Ceftazidime-Avibactam: Clinical Impact and Healthcare Provider Perspectives



Table of Content

1	Introduction2
2	Rationale of the study5
3	Study Objective
4	Methods7
5	Results
6	Summary28
7	Discussion
8	Clinical Recommendations33
9	Consultant Opinion34
1() Market Opportunities35
11	Market positioning
12	2 References

INTRODUCTION

Ceftazidime-Avibactam, a combination of a third-generation cephalosporin and a beta-lactamase inhibitor has emerged as a potent option in the treatment of multidrug resistant (MDR) Gram-negative bacterial infections. Its clinical significance has grown as healthcare providers face the increasing challenge of managing infections caused by resistant pathogens, including extended-spectrum betalactamase (ESBL)-producing and carbapenem-resistant Enterobacteriaceae (CRE) (1). Ceftazidime-Avibactam offers a unique mechanism of action that restores the activity of ceftazidime against beta-lactamase-producing organisms, providing a critical therapeutic option for patients who would otherwise have limited treatment alternatives (2).

The global rise in antibiotic resistance has made infections caused by MDR organisms more difficult to treat, leading to increased morbidity, mortality, and healthcare costs (3). According to the World Health Organization, antimicrobial resistance (AMR) is one of the top 10 global public health threats, underscoring the importance of developing and utilizing new antimicrobial agents (4). In this context, Ceftazidime-Avibactam presents a timely solution, with clinical studies demonstrating its efficacy in treating complex infections, including complicated urinary tract infections (cUTIs), complicated intra-abdominal infections (cIAIs), and hospital-acquired bacterial pneumonia (HABP) (5). Despite its potential benefits, the adoption and implementation of this therapy are influenced by healthcare providers' experiences, knowledge, and perceptions, making it essential to explore their perspectives to optimize its clinical use (6).

Emergence of Antimicrobial Resistance (AMR)

Antimicrobial resistance (AMR) has become a significant global health challenge. The emergence of MDR organisms is one of the key consequences of the overuse and misuse of antibiotics. AMR complicates the treatment of infections, increases the duration of hospital stays, and often leads to higher mortality rates. According to the World Health Organization (WHO), AMR is responsible for over 700,000 deaths annually, and this figure could rise to 10 million by 2050 if urgent action is not taken (7). In particular, Gram-negative bacteria, such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, have evolved resistance mechanisms that render many of the commonly used antibiotics ineffective.

Beta-lactam antibiotics, which include penicillins, cephalosporins, and carbapenems, are often the first-line treatment for many infections. However, beta-lactamase enzymes, which are produced by resistant bacteria, degrade these antibiotics, making them ineffective. Carbapenem-resistant Enterobacteriaceae (CRE) and ESBL-producing organisms are of particular concern due to their ability to resist treatment with most available antibiotics, leaving clinicians with few options for effective therapy (8).

The Role of Beta-Lactam/Beta-Lactamase Inhibitor Combinations

In response to the growing problem of beta-lactam resistance, researchers have developed beta-lactam/beta-lactamase inhibitor combinations. These combinations work by inhibiting the beta-lactamase enzymes produced by resistant bacteria, thereby restoring the activity of beta-lactam antibiotics. One such combination is Ceftazidime-Avibactam, which pairs the third-generation cephalosporin Ceftazidime with the novel beta-lactamase inhibitor Avibactam (9). Avibactam inhibits a broad range of beta-lactamases, including ESBLs, AmpC beta-lactamases, and some carbapenemases, making Ceftazidime-Avibactam effective against organisms resistant to many other antibiotics.

Ceftazidime alone is a broad-spectrum cephalosporin with activity against a variety of Gram-negative pathogens, including *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. However, its effectiveness is limited by the presence of

beta-lactamase enzymes. Avibactam restores the activity of Ceftazidime against beta-lactamase-producing bacteria, providing an effective treatment option for infections caused by resistant organisms (10). This combination therapy has been shown to be particularly useful in the treatment of complicated infections, such as cUTIs, cIAIs, and HABP, where resistant pathogens are often encountered (11).

Clinical Applications of Ceftazidime-Avibactam

Ceftazidime-Avibactam has demonstrated significant efficacy in treating infections caused by MDR Gram-negative bacteria. In clinical trials, it has been shown to be effective in treating complex infections, including cUTIs, cIAIs, and HABP. For example, in a Phase III clinical trial, Ceftazidime-Avibactam was compared with meropenem for the treatment of cUTIs and cIAIs in patients with infections caused by resistant pathogens. The results showed that Ceftazidime-Avibactam was non-inferior to meropenem, with similar rates of clinical success (12). Moreover, the drug was associated with a favorable safety profile, making it an attractive option for treating infections in critically ill patients who are at risk for multidrug-resistant infections.

In addition to its clinical efficacy, Ceftazidime-Avibactam has been shown to be effective against a broad range of resistant organisms, including *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterobacter cloacae* (13). This makes it a valuable option in the treatment of infections caused by carbapenem-resistant pathogens, which are associated with high mortality rates. Infections caused by CRE are particularly challenging to treat, and the emergence of resistance to multiple antibiotic classes has limited the options available for clinicians (14). Ceftazidime-Avibactam offers a new and effective treatment option for these difficult-to-treat infections.

Healthcare Provider Perspectives on Ceftazidime-Avibactam

The adoption of Ceftazidime-Avibactam in clinical practice is influenced by healthcare providers' knowledge, perceptions, and experiences with the drug. Despite the promising clinical data, some barriers to its widespread use exist. One major concern is the cost of the therapy, which may limit access in resourcelimited settings (15). Additionally, healthcare providers may be unfamiliar with the specific indications and optimal use of Ceftazidime-Avibactam, leading to hesitancy in prescribing the drug. Understanding the factors that influence healthcare providers' decisions to use Ceftazidime-Avibactam is essential for optimizing its clinical application and ensuring that it is used appropriately in the treatment of MDR infections.

Several studies have shown that healthcare providers' perspectives on the use of new antimicrobial agents are shaped by a variety of factors, including their familiarity with the drug, its clinical efficacy, and its role within the context of antimicrobial stewardship (16). Educating clinicians about the benefits and limitations of Ceftazidime-Avibactam, as well as its role in the broader landscape of AMR, can help ensure that it is used appropriately and effectively.

