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The Sri Lanka Prescriber

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Management of Urinary Tract Infections in Children

Abstract

Background: Urinary tract infection (UTI) is one of the most common bacterial infections in children, accounting for approximately 5% of febrile illnesses in those younger than two years. Prompt diagnosis and appropriate treatment is essential to prevent renal scarring, hypertension, and chronic kidney disease. This review provides an evidence-based overview of the diagnosis, management, prevention, and follow-up of childhood UTI, supported by illustrative clinical scenarios.

Clinical presentation and diagnosis: Clinical manifestations vary with age. Infants often present with non-specific symptoms such as fever, irritability, poor feeding, vomiting, or failure to thrive, whereas older children commonly experience dysuria, urinary frequency, loin pain, haematuria, and new-onset incontinence. Diagnosis requires urinalysis and urine culture, with a clean-catch midstream urine specimen as the preferred collection method. Interpretation of culture results depends on the method of urine collection.

Management: Treatment is guided by the site and severity of infection. Lower UTI is managed with oral antibiotics for 7 days, whereas pyelonephritis requires 10-14 days of therapy. Intravenous antibiotics are recommended for neonates, infants younger than three months, and children with severe illness or inability to tolerate oral treatment. Imaging studies, including renal ultrasonography, micturition cystourethrogram, and DMSA scintigraphy, should be performed selectively according to clinical indications rather than routinely.

Conclusion: Prevention focuses on adequate hydration, management of constipation, regular bladder emptying, and good perineal hygiene. Long-term antibiotic prophylaxis is reserved for selected high-risk children. A systematic approach to diagnosis, evidence-based antimicrobial therapy, appropriate imaging, and structured follow-up is essential to optimise outcomes and minimise long-term renal complications in children with UTI.

Background

Urinary tract infections (UTIs) are among the most common bacterial infections encountered in childhood, accounting for approximately 5% of febrile illnesses in children less than two years of age. A UTI is defined as the presence of a pathogenic microorganism in the urinary tract together with symptoms of infection [1].

Clinical Presentation

The clinical presentation of UTI in children varies considerably with age. In infants and toddlers, the condition typically manifests with non-specific features such as fever, irritability, poor feeding, vomiting, and failure to thrive [2]. In older children, the presentation more closely resembles that seen in adults, with symptoms including dysuria, increased urinary frequency, haematuria, lower abdominal or loin pain, secondary incontinence, and enuresis [3].

Clinical Evaluation

A thorough clinical evaluation should include a systematic review for underlying risk factors that may predispose to UTI or its recurrence [4]. These include a history of congenital abnormalities of the kidney and urinary tract (CAKUT), constipation, bladder dysfunction (such as poor urinary stream or incontinence), anatomical variants including labial adhesions, tight prepuce or phimosis, as well as physical findings such as a palpable bladder, ballotable kidneys or spinal lesions.

Diagnosis

Urine Sample Collection

Urine culture is essential for the confirmation of UTI. The preferred method of urine sample collection for both urinalysis and culture is the clean catch midstream urine (CCMSU) sample. In children under two years of age, a clean catch urine (CCU) or bag urine specimen is acceptable for urinalysis only [5]. In acutely ill children requiring urgent antibiotic therapy, or when CCMSU is difficult to obtain, an in-out catheter sample is appropriate. Suprapubic aspiration (SPA) represents the most sterile collection method and should be performed under ultrasound guidance [6].

Urinalysis and Culture Interpretation

A positive urinalysis is defined as greater than 5 white blood cells per high power field (WBC/HPF) in centrifuged urine. The interpretation of urine culture results depends on the method of collection, as summarised in Table 1. Contamination during collection should be suspected in the presence of more than one species of colony-forming organisms, non-uropathogenic organisms, insignificant colony-forming unit counts, or epithelial cells on urine microscopy [7].

Table 1: Interpretation of Urine Culture Results by Collection Method

Method of Collection	Colony Count of a Single Uropathogen
CCMSU	$>10^5$ (10^4-10^5 may be positive if clinically or urinalysis is suggestive)
In-out catheter	$>10^5$
Supra-pubic aspiration	Any growth is significant. Performed under ultrasound guidance and when in-out catheter samples cannot be obtained

Management

General Principles

Early initiation of antibiotic therapy is critical, particularly in cases of suspected pyelonephritis. Children who are very ill should be admitted for further assessment, including a full blood count (FBC), renal profile, C-reactive protein (CRP) and blood culture.

Antibiotic Therapy and Duration (Table 2)

Upper UTI / Pyelonephritis requires 10 to 14 days of antibiotic therapy. Infants under three months of age should initially receive intravenous (IV) antibiotics for 48 to 72 hours before changing to oral therapy to complete the course. Children over three months of age who are sick (having vomiting, poor perfusion or diarrhoea) should likewise be commenced on IV antibiotics initially, while those with less severe presentations may be managed with oral antibiotics alone [8].

Lower UTI (Cystitis) is treated with oral antibiotics for 7 days.

Classification of UTI

UTI may be classified as atypical or complicated, and as recurrent. Atypical or complicated UTI is defined by one or more of the following features: a seriously ill child, obstructive uropathy (poor urine stream, palpable bladder or kidneys), raised serum creatinine, septicaemia, poor response to antibiotics within 48 hours or infection with atypical organisms such as *Pseudomonas aeruginosa*. Recurrent UTI is defined as two or more UTIs with at least one upper UTI, or three or more lower UTIs.

Radiological Investigations

Radiological evaluation is guided by the clinical classification of UTI [9]. An ultrasound scan (USS) of the kidneys, ureters, and bladder (KUB) is recommended for all children following the first episode of upper UTI or pyelonephritis. A micturition cystourethrogram (MCUG) is indicated in infants with complicated or recurrent UTI or in those with an abnormal USS suggesting outflow obstruction or vesico-ureteric reflux (VUR). A DMSA (dimercaptosuccinic acid) scan is recommended in cases of complicated or recurrent UTI and should be performed no earlier than four to six months after the acute infection. A DTPA (diethylenetriaminepentaacetic acid) scan is indicated when USS suggests urinary tract obstruction at the pelvi-ureteric junction (PUJ) or vesico-ureteric junction (VUJ), or to assess differential renal function.

Practices Not Recommended

Routine urine culture in asymptomatic children at the completion of an antibiotic course or during clinic follow-up is not recommended. Antