# Experience of Faropenem for the management of urinary tract infection: Real-world experience from India

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## Abstract

**Background:** Urinary tract infections (UTIs) is the infectious diseases affecting both the genders. The prevalence of drug-resistant microbes in patients with UTIs is increasing. Faropenem due to its broad spectrum antimicrobial activity and lower chances of resistance is becoming popular among the Indian urologist however, real-world data is scarce.

**Aim and Objective:** To record the real-world responses from the urologist of India on the use of faropenem in the management of UTIs.

**Materials and Methods:** Responses of Indian urologists were obtained on the usage of faropenem in the management of complicated urinary tract infection (cUTI) after providing a set of eight questions having both multiple-choice responses and open-ended answers.

**Results:** Responses of 391 participants were collected. In majority of the urology clinics prevalence of cUTI was 5-10% whereas others found it to be 10-20%. Majority believes that faropenem is an effective pharmacotherapy for the management of UTIs (66.4%) including cUTI as a step-down therapy (66.4%). Faropenem 300 mg provides more compliance. Overall perception on the use of faropenem in their practice was that (out of 391 responses) majority found it to be effective (72.7%) and 4.6% participants have used faropenem as an alternative in cUTI. Majority found it safe (68.5) to be used in cUTI.

**Conclusion:** Real world data from the Indian urologist highlight the shifting trend. Faropenem is being referred for the treatment of urinary tract infections due to its effectiveness, ability to cause less resistance and safety profile.

**Keywords:** Resistance, Urinary tract infection, Extended-spectrum β – lactamase, Penems.

## Introduction

India has witnessed the highest rates of extended-spectrum β - lactamase (ESBL) –producing organisms in the world. (Gandra S 2016, Paterson DL 2005) There is a need for oral administration as it is the preferred dosage form and route for patients discharged from the hospital.

In India, an alternative to intravenous carbapenems is often prescribed by clinicians. Faropenem is an oral antibiotic that belongs to the "penems" class of β-lactam antibiotics. Penems are a hybrid of penam (penicillin) and cepham (cephalosporins) nuclei and are structurally most similar to carbapenems. (Gettig JP 2008)

Faropenem has broad antimicrobial activity, is active against aerobic gram-positive, gram-negative, and anaerobic bacteria, and is also resistant to TEM-, SHV-, and CTX-M–type ESBLs. In India, faropenem is approved for the treatment of respiratory tract, urinary tract, skin, soft-tissue, and gynecological infections. (Central Drugs Standard Control Organization 2020) It is often used to treat invasive ESBL-producing Enterobacteriaceae infections even though its efficacy in these cases is not clinically proved.

UTIs are among the most prevailing infectious diseases in the community with the substantial clinical and financial burden. (Ejrnæs K 2011) Almost 95% of all UTIs are caused by bacteria, most of them by E-coli (30%–90%, depending on the clinical setting). Klebsiella, Enterobacter, Proteus, Pseudomonas, Enterococcus, Staphylococcus, and others can also cause UTIs. (Patel HB 2019)

Real-world clinical experiences at the urologist's level for Faropenem is scarce. To the best of our knowledge, this is the first study where the clinical experience and satisfaction level of urologists using the

faropenem for the treatment of UTIs. Hence in the present survey, we tried to record the responses and feedback of the use of faropenem from the urologist of India.

## Materials and Methods

In the present study, we collected the response from 391 Indian urologists across India on the usage of faropenem for the management of cUTI.

A set of eight questions having both multiple-choice and open answers were presented to each participant and the responses were collected.

The list of questions are as follows;

| Question number | Question details |
|---|---|
| 1 | What proportion of your patients present with cUTI?<br>a. 5-10%<br>b. 10-20%<br>c. 20-30%<br>d. >30% |
| 2 | According to your clinical expertise, what is the line of treatment of cUTI?<br>a. First line<br>b. Second line<br>c. Third line<br>d. Any other |
| 3 | According to your clinical expertise, what are the indications where faropenem has an advantage over other antibiotics?<br>a. cUTI<br>b. cUTI for resistant infections<br>c. cUTI for step down therapy<br>d. cUTI for hospital acquired infections<br>e. Pyelonephritis<br>f. Prostatitis<br>g. Post-operative care<br>h. Abscess<br>i. Any other |
| 4 | In your opinion what is the place of faropenem in UTIs management? |
| 5 | As per your clinical experience management of UTIs with faropenem is?<br>a. Extremely effective<br>b. Very effective<br>c. Moderately effective<br>d. Slightly effective<br>e. Not at all effective |
| 6 | How do you perceive faropenem in your practice? |
| 7 | How efficacious is Faropenem as compared to other available options? |
| 8 | How is the safety profile of Faropenem? |

Data analysis was performed using IBM SPSS ver. 20 software. A frequency distribution was performed to obtain the frequency of each response. Data are presented as a number or percentage. No further data analysis was performed.

