode of UTI during their lifetime, and between 20 and 40% will have recurrent episodes. The discovery of a broad-spectrum antibiotic, fosfomycin tromethamine, occurred in Spain in 1969 and is prominently used in the management of uncomplicated UTIs. As a phosphonic acid derivative, fosfomycin acts by disrupting bacterial cell wall synthesis by inhibiting the enzyme MurA, demonstrating effective activity against a wide variety of gram-negative and gram-positive pathogens, comprising multidrug-resistant strains such as *Escherichia coli* and *Klebsiella pneumoniae*. Fosfomycin is not metabolized and is predominantly excreted unchanged in the urine through glomerular filtration. Mean peak urinary concentrations of fosfomycin ranging from 1053 to 4415 mg/L occur within 4 hours of administration of a single oral dose of fosfomycin tromethamine correspondent to fosfomycin 3 gm. Urinary concentrations >128 mg/L, which are adequate to inhibit most urinary pathogens, are maintained for 24–48 hours following a single oral dose of fosfomycin tromethamine. This makes it particularly advantageous for uncomplicated UTIs, where it offers a convenient and effective single-dose treatment option. Clinical trials and observational studies have consistently shown high cure rates and patient compliance, attributing this to its minimal side effects and broad-spectrum efficacy. A single oral dose of fosfomycin tromethamine, equivalent to 3 gm of fosfomycin, is indicated for treating acute uncomplicated lower UTIs in adults. It is classified as pregnancy category B. Various clinical guidelines, such as the Infectious Diseases Society of America (IDSA), European Association of Urology (EAU), and National Institute for Health and Care Excellence (NICE), also recommend fosfomycin tromethamine for the treatment of UTI. In conclusion, fosfomycin tromethamine remains a robust and indispensable antibiotic in the management of uncomplicated UTIs, with a distinct pharmacological profile that ensures both efficacy and safety, and patient compliance due to its single-dose regimen.

Journal of The Association of Physicians of India (2025): 10.59556/japi.73.1103

Introduction

In India, patients suffering from lower urinary tract infections (UTIs) can be managed not only by urologists but also by family physicians/general practitioners (GPs), geriatricians, pediatricians, and gynecologists. The global pooled incidence of UTI accounted for 1.6%. With respect to a systematic review and meta-analysis, the prevalence of UTIs in India has been rising, with *Escherichia coli* being the most commonly isolated pathogen, found in 49.6% of cases, followed by *Klebsiella* spp. at 12.8%.[1] Uncomplicated UTIs occur at a rate of 50 per 1,000 women per year. Approximately 50% of all women will experience at least one UTI during their lifetime, and between 20 and 40% of women will have recurrent UTI episodes.[2] During pregnancy, UTIs are highly prevalent, affecting approximately 20% of pregnant women.[3]

Treating UTIs in India presents several significant challenges, including:

- Antimicrobial resistance: One of the most pressing issues in treating UTIs in India is the high prevalence of antimicrobial resistance (AMR) among common uropathogens like *E. coli* and *Klebsiella pneumoniae*. The misuse and overuse of antibiotics contribute significantly to this problem.
- Diagnostic challenges: In India, the accuracy of UTI diagnosis is often compromised due to reliance on less sensitive methods, which can lead to both false positives and negatives. Proper diagnostic infrastructure is crucial for identifying the specific causative agents and their resistance patterns to tailor effective treatments.
- Socioeconomic factors: Many patients may not complete their prescribed antibiotic courses due to financial constraints, leading to incomplete eradication of the infection and increased resistance. Additionally, there is a lack of awareness about proper hygiene practices and the importance of adhering to prescribed treatments, which can contribute to recurrent infections and resistance issues.
- Right selection of antibiotic: Right selection of antibiotic while treating UTI is a key factor in clinical practice. Different factors should be considered while choosing antibiotic therapy for treating UTI, including: (1) pharmacokinetic (PK) properties of antibiotic—antibiotics with renal excretion should be preferred, (2) activity of the antibiotic against pathogens causing UTI, (3) local resistance pattern against causative pathogens, (4) dosing frequency (simplified dosing regimen or frequency is always preferred), (5) safety and efficacy, and (6) consideration of patient compliance.[4]

Developmental Aspect of Fosfomycin

Fosfomycin is an old antibiotic. Merck, Sharp, and Dohme (MSD) and Compañía Española de Penicilina y Antibióticos (CEPA) discovered fosfomycin in 1969. Fosfomycin is a derivative of phosphonic acid, isolated from *Streptomyces* spp. Originally called phosphonomycin, fosfomycin has a broad bactericidal spectrum that acts by interfering with cell wall synthesis of both gram-negative and gram-positive bacteria.