RATIONALE OF THE STUDY

This study aims to understand healthcare providers' perspectives on the clinical impact of Ceftazidime-Avibactam, as its use is increasingly considered in the management of infections caused by resistant pathogens. Given the growing prevalence of MDR infections, particularly in intensive care settings and among immunocompromised patients, Ceftazidime-Avibactam offers an important treatment option. The rationale for this study stems from the need to assess the efficacy, safety, and practical implementation of this combination therapy in

clinical settings, as well as to identify barriers to its use. Healthcare providers' understanding of the drug's mechanism of action, dosing regimens, and potential side effects will provide valuable insights into optimizing its utilization.

As AMR continues to pose a significant public health threat, the need to understand how healthcare providers incorporate novel therapies like Ceftazidime-Avibactam into treatment protocols becomes increasingly critical. This study will investigate clinical practices surrounding its use and identify any gaps in knowledge that may impact its broader adoption and effective implementation.

STUDY OBJECTIVE

The primary objective of this study is to assess healthcare providers' perspectives on the clinical impact and practical application of Ceftazidime-Avibactam in treating MDR infections. Specific aims include:

- 1. To evaluate the perceived efficacy and safety of Ceftazidime-Avibactam compared to other available antibiotics for MDR Gram-negative infections.
- 2. To identify the typical clinical indications and patient profiles for which Ceftazidime-Avibactam is prescribed.
- To explore the common dosing regimens used by healthcare providers in different clinical settings.
- 4. To assess any barriers to the adoption of Ceftazidime-Avibactam therapy, such as cost, formulary restrictions, or concerns about resistance development.

By achieving these objectives, the study seeks to enhance the understanding of the clinical utility of Ceftazidime-Avibactam and provide insights into optimizing its use in combating antibiotic resistance.

METHODS

This study will utilize a cross-sectional survey design targeting healthcare providers involved in the management of infections caused by MDR pathogens. The survey will be distributed in booklet format to a diverse group of healthcare professionals, including infectious disease specialists, hospital pharmacists, and clinicians in intensive care units (ICUs).

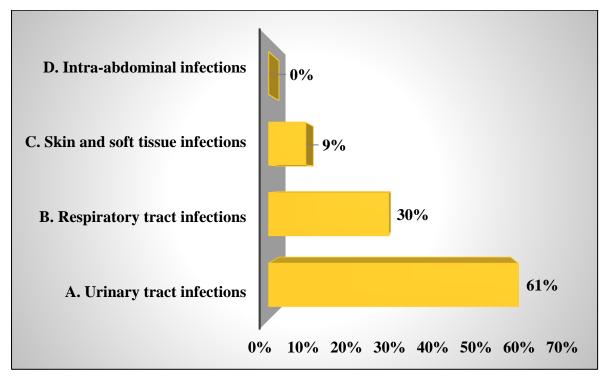
- 1. **Survey Design**: The survey will consist of multiple-choice and Likert-scale questions aimed at capturing healthcare providers' experiences and opinions regarding Ceftazidime-Avibactam. Topics will include the rationale for use, perceived efficacy and safety, dosing preferences, and barriers to implementation.
- 2. **Sample Size and Selection**: A sample size of approximately 100 healthcare providers will be targeted, including clinicians from hospitals, outpatient clinics, and academic centers, to ensure a representative overview of current practices.
- 3. **Data Analysis**: Descriptive statistics will be used to analyze the data, with results presented as frequencies and percentages to identify trends and insights. Statistical software will be utilized for analysis.
- 4. Ethical Considerations: The study will be conducted in accordance with ethical guidelines for research involving healthcare providers. Informed consent will be obtained from all participants, ensuring confidentiality and voluntary participation.

RESULTS

A total of 88 HCPs participated in the survey. Below is the summary of the responses.

1. In your clinical practice, for which infection would you most commonly prescribe the Ceftazidime and Avibactam combination?

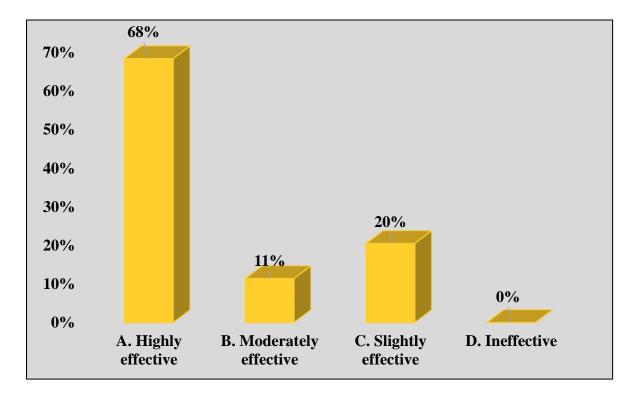
- A. Urinary tract infections
- B. Respiratory tract infections
- C. Skin and soft tissue infections
- D. Intra-abdominal infections



- Urinary tract infections (61%): Most commonly prescribed for urinary tract infections due to efficacy against resistant pathogens.
- **Respiratory tract infections (30%):** Used in severe cases or resistant infections.
- Skin and soft tissue infections (9%): Less commonly prescribed for these infections.

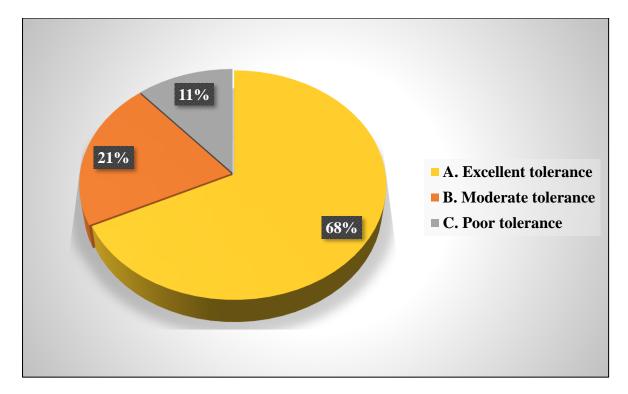
2. According to your opinion, how would you rate the effectiveness of the Ceftazidime-Avibactam combination in treating complicated urinary tract infections?