## Results

In present survey responses of a total 391 participants were recorded. In majority of the urology clinics prevalence of cUTI was 5-10% [266 (68%)] whereas other participants revealed a prevalence between 10-20% [68 (17.4%)] and 20-30% [57 (14.6%)].

As a first line and second line management therapy for cUTI mixed response were recorded. 3rd generation cephalosporin, aminoglycoside, combination of aminoglycoside with cefalosoporin, beta lactam carbapenem like faropenem, cephalosporin, ceftriaxone, combination of ceftriaxone + amikacin and fluoroquinolone and its combination with cefalosporins were some of them.

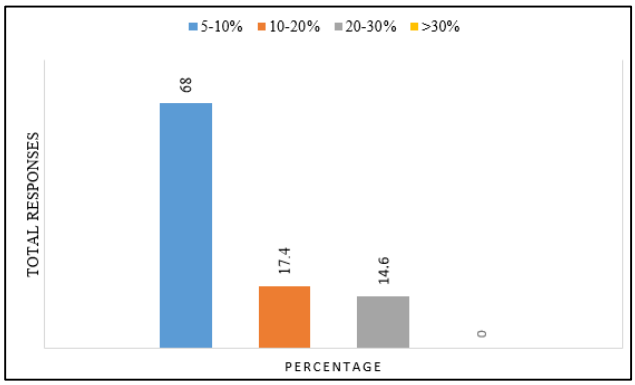


**Fig. 1:** Showing the prevalence of cUTI in urology clinic

Participants were asked to share their clinical experience management of UTIs with faropenem. It was found that the majority believe that faropenem is very effective for the management of UTIs [260 (66.4%)] whereas [131 (33.5%)] found that it is extremely effective. Overall all the participants believe that faropenem is effective for the management of UTIs.

In response to the scope of faropenem, it was revealed that faropenem is an effective drug for the management of cUTI and as step-down therapy [260 (66.4%)].

The majority of the participants believe that faropenem 200 mg is an effective option for step-down therapy for cUTI due to fewer chances of resistance. For faropenem 300mg, majority of the participants believed that it has excellent patient compliance and is an effective step-down option for cUTI due to its high efficacy and fewer side effects.

In response to the perception of the use of faropenem in their practice (out of 391 responses) majority found it to be effective [284 (72.7%)] and [18 (4.6%)] participants have used faropenem as an alternative in cUTI. There were [56 (14.3%)] participants who have rarely used, do not prefer, or are not used it as the first-line drug in the management of cUTI. However, [6 (1.5%)] participants have used faropenem as the second-line antibiotics in their practice.

In response to the question on how efficacious is faropenem as compared to other available options?, majority believed that faropenem is highly efficacious [345 (88.14%)] in the management of cUTI however, [23 (5.8%)] participants believed that faropenem is equally efficacious than the other available options. However, [20 (5.1%)] participants did not have enough clinical experience of using faropenem.

In response to safety concerns of faropenem use, the majority [268 (68.5%)] of the participants found is safe, 87 (22.2%) believed that it has an excellent safety profile however, only 37 (9.4%) participants believe that it is not safe and causes acidity or gastritis.

## Discussion

Faropenem has good activity against E. coli and Klebsiella spp. with ESBLs which are the major causative organism for the development of cUTIs. Its clinical utility will depend on minimum effective concentration achieved in the urinary tract, the site of most of the community infections caused by extended-spectrum β-lactamase (ESBL) producers. (Livermore DM 2007, Potz NA 2006).

In urological clinics, recurrent or cUTIs are one of the most common problems encountered. This may be due to in increased prevalence of cUTI. This was also highlighted in present survey where in majority of the urology clinics prevalence of cUTI was 5-10% whereas other participants revealed a prevalence between 10-20% and 20-30% which is alarming.

As a first line and second line management therapy for cUTI mixed response were recorded in present survey. Few most commonly used pharmacotherapy were 3rd generation cephalosporin, aminoglycoside, combination of aminoglycoside with cefalosoporin, beta lactam carbapenem like faropenem, cephalosporin,

ceftriaxone, combination of ceftriaxone with amikacin and fluoroquinolone and its combination with cefalosporins. This highlight that there is no particulate drug being used for the management of cUTI.