Fosfomycin is available in three different formulations. When it is combined with calcium, it is called fosfomycin calcium. When combined with tromethamine (trometamol), it is called fosfomycin tromethamine, and both are for oral treatment, and when combined with sodium, it is called disodium fosfomycin and is for intravenous treatment.[5]

Difference between Fosfomycin Calcium and Fosfomycin Tromethamine/Trometamol

The oral bioavailability of fosfomycin tromethamine/trometamol is 34–58%, with absorption predominantly occurring in the small intestine. Absorption of fosfomycin tromethamine is six times more than that of

[1]Head, Department of Medical Affairs, Indoco Remedies Limited; [2]Consultant Physician and Diabetologist, Department of Medical, Shilpa Medical Research Centre, Mumbai, Maharashtra, India; *Corresponding Author

How to cite this article: Trailokya AA, Tiwaskar M. Fosfomycin Tromethamine: A Urinary Antibiotic. J Assoc Physicians India 2025;73(10):79–82.

© The Author(s). 2025 Open Access. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by-nc/4.0/). Please refer to the link for more details.

fosfomycin calcium during the first 2 hours and three to four times more in the first 12 hours; the probable explanation could be that the calcium salt is hydrolyzed and inactivated by gastric enzymes.[6]

Ideal Urinary Antibiotic

Ideal antibiotics for treating UTIs are the dream of clinicians and should possess several key properties to ensure efficacy, safety, and minimal resistance development (Fig. 1).

These properties help ensure that antibiotics for UTIs are both effective and practical for widespread use, reducing the incidence of complications and the spread of resistant bacteria.

Fosfomycin Tromethamine

Though the name fosfomycin ends with "-omycin," it does not belong to the macrolide class of antibiotics. Instead, it is classified as phosphonic acids or phosphonic antibiotics, a novel class of antibiotics.[7]

Chemical Structure

Fosfomycin trometamol is a monobasic hydrosoluble fosfomycin salt. After absorption, fosfomycin is released from fosfomycin trometamol through hydrolysis.[7]

Mechanism of Action

Fosfomycin acts by inhibiting the bacterial cell wall, thereby inactivating the enzyme enolpyruvyl transferase.[7,8] This action blocks the condensation of uridine diphosphate *N*-acetylglucosamine with phosphoenolpyruvate, an essential step in peptidoglycan synthesis, which is crucial for bacterial cell wall formation. This inhibition leads to a bactericidal effect, particularly in the urinary tract, as fosfomycin is highly concentrated in the urine after administration.[8]

Microbiology

Fosfomycin is effective against a broad range of gram-negative and gram-positive bacteria.[7,9] It has shown activity against *E. coli*, *Enterococcus faecalis*, and other pathogens involved in UTIs. It is bactericidal in urine at therapeutic doses with MIC: *E. coli* (MIC_{90} ≤12.3 µg/mL). Its lack of cross-resistance with other antibiotic classes makes it a valuable option in the treatment of resistant infections.

Pharmacokinetic Properties of Fosfomycin Tromethamine

Absorption

Fosfomycin tromethamine is well absorbed after oral administration, although its bioavailability is <50% (absorption of fosfomycin occurs primarily in the small intestine) (Table 1). The absorption of the drug may reduce when coadministered with food. Concomitant administration of metoclopramide should be avoided, as it fails to maintain adequate drug levels for therapeutic efficacy.

Distribution

Once absorbed, fosfomycin is widely distributed in body tissues, including the kidneys, bladder wall, and prostate, which is beneficial for treating UTIs. It does not bind to plasma proteins, facilitating its rapid action at infection sites. The evidence shows that a single 3 gm dosage of oral fosfomycin trometamol achieves adequate concentrations in noninflamed prostatic tissue.