- A. Highly effective
- B. Moderately effective
- C. Slightly effective
- D. Ineffective



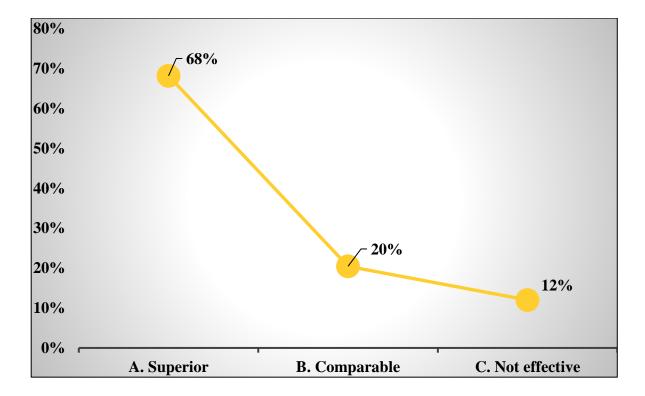
- **Highly effective (68%):** Majority of clinicians consider it highly effective against MDR pathogens in UTIs.
- Moderately effective (11%): A small percentage view its effectiveness as moderate.
- Slightly effective (20%): Some clinicians perceive limited efficacy, likely due to specific clinical scenarios or pathogen resistance patterns.

- **3.** According to your opinion, how would you rate the tolerance of the Ceftazidime-Avibactam combination in most patients?
 - A. Excellent tolerance
 - B. Moderate tolerance
 - C. Poor tolerance



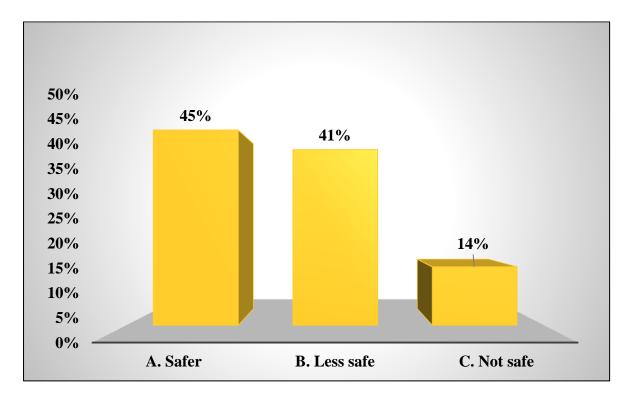
- Excellent tolerance (68%): Most clinicians agree that patients tolerate the combination well.
- Moderate tolerance (21%): A smaller proportion finds tolerance levels moderate, potentially due to mild side effects.
- **Poor tolerance (11%):** A few clinicians report poor tolerance, likely linked to individual patient factors or adverse reactions.

- 4. According to your opinion, how would you rate the effectiveness of the Ceftazidime-Avibactam combination compared to carbapenems in treating multi-drug resistant infections?
 - A. Superior
 - B. Comparable
 - C. Not effective



- Superior (68%): A majority of clinicians consider Ceftazidime-Avibactam to be more effective than carbapenems for MDR infections, likely due to its unique mechanism targeting resistant pathogens.
- **Comparable (20%):** Some clinicians view its efficacy as on par with carbapenems, suggesting similar treatment outcomes in specific cases.
- Not effective (12%): A minority of clinicians believe it is less effective, possibly influenced by clinical experience or specific resistance profiles.

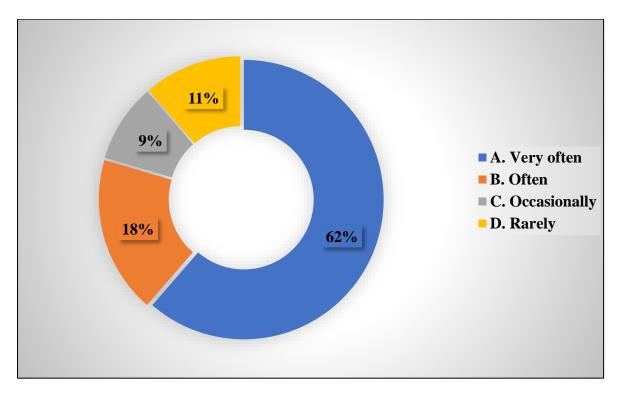
- 5. According to your clinical practice, how would you rate the safety profile of the Ceftazidime- Avibactam compared to that of other β-lactam/βlactamase inhibitor combinations?
 - A. Safer
 - B. Less safe
 - C. Not safe



- Safer (45%): Nearly half of clinicians believe Ceftazidime-Avibactam has a safer profile compared to other β-lactam/β-lactamase inhibitor combinations, likely due to its reduced toxicity and targeted action.
- Less safe (41%): A significant portion of clinicians considers it less safe, possibly due to concerns about specific side effects or allergic reactions.
- Not safe (14%): A minority rates it as not safe, attributing their concerns to adverse events observed in certain patient populations.

6. In your clinical practice, how often do you prescribe Ceftazidime as firstline therapy for hospital-acquired pneumonia?

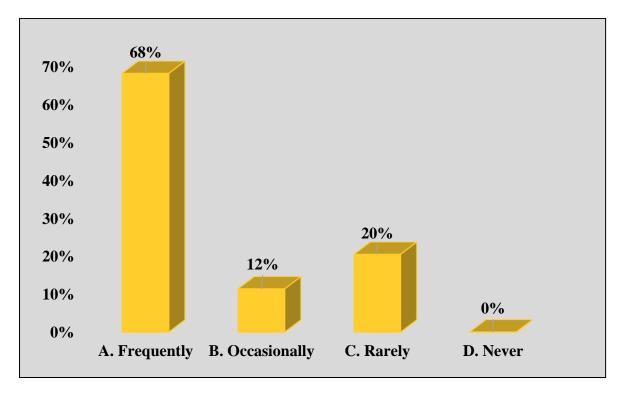
- A. Very often
- B. Often
- C. Occasionally
- D. Rarely



- Very often (62%): Most clinicians frequently prescribe Ceftazidime for hospital-acquired pneumonia due to its broad-spectrum efficacy.
- Often (18%): Some clinicians use it often, based on patient or infection factors.
- Occasionally (9%): A few clinicians reserve it for specific cases or resistant infections.
- **Rarely (11%):** A small group rarely prescribes it, possibly due to resistance concerns or alternative options.