However, when participants were asked to share their clinical experience management of UTIs with faropenem. It was found that the majority believe that faropenem is very effective for the management of UTIs (66.4%) whereas 33.6% found that it is extremely effective. Overall all the participants believed that faropenem is effective for the management of UTIs. This was highlighted by Gandra et al where they reported that faropenem consumption increased by 154% since it was approved in 2010 (from 7.4 million standard units in 2010 to 18.9 million standard units in 2014). (Gandra S 2016) It was also revealed that meropenem consumption was also increased from 2010 to 2014 however, faropenem consumption exceeded total carbapenem consumption in India. (Gandra S 2016).

Complicated urinary tract infections (cUTI) are universal reasons for hospitalization, and highly likely to develop into sepsis or septic shock. (Tan X 2020).

In response to the scope of faropenem in cUTI from the urologist, it was revealed that faropenem is an effective drug for the management of cUTI and as a step-down therapy (66.4%). This highlight the increase in belief on faropenem among the urologist in the management of cUTI.

Resistance and prevalence of cephalosporin-resistant Enterobacteriaceae is changing and increasing in nature. Faropenem is active against extended-spectrum β-lactamase (ESBL) producers which increasingly cause community-onset infections. (Mushtaq S 2007) The same was highlighted from the response recorded from the present study participants where the majority of the participants believe that faropenem 200 mg is an effective option step-down therapy for cUTI due to fewer chances of resistance. This was supported by a previous study that compared faropenem to cephalosporins and imipenem concerning β-Iactamase stability. It was found that faropenem as well as other cephalosporins tested were highly stable to penicillinase derived from S. aureus and E. coli. However, E. coli- and P. vulgaris-derived cephalosporinase hydrolyzed cephaloridine, cefaclor, and cefotiam considerably, whereas faropenem was highly stable. (Dalhoff A 2003)

For faropenem 300 mg extended release, majority of the participants believed that it has excellent patient compliance and is an effective step-down option for cUTI due to its high efficacy and fewer side effects. The increase in compliance with 300 mg faropenem is may be due to the availability of extended release tablets. The benefits offered by faropenem may also be due to its chiral tetrahydrofuran substituent at position C2 which provides improved chemical stability. (Schurek KN 2007) Though few clinical trials are showing the clinical effectiveness of 300 mg in UTIs, one Phase III trial found faropenem 300 mg twice daily less effective than co-trimoxazole in acute uncomplicated urinary tract infections; (Richard G 2005) however, a small Japanese trial found faropenem 300 mg three times daily was equivalent to levofloxacin given as a 100 mg three times daily regimen in cUTI. (Muratani T 2002)

Faropenem demonstrates broad-spectrum in-vitro antimicrobial activity against many gram-positive and gram-negative aerobes and anaerobes and is resistant to hydrolysis by nearly all β-lactamases, including extended-spectrum β-lactamases and AmpC β - lactamases. (Schurek KN 2007) In line with that, the responses on perception on the use of faropenem in the practice of the present study participants majority found it to be effective (72.7%) and (4.6%) participants have used faropenem as an alternative in cUTI. There were 14.3% participants who have rarely used, do not prefer, as a first-line drug in the management of cUTI. There were 5.8% of participants who believe that faropenem is equally efficacious compared to other available options. However, 5.1% participants did not have enough clinical experience of using faropenem.

In response to safety concerns of faropenem use, the majority (68.5%) of the participants found it safe whereas, 22.2% believed that it has an excellent safety profile, however, only 9.3% participants believe that it is not safe and causes acidity or gastritis. The safety of faropenem is may be due to the presence of chiral tetrahydrofuran substituent at position C2 which has provided greater stability and reduced CNS effects, compared with imipenem.

## Conclusion

Despite limited evidence available on the effectiveness of faropenem in the management of UTIs. The present study records real-world evidence from India. Among Indian urologists, faropenem is gaining acceptance for the management of UTIs and cUTI as a step-down therapy. Compliance is more with faropenem 300 mg extended release. The overall perception which we found through this study was that majority found it to be an effective and excellent alternative to current available options for the management of cUTI. To conclude faropenem has the potential for the treatment of urinary tract infections due to ESBL producers and other cephalosporin-resistant Enterobacteriaceae, but that further clinical work is needed to optimize regimens for this purpose.

## Conflict of Interest

The authors declare that there have no competing interests.

## Source of Funding

None.

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**How to cite:** Shah A, Sharma S, Unnikrishnan TK. Experience of Faropenem for the management of urinary tract infection: Real-world experience from India. *IP J Urol Nephrol Hepatol Sci* 2020;3(4):