Metabolism and Excretion

Fosfomycin is primarily excreted unchanged in the urine. The half-life of fosfomycin trometamol is 5.7 hours in patients with normal renal function but can be significantly prolonged in those with renal impairment (up to 50 hours). After oral dosing, urinary concentrations exceed the MICs of susceptible pathogens for over 24 hours. A total of 32–43% of fosfomycin is excreted renally within 48 hours, and about 85–95% is excreted in the first 24 hours. Concentrations >128 mg/L, sufficient to inhibit most urinary pathogens, are maintained for 24–48 hours after a single oral dose of fosfomycin. After a single 3 gm dose, >99% of common urinary pathogens are eradicated. Additionally, bacterial adhesiveness to uroepithelial mucosa decreases significantly within 1 hour of exposure to fosfomycin at a concentration of 1000 mg/L.[7,9]

Special Populations

In Geriatric Patients

No dose adjustment is necessary, as there are no significant differences in the PK of fosfomycin.

Renal Impairment

In patients with varying degrees of renal impairment, the elimination half-life of fosfomycin trometamol increases, and its excretion in urine decreases significantly.

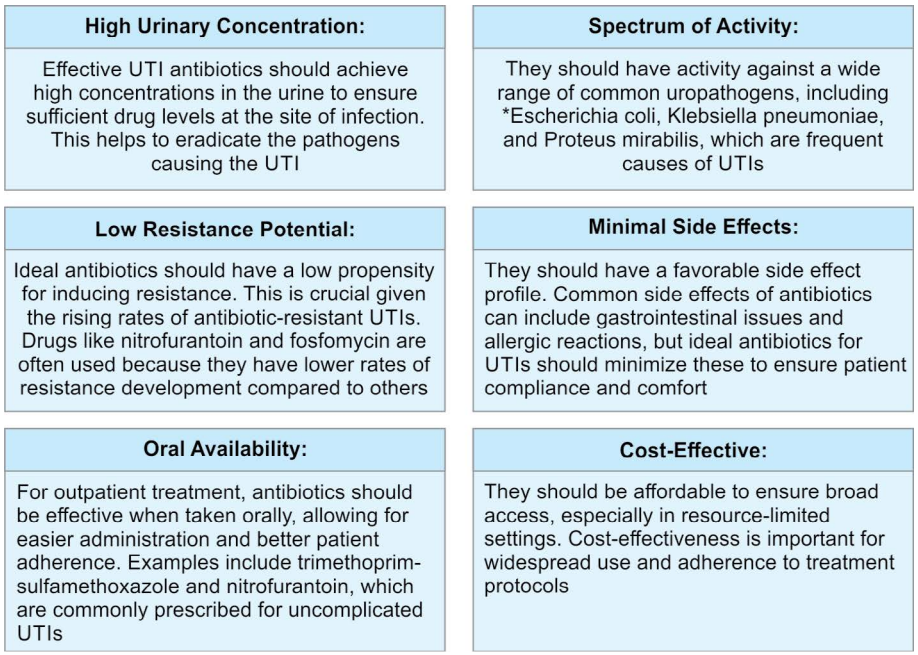

Fig. 1: Properties of ideal urinary antibiotic

Table 1: PK properties of fosfomycin trometamol[7,9]

Parameters	*Serum/plasma*	*Parameters*	*Urine*
Bioavailability	34–41%		
Maximum plasma concentration (C_{max})	22–32 µg/mL	Maximum urinary concentration (U_{max})	1053–4415 µg/mL
Time to C_{max} (T_{max})	2–2.5 hours	Time to U_{max} (urinary T_{max})	4 hours
Half-life ($t_{1/2}$)	5.7 hours	Urinary concentration at 48 hours	~100 µg/mL

Fosfomycin in Pregnancy[7,9,10]

Pregnant women are more prone to develop UTIs in the third trimester, with *E. coli* being the most common pathogen. Around 20–40% of *E. coli* cases are resistant to ampicillin and amoxicillin, making these antibiotics less effective. Fosfomycin is a valuable alternative treatment.

The US FDA classified fosfomycin in pregnancy category B, that is, "no evidence of risk in humans and can be used in pregnancy if clearly needed." Fosfomycin is excreted in breast milk.[7]

Indication and Approval Status

Fosfomycin is approved in major countries like the US, UK, and India (Fig. 2).