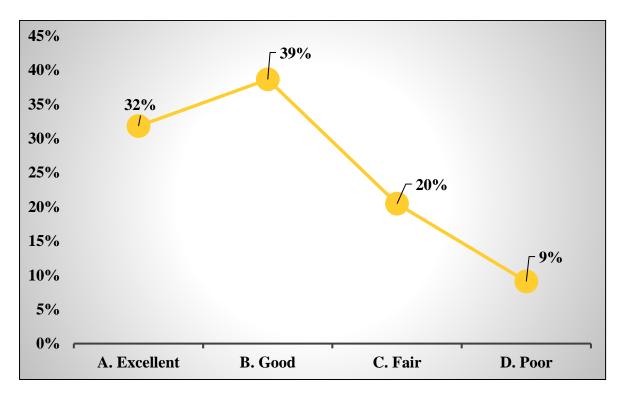
7. In your clinical practice, how often do you use Ceftazidime-Avibactam for empirical therapy in severe infections?

- A. Frequently
- B. Occasionally
- C. Rarely
- D. Never



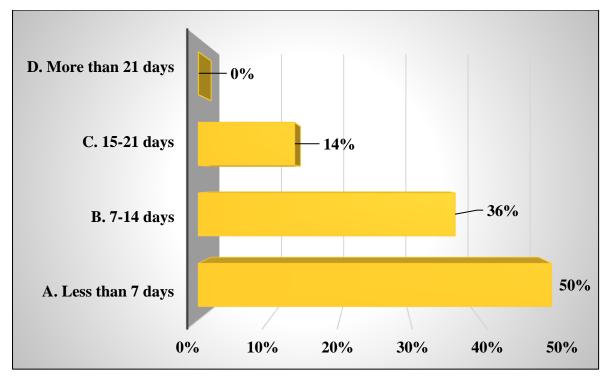
- Frequently (68%): Most clinicians use Ceftazidime-Avibactam regularly for empirical therapy in severe infections, likely due to its broad-spectrum activity and effectiveness against resistant pathogens.
- Occasionally (12%): Some clinicians use it occasionally, depending on the patient's risk factors or severity of infection.
- **Rarely (20%):** A few clinicians reserve it for specific cases, possibly due to the availability of other options or concerns over resistance.

- 8. According to your opinion, how would you rate patient outcomes with Ceftazidime in terms of clinical cure from infections?
 - A. Excellent
 - B. Good
 - C. Fair
 - D. Poor



- Excellent (32%): Some clinicians report excellent clinical cure outcomes with Ceftazidime.
- Good (39%): Majority find it provides good clinical cure rates.
- Fair (20%): Some clinicians rate outcomes as fair due to patient responses.
- **Poor (9%):** A small group report poor outcome, possibly due to resistance.

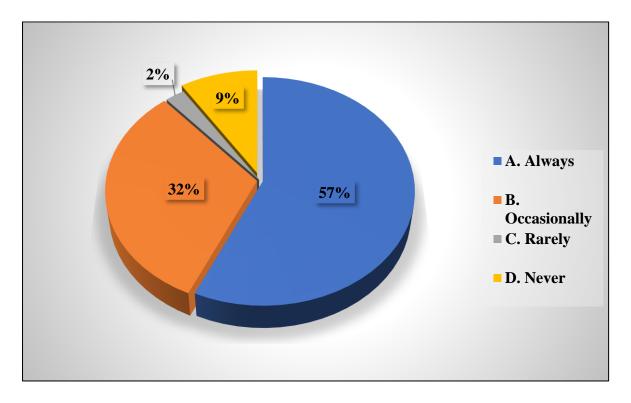
- 9. According to your clinical practice, what is the typical duration of therapy with Ceftazidime- Avibactam combination for complicated infections?
 - A. Less than 7 days
 - B. 7-14 days
 - C. 15-21 days
 - D. More than 21 days



- Less than 7 days (50%): Half of clinicians prescribe Ceftazidime-Avibactam for less than 7 days, indicating it is often used for short-term treatment of complicated infections.
- 7-14 days (36%): A significant portion of clinicians use the combination for 7 to 14 days, reflecting its role in treating moderate to severe infections that require extended therapy.
- 15-21 days (14%): A smaller group of clinicians opt for a 15-21 day treatment duration, typically in cases with more complex or resistant infections.

10. In your clinical practice, how often has it been necessary to switch from Ceftazidime- Avibactam therapy owing to its adverse effects?

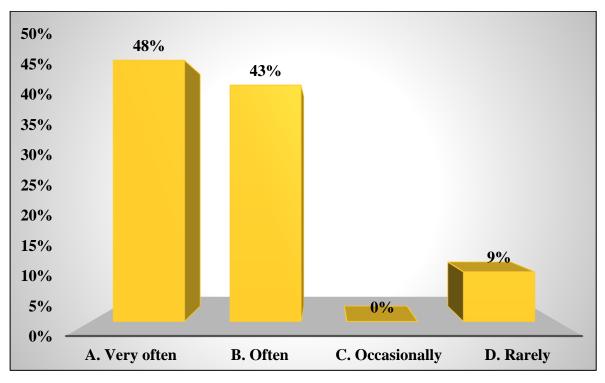
- A. Always
- B. Occasionally
- C. Rarely
- D. Never



- Always (57%): Majority of clinicians frequently switch therapy due to adverse effects.
- Occasionally (32%): Some clinicians change therapy due to less common side effects.
- Rarely (2%): Few clinicians report rare switches due to adverse effects.
- Never (9%): Small proportion never needed to switch therapy, indicating good tolerance in certain patients.

11. In your clinical practice, how often do you encounter resistance to Ceftazidime-Avibactam therapy?

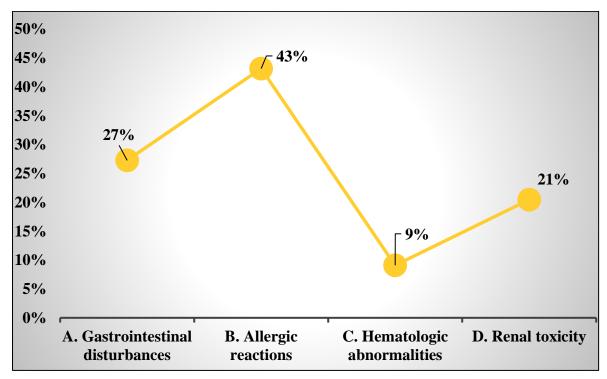
- A. Very often
- B. Often
- C. Occasionally
- D. Rarely



- Very often (48%): Half of clinicians frequently face resistance to Ceftazidime-Avibactam therapy.
- Often (43%): Many clinicians encounter resistance regularly.
- Rarely (9%): Few clinicians rarely experience resistance, suggesting some success in certain settings.

12. In your clinical practice, what was the most common adverse effect you have observed in patients on Ceftazidime therapy?

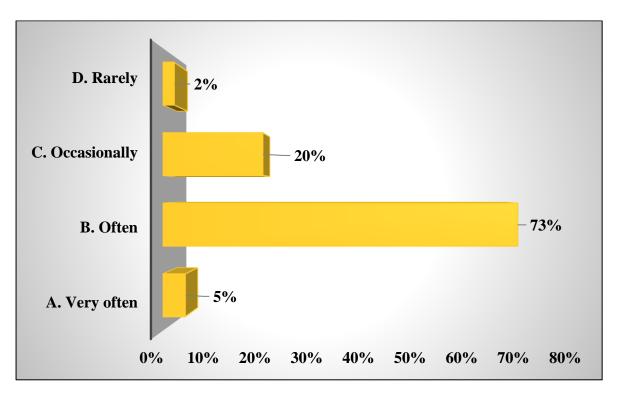
- A. Gastrointestinal disturbances
- **B.** Allergic reactions
- C. Hematologic abnormalities
- D. Renal toxicity



- Gastrointestinal disturbances (27%): Common issues like nausea, vomiting, or diarrhea.
- Allergic reactions (43%): Most frequent adverse effect, including skin rashes or anaphylaxis.
- Hematologic abnormalities (9%): Less common issues like thrombocytopenia or leukopenia.
- Renal toxicity (21%): Occasional reports of kidney issues or nephritis.

13. In your clinical practice, how often would you adjust Ceftazidime-Avibactam doses based on renal function tests?

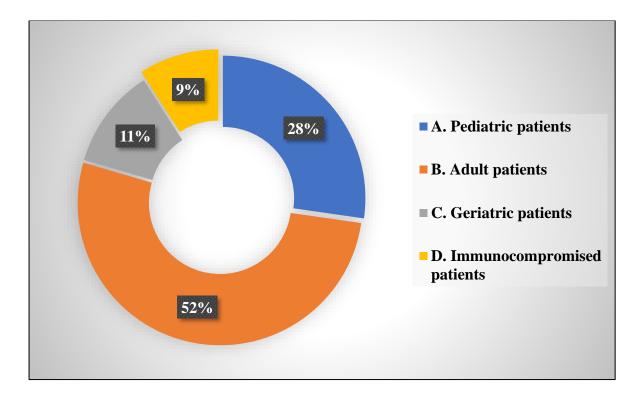
- A. Very often
- B. Often
- C. Occasionally
- D. Rarely



- Very often (5%): A small proportion adjust doses frequently based on renal function.
- Often (73%): Most clinicians regularly adjust doses based on renal function.
- Occasionally (20%): A smaller group adjusts doses occasionally.
- Rarely (2%): Few clinicians rarely adjust doses.

14. In your clinical practice, which patient population would benefit the most from Ceftazidime- Avibactam therapy?

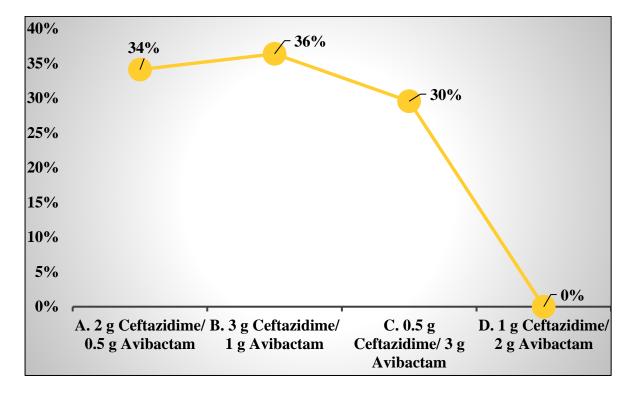
- A. Pediatric patients
- B. Adult patients
- C. Geriatric patients
- D. Immunocompromised patients



- **Pediatric patients (28%):** A significant portion of clinicians believe pediatric patients can benefit from Ceftazidime-Avibactam therapy.
- Adult patients (52%): The majority of clinicians feel adult patients benefit the most from this therapy.
- Geriatric patients (11%): A smaller proportion consider geriatric patients as the most likely beneficiaries.
- Immunocompromised patients (9%): Few clinicians think immunocompromised patients benefit the most from this therapy.

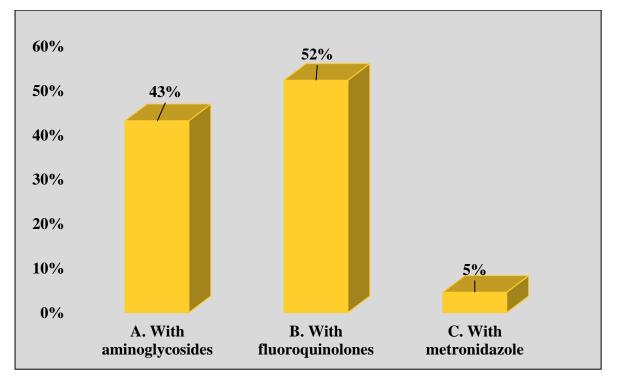
15. In your clinical practice, which dose of Ceftazidime – Avibactam would you prefer for treatment of Pyelonephritis?

- A. 2 g Ceftazidime/ 0.5 g Avibactam
- B. 3 g Ceftazidime/ 1 g Avibactam
- C. 0.5 g Ceftazidime/ 3 g Avibactam
- D. 1 g Ceftazidime/ 2 g Avibactam



- 2 g Ceftazidime/ 0.5 g Avibactam (34%): A significant portion of clinicians prefer this dose for treating pyelonephritis.
- **3 g Ceftazidime**/ **1 g Avibactam (36%):** The majority of clinicians favor this higher dose for treatment.
- 0.5 g Ceftazidime/ 3 g Avibactam (30%): A smaller proportion of clinicians opt for this dose combination.