Approval Status

Fosfomycin has been available in several European countries, as well as in Japan, South Africa, and Brazil, in both oral and parenteral formulations, for four decades. In India, the Drug Controller General of India (DCGI) approved fosfomycin in 2008.[12]

Safety and Tolerability of Fosfomycin

Fosfomycin is generally well tolerated, with few common side effects such as diarrhea, nausea, and abdominal pain. It should be avoided in individuals with a known allergy to the drug, children under 12 years old, those with severe renal insufficiency (CLcr <10 mL/min), or patients undergoing hemodialysis.[7,11]

Dosage of Fosfomycin

The rationale for using a single dose of fosfomycin trometamol is based on its PK properties (Table 2).[7] After single oral administration, the maximum concentration of 22–32 µg/mL is achieved in about 2 hours, with an elimination half-life of 2.4–7.3 hours and an area under the curve of 145–228 µg/mL·hour. This results in high urinary concentrations (1000–4000 µg/mL), maintaining levels above 100 µg/mL for 30–48 hours.

Method of Administration

- It is advisable to take fosfomycin on an empty stomach.[7]
- About 2–3 hours before or 2–3 hours after meals, and preferably before bedtime after emptying the bladder.
- A sachet has to be dissolved in a glass of water and consumed immediately after preparation.

Clinical Efficacy and Safety

Fosfomycin tromethamine is clinically effective for treating uncomplicated UTIs. A meta-analysis comparing fosfomycin to other antibiotics like nitrofurantoin and ciprofloxacin found that a single dose of fosfomycin achieved similar clinical and microbiological cure rates. It is particularly effective against common uropathogens, including multidrug-resistant *E. coli*. Studies show that fosfomycin is generally well tolerated, with fewer gastrointestinal side effects compared to other treatments.[13]

Guidelines Recommending Fosfomycin Use in Clinical Practice

Fosfomycin tromethamine is recommended for the treatment of uncomplicated UTIs due to its effectiveness, safety, and convenient single-dose administration. It is particularly beneficial against a broad range of uropathogens, including multidrug-resistant strains like *E. coli* and *E. faecalis*.

European Association of Urology Guidelines

The European Association of Urology (EAU) guidelines for the management of uncomplicated UTIs recommend fosfomycin as one of the first-line options for empirical treatment in regions with low rates of resistance (<10–20%). Fosfomycin is particularly favored for the treatment of acute uncomplicated cystitis in women, owing to its high efficacy and favorable safety profile.[14]

Infectious Diseases Society of America Guidelines

The Infectious Diseases Society of America (IDSA) guidelines for the treatment of uncomplicated cystitis in adult women recommend fosfomycin as one of the first-line agents, particularly in settings where the prevalence of multidrug-resistant pathogens is low. Fosfomycin is recommended as a single-dose regimen for uncomplicated cystitis caused by susceptible pathogens, such as *E. coli*.[15]

Society of Infectious Diseases Pharmacists Recommendations

The Society of Infectious Diseases Pharmacists (SIDP) recommendations for the management of complicated urinary tract infections (cUTIs) and acute pyelonephritis (AP) highlight the role of fosfomycin in combination therapy for the treatment of multidrug-resistant pathogens, including extended-spectrum β-lactamase (ESBL)-producing *Enterobacterales* and carbapenem-resistant organisms. Fosfomycin is often recommended in combination with other agents, such as aminoglycosides or carbapenems, for the treatment of cUTIs and AP caused by difficult-to-treat pathogens.[16]

As per National Institute for Health and Care Excellence (NICE) and Public Health England (PHE)

Fosfomycin is recommended for uncomplicated UTI caused by ESBL-producing *E. coli* in adults. Guidelines suggest a single dose of 3 gm in women and two 3 gm doses at an interval of 3 days in men.[17]

Table 2: Dosing schedule of fosfomycin

Availability	*Dose*
Fosfomycin is available as sachet of 3 gm	A single oral dose of fosfomycin trometamol is suggested for treating acute uncomplicated lower UTIs in adults