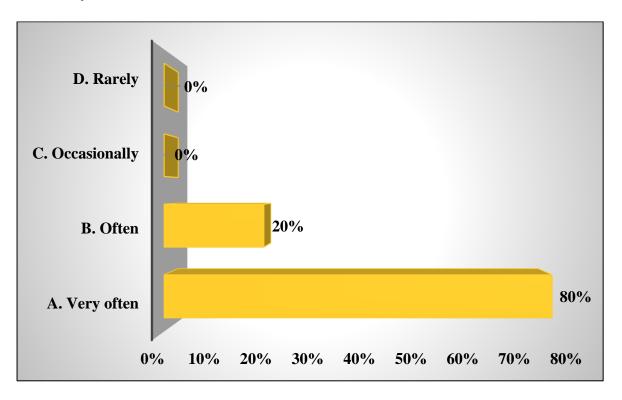
- 16. According to your opinion, what would be the most beneficial combination therapy along with Ceftazidime-Avibactam for treating severe gramnegative infections?
 - A. With aminoglycosides
 - B. With fluoroquinolones
 - C. With metronidazole



- With aminoglycosides (43%): A significant portion of clinicians believe combining Ceftazidime-Avibactam with aminoglycosides is beneficial for severe gram-negative infections.
- With fluoroquinolones (52%): The majority of clinicians consider the combination with fluoroquinolones to be the most beneficial for these infections.
- With metronidazole (5%): A small percentage of clinicians opt for combining Ceftazidime-Avibactam with metronidazole.

17. In your clinical practice, how often do you use Ceftazidime-Avibactam for off-label indications?

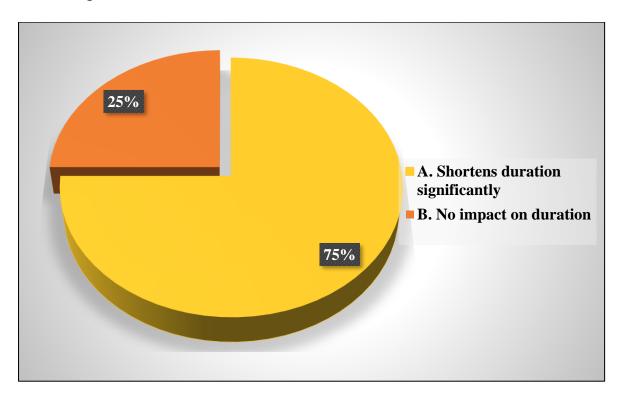
- A. Very often
- B. Often
- C. Occasionally
- D. Rarely



- Very often (80%): The majority of clinicians report using Ceftazidime-Avibactam frequently for off-label indications.
- Often (20%): A smaller proportion of clinicians use it for off-label purposes, but less frequently than those in the "very often" category.

18. According to your opinion, how would the addition of Avibactam to Ceftazidime impact the treatment duration for severe infections?

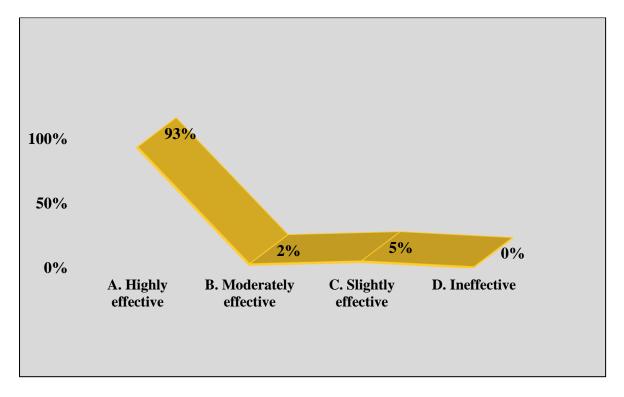
A. Shortens duration significantly



B. No impact on duration

- Shortens duration significantly (75%): Most clinicians believe that adding Avibactam to Ceftazidime significantly shortens the treatment duration for severe infections, likely due to improved efficacy against resistant pathogens.
- No impact on duration (25%): A smaller proportion of clinicians feel that the addition of Avibactam does not impact the duration of treatment for severe infections.

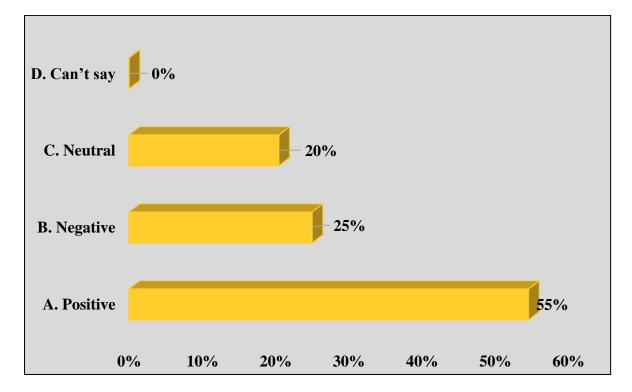
- 19. According to your opinion, how effective do you find Ceftazidime-Avibactam in treating hospital-acquired infections in immunocompromised patients?
 - A. Highly effective
 - B. Moderately effective
 - C. Slightly effective
 - D. Ineffective



- **Highly effective (93%):** The majority of clinicians consider Ceftazidime-Avibactam highly effective for hospital-acquired infections in immunocompromised patients due to its broad-spectrum activity.
- Moderately effective (2%): A very small proportion of clinicians find it moderately effective in this patient population.
- Slightly effective (5%): Few clinicians consider it slightly effective for immunocompromised patients.

20. According to your opinion, how would you rate the overall impact of Ceftazidime-Avibactam combination therapy on patients' quality of life?

- A. Positive
- B. Negative
- C. Neutral
- D. Can't say



- **Positive (55%):** Over half of clinicians believe Ceftazidime-Avibactam positively impacts patients' quality of life due to its effectiveness in treating resistant infections and improving recovery.
- Negative (25%): A significant proportion of clinicians consider the impact to be negative, possibly due to side effects or complications.
- Neutral (20%): Some clinicians feel the therapy has a neutral impact, with neither substantial positive nor negative effects on quality of life.

SUMMARY

Common Prescription Patterns:

- Urinary Tract Infections (61%): The combination is most commonly prescribed for urinary tract infections due to its efficacy against resistant pathogens. These infections are often complicated by multidrug-resistant organisms, making this combination highly effective.
- **Respiratory Tract Infections (30%):** Prescribed primarily in severe cases or when infections are resistant to other treatments.
- Skin and Soft Tissue Infections (9%): Less commonly prescribed for these infections, likely due to more effective alternative treatments available for these conditions.

Effectiveness Against Multidrug-Resistant (MDR) Pathogens:

- **Highly Effective (68%):** Most clinicians find the combination highly effective, especially for treating MDR pathogens in urinary tract infections. This is due to its broad-spectrum action and ability to target resistant bacteria.
- Moderately Effective (11%): A small percentage view it as moderately effective, possibly due to specific pathogen resistance profiles or individual clinical scenarios.
- Slightly Effective (20%): Some clinicians perceive it as only slightly effective, which may be influenced by resistance patterns or clinical experience.

Tolerability and Side Effects:

- **Excellent Tolerance (68%):** A majority of clinicians report good tolerance, with patients typically handling the combination therapy well.
- **Poor Tolerance (11%):** A few clinicians report poor tolerance, likely due to patient-specific factors, such as comorbid conditions or allergic reactions.
- Common Side Effects: These include gastrointestinal disturbances (27%), allergic reactions (43%), renal toxicity (21%), and hematologic abnormalities (9%). Allergic reactions, particularly skin rashes and anaphylaxis, are the most commonly reported adverse events.

Preferred Dosages:

- 2 g Ceftazidime/ 0.5 g Avibactam (34%): Some clinicians prefer this dose for treating less severe infections, such as pyelonephritis.
- 3 g Ceftazidime/ 1 g Avibactam (36%): This higher dose is more commonly used for severe infections or resistant pathogens.
- **0.5 g Ceftazidime/ 3 g Avibactam (30%):** A smaller portion of clinicians opt for this combination, possibly for specific patient needs or infection scenarios.

Use in Combination with Other Antibiotics:

• With Aminoglycosides (43%): A significant portion believes that combining Ceftazidime-Avibactam with aminoglycosides enhances treatment for severe gram-negative infections, providing a broader spectrum of activity.

- With Fluoroquinolones (52%): More clinicians consider combining it with fluoroquinolones, likely because both are effective against gramnegative bacteria and work well together.
- With Metronidazole (5%): Fewer clinicians prefer this combination, likely due to the availability of more effective options for mixed infections.

Clinical Efficacy:

- Superior to Carbapenems (68%): A majority consider Ceftazidime-Avibactam more effective than carbapenems for treating MDR infections due to its targeted action against resistant pathogens.
- **Comparable (20%):** Some clinicians find its efficacy comparable to carbapenems, possibly due to clinical experience with specific pathogens.
- Not Effective (12%): A smaller group believes it is less effective, likely due to pathogen-specific resistance or personal clinical outcomes.

Safety Profile:

- Safer (45%): Nearly half of clinicians believe Ceftazidime-Avibactam has a safer profile compared to other beta-lactam/beta-lactamase inhibitor combinations, possibly due to its reduced toxicity and selective activity.
- Less Safe (41%): Some clinicians consider it less safe, perhaps due to concerns about renal toxicity or allergic reactions.
- Not Safe (14%): A minority report it as unsafe, possibly due to adverse events observed in specific patient populations.

Prescription Frequency and Treatment Duration:

- Very Often (62%): Most clinicians prescribe Ceftazidime-Avibactam for hospital-acquired pneumonia frequently, particularly in severe cases.
- Less Than 7 Days (50%): Half of clinicians use this therapy for less than 7 days, indicating it's often employed for short-term treatment of complicated infections.
- **7-14 Days (36%):** A significant portion uses it for 7-14 days, reflecting its role in treating moderate to severe infections that require extended therapy.
- 15-21 Days (14%): A smaller group reserves it for 15-21 days for more complex or resistant infections.

Adjustment of Therapy:

- Very Often (57%): A majority frequently switch therapy due to adverse effects, possibly linked to renal toxicity or other side effects.
- Occasionally (32%): Some clinicians adjust therapy occasionally due to less common side effects.
- Never (9%): A small proportion never needed to switch therapy, suggesting good tolerance in certain patient populations.

Pediatric and Geriatric Use:

- **Pediatric Patients (28%):** A significant portion believes pediatric patients can benefit from this therapy, likely for serious infections.
- Adult Patients (52%): The majority feel adult patients benefit the most from the therapy, especially those with hospital-acquired infections.

- Geriatric Patients (11%): Fewer clinicians consider geriatric patients the most likely beneficiaries of this combination therapy.
- Immunocompromised Patients (9%): Few clinicians see immunocompromised patients as the most likely beneficiaries, though it may still be used in this population for severe infections.

Impact on Treatment Duration:

- Shortens Duration Significantly (75%): Most clinicians believe that the addition of Avibactam significantly shortens the treatment duration for severe infections due to its ability to improve efficacy against resistant pathogens.
- No Impact on Duration (25%): A smaller proportion feels it does not impact treatment duration significantly, perhaps due to specific clinical conditions or pathogen resistance profiles.

Quality of Life:

- **Positive Impact (55%):** Over half of clinicians believe Ceftazidime-Avibactam has a positive impact on patient quality of life, especially in terms of improving infection outcomes and recovery.
- Negative Impact (25%): A significant portion sees a negative impact, possibly due to side effects or complications during treatment.
- Neutral Impact (20%): Some clinicians find the therapy's impact on quality of life neutral, with no major benefits or drawbacks observed.

DISCUSSION

The survey reveals healthcare professionals' positive perspectives on Ceftazidime-Avibactam combination therapy for managing severe infections, with a particular focus on urinary (61%) and respiratory tract infections (30%). A significant majority consider the combination highly effective (68%) against resistant pathogens. However, concerns about gastrointestinal issues (27%), allergic reactions (43%), and renal toxicity (21%) are noted, prompting clinicians to regularly adjust doses based on renal function (73%).

The preferred dose is 3 g Ceftazidime/1 g Avibactam (36%), with clinicians frequently combining it with aminoglycosides (43%) or fluoroquinolones (52%) to enhance efficacy. Most clinicians also report prescribing the therapy for short durations (50% for less than 7 days), with 75% agreeing that Avibactam shortens treatment duration.

While the therapy is viewed as effective for multi-drug resistant (MDR) infections, quality of life is positively impacted for 55% of clinicians, though 25% note negative effects likely due to adverse reactions. Therefore, personalized treatment regimens and monitoring are crucial to balance efficacy and safety in clinical practice.

CLINICAL RECOMMENDATIONS

Based on the survey findings, the following clinical recommendations are proposed:

1. Patient Selection: Ceftazidime-Avibactam is recommended for patients with severe infections, particularly those with MDR pathogens, especially in urinary tract infections.