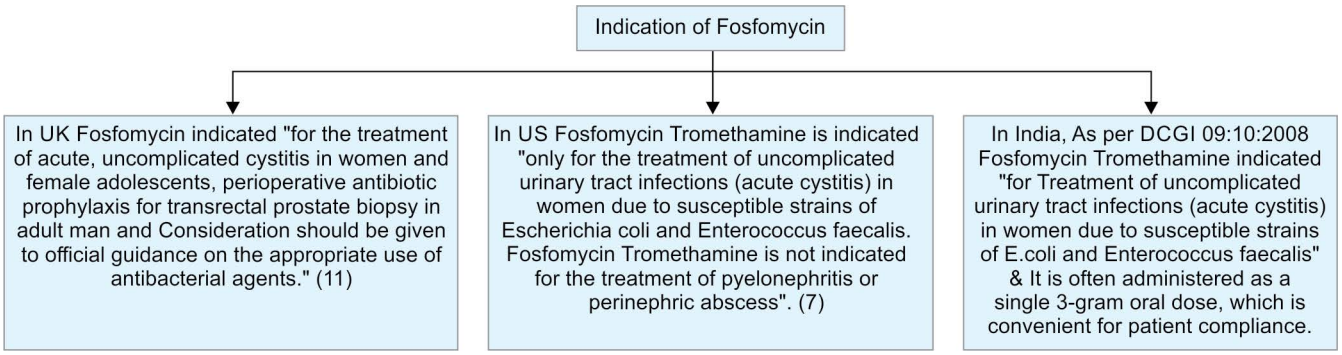

Fig. 2: Indications approval of fosfomycin in various countries like US, UK, and India

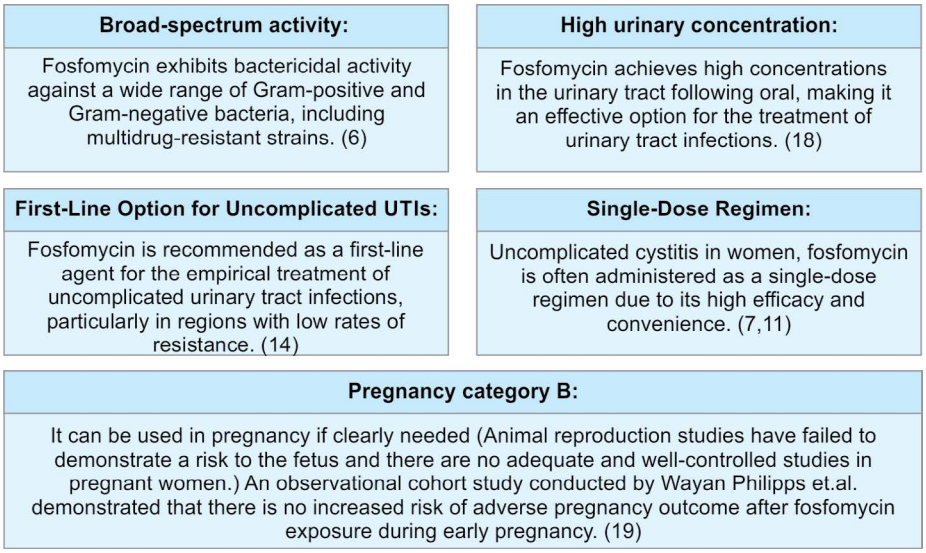

Fig. 3: Important pointers on fosfomycin from a clinical perspective

Important points regarding fosfomycin from a clinical perspective can be seen in Figure 3.

Conclusion

Fosfomycin tromethamine is a broad-spectrum antibiotic prominently used in the management of uncomplicated UTIs. This agent is highly valued for its unique mechanism of action, which involves the inhibition of bacterial cell wall synthesis by blocking the initial step in peptidoglycan formation. Its efficacy against both gram-positive and gram-negative bacteria, including multidrug-resistant strains like ESBL-producing *Enterobacteriaceae*, makes it an essential option in antimicrobial therapy. Clinically, fosfomycin tromethamine is administered as a single-dose regimen, enhancing patient compliance compared to traditional multidose therapies. Its PK profile allows for high urinary concentrations, which is critical for effectively targeting urinary pathogens. Furthermore, the drug demonstrates a favorable safety profile with minimal adverse effects, making it suitable for a broad patient population. Given the rising issue of antibiotic resistance, fosfomycin tromethamine's role in the therapeutic landscape is increasingly significant. It offers a viable alternative in instances where other antibiotics may fail due to resistance or adverse reactions. A recent systematic review and network meta-analysis published in World Journal of Urology 2024 confirmed that fosfomycin is the most effective antibiotic in treating uncomplicated UTIs with respect to microbiological cure, clinical cure, and adverse events profile.[20]

In conclusion, fosfomycin tromethamine remains a robust and indispensable antibiotic in the management of uncomplicated UTIs, with a distinct pharmacological profile that ensures both efficacy and safety. Its relevance is further underscored in the current era of escalating AMR, positioning it as a critical tool in contemporary infectious disease therapy. Appropriate antibiotic therapy is essential for achieving clinical cure and preventing complications. However, the increasing prevalence of antibiotic resistance necessitates a thoughtful, evidence-based approach to antibiotic selection and management.