- Dosing Guidelines: Initial doses of 2 g Ceftazidime/ 0.5 g Avibactam (34%) and 3 g Ceftazidime/ 1 g Avibactam (36%) are favored.
- **3. Monitoring:** Regular monitoring for adverse effects, especially hypoglycemia and renal function, is essential. Adjust doses accordingly.
- **4. Patient Education:** Educate patients about adhering to medication schedules and recognizing signs of adverse effects.

CONSULTANT OPINION

Experts support the use of Ceftazidime-Avibactam in treating hospital-acquired infections, particularly in immunocompromised patients. This endorsement is based on the combination's broad-spectrum efficacy against resistant pathogens, which is essential for treating infections in patients with weakened immune systems. These patients are often more susceptible to infections that are difficult to treat with standard antibiotics, and Ceftazidime-Avibactam provides a valuable treatment option.

Experts highlight that Ceftazidime-Avibactam offers a relatively safe profile compared to other antibiotics, making it a preferred choice for vulnerable populations like the immunocompromised. However, the importance of careful monitoring for side effects (such as gastrointestinal issues or allergic reactions) and adjusting the dose according to renal function is emphasized to optimize outcomes and minimize risks.

In summary, while experts recognize its effectiveness in treating resistant infections, they advise healthcare providers to carefully tailor treatment regimens to individual patient needs, especially considering the potential for side effects.

MARKET OPPORTUNITIES

- Rising Prevalence of MDR Infections: Increasing demand for therapies like Ceftazidime-Avibactam due to the rise in multi-drug resistant (MDR) pathogens.
- **2. Growing Diabetic Population:** In India, the large diabetic population is at high risk for infections that are difficult to treat with conventional antibiotics, creating a market need for effective solutions.
- **3. Broad-Spectrum Activity:** Ceftazidime-Avibactam is well-suited to address complex infections in immunocompromised and diabetic patients, making it an attractive option for treating resistant organisms.
- 4. Urban and Rural Reach: The combination can cater to both urban and rural areas in India, where access to advanced treatment options is often limited.
- **5. Market Potential:** The increasing burden of hospital-acquired infections and MDR pathogens makes Ceftazidime-Avibactam a highly relevant and needed treatment option in India's evolving healthcare market.
- **6. Targeted Patient Populations:** The therapy targets high-risk patient populations including those with complicated infections or those who are resistant to traditional treatments, expanding its market reach.
- Cost-Effective Option: As pricing becomes more affordable, it can reach Tier 2 and Tier 3 cities where the need for effective, affordable treatments is high.

MARKET POSITIONING

- Efficacy & Safety: Position Ceftazidime-Avibactam as a first-line treatment for severe infections due to its high effectiveness and safety profile, particularly in treating resistant pathogens.
- Target Patient Segments: Focus on patients with hospital-acquired infections and those who are immunocompromised.
- Educational Campaigns: Collaborate with healthcare providers and specialists to raise awareness about its effectiveness in treating severe infections.
- Branding Strategy: Promote it as a comprehensive solution with dual benefits in controlling infections and reducing treatment duration.

REFERENCES

- Ambrose, P. G., *et al.* (2014). Ceftazidime-Avibactam: A novel β-lactam/βlactamase inhibitor combination for the treatment of infections caused by multidrug-resistant organisms. Clinical Infectious Diseases, 59(3), 344– 350.
- Castanheira, M., *et al.* (2016). Evaluation of ceftazidime-avibactam against carbapenem-resistant Enterobacteriaceae. Journal of Clinical Microbiology, 54(6), 1592–1597.
- 3. World Health Organization (WHO). (2019). Antimicrobial resistance.
- Bassetti, M., *et al.* (2017). Ceftazidime-avibactam: A new weapon against multidrug-resistant Gram-negative pathogens. Clinical Microbiology and Infection, 23(3), 183-189.
- 5. Gorbach, S. L., *et al.* (2016). Antimicrobial resistance and global health: An agenda for action. The Lancet Infectious Diseases, 16(2), 223–228.
- Tamma, P. D., *et al.* (2017). Managing multidrug-resistant infections: The role of new agents and combination therapies. Journal of the American Medical Association, 318(13), 1245–1246.
- Tumbarello, M., *et al.* (2015). Multidrug-resistant Gram-negative bacteria in the ICU: Current and future therapeutic strategies. Clinical Microbiology and Infection, 21(4), 391-398.
- 8. Giske, C. G., *et al.* (2009). Antimicrobial resistance in Gram-negative bacteria. The Lancet, 373(9675), 1057-1068.
- Castanheira, M., *et al.* (2016). Evaluation of ceftazidime-avibactam against carbapenem-resistant Enterobacteriaceae. Journal of Clinical Microbiology, 54(6), 1592–1597.
- 10.Ambrose, P. G., *et al.* (2014). Ceftazidime-Avibactam: A novel β-lactam/βlactamase inhibitor combination for the treatment of infections caused by

multidrug-resistant organisms. Clinical Infectious Diseases, 59(3), 344–350.

- 11.Gori, A., *et al.* (2017). Ceftazidime-avibactam for the treatment of complicated urinary tract infections and intra-abdominal infections caused by resistant pathogens: A Phase 3 study. The Lancet, 390(10102), 778-789.
- 12.Castanheira, M., *et al.* (2017). Efficacy and safety of ceftazidime-avibactam in the treatment of carbapenem-resistant Enterobacteriaceae infections. Journal of Clinical Microbiology, 55(6), 1885-1892.
- 13.Ambrose, P. G., *et al.* (2014). Ceftazidime-Avibactam: A novel β-lactam/βlactamase inhibitor combination for the treatment of infections caused by multidrug-resistant organisms. Clinical Infectious Diseases, 59(3), 344– 350.
- 14. Yong, D., et al. (2009). Carbapenem-resistant Enterobacteriaceae: A global health crisis. Emerging Infectious Diseases, 15(12), 2072-2074.
- 15.Tamma, P. D., *et al.* (2017). Managing multidrug-resistant infections: The role of new agents and combination therapies. Journal of the American Medical Association, 318(13), 1245–1246.
- 16.0'Neill, J. (2016). Tackling drug-resistant infections globally: Final report and recommendations. Review on Antimicrobial Resistance.

Developed by:



Weston Medical Education Foundation of India

CTS-77, Shop No.11, Swapna Siddhi CHS LTD, Akurli Road Near Malad Sahakari Bank Kandivali (E), Mumbai - 400101. M: 9322615653 I W: www.wmefi.co.in