Conflict of Interest

Dr Abhijit A Trailokya is associated with Indoco Remedies Limited, Mumbai.

Orcid

Abhijit A Trailokya https://orcid.org/0009-0002-7657-8119
Mangesh Tiwaskar https://orcid.org/0000-0003-4024-0095

References

1. Faraz MAA, Mendem S, Swamy MV, et al. Prevalence of urinary tract infections and related anti-microbial resistance in India: a systematic review and meta-analysis. Int J Pharm Sci Res 2021;12(8):4314–4321.
2. Pardeshi P. Prevalence of urinary tract infections and current scenario of antibiotic susceptibility pattern of bacteria causing UTI. Indian J Microbiol Res 2018;5(3):334–338.
3. Salari N, Khoshbakht Y, Hemmati M, et al. Global prevalence of urinary tract infection in pregnant mothers: a systematic review and meta-analysis. Public Health 2023;224:58–65.
4. Yakovlev SV, Suvorova MP. [Rationale for the choice of an antibiotic for urinary tract infections with an emphasis on the environmental safety of therapy]. Urologiia 2021;(4):97–105.
5. Arteche-Eguizabala L, Domingo-Echaburua S, Urrutia-Losadaa A, et al. Fosfomycin: salt is what really matters. Enferm Infecc Microbiol Clin 2021;39(4):206–207.
6. Falagas ME, Vouloumanou EK, Samonis G, et al. Fosfomycin. Clin Microbiol Rev 2016;29:321–347.
7. FOSFOMYCIN TROMETHAMINE—granules for oral solution powder. XIROMED LLC; 2020.
8. Werth BJ. Fosfomycin. MSD Manual Professional Edition.
9. Patel SS, Balfour JA, Bryson HM. Fosfomycin tromethamine. A review of its antibacterial activity, pharmacokinetic properties and therapeutic efficacy as a single-dose oral treatment for acute uncomplicated lower urinary tract infections. Drugs 1997;53(4):637–656.
10. Kalinderi K, Delkos D, Kalinderis M, et al. Urinary tract infection during pregnancy: current concepts on a common multifaceted problem. J Obstet Gynaecol 2018;38:448–453.
11. Monuril 3g granules for oral solution—Summary of Product Characteristics.
12. DCGI approval list of new drugs approval in India. https://cdsco.gov.in/opencms/resources/UploadCDSCOWeb/2018/UploadApprovalMarketingFDC/LIST%20OF%20APPROVED%20DRUG%20FROM%2001-01-2008%20to%2031-12-2008.pdf
13. Derington CG, Benavides N, Delate T, et al. Multiple-dose oral fosfomycin for treatment of complicated urinary tract infections in the outpatient setting. Open Forum Infect Dis 2020;7:ofaa034.
14. European Association of Urology Guidelines on Urological Infections. Arnhem, The Netherlands: European Association of Urology; 2020.
15. Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis 2011;52(5):e103–e120.
16. Zasowski EJ, Rybak JM, Rybak MJ. The β-lactams strike back: fosfomycin for multidrug-resistant urinary tract infections. Antimicrob Agents Chemother 2019;63(9):e01043.
17. Matthews PC, Barrett LK, Warren S, et al. Oral fosfomycin for treatment of urinary tract infection: a retrospective cohort study. BMC Infect Dis 2016;16(1):556.
18. Sastry S, Doi Y. Fosfomycin: resurgence of an old companion. J Infect Chemother 2016;22(5):273–280.
19. Philipps W, Fietz AK, Meixner K, et al. Pregnancy outcome after first-trimester exposure to fosfomycin for the treatment of urinary tract infection: an observational cohort study. Infection 2020;48(1):57–64.
20. Hadidi MF, Alhamami N, Alhakami M, et al. Antibiotics efficacy in clinical and microbiological cure of uncomplicated urinary tract infection: a systematic review and network meta-analysis. World J Urol 2024;42(1):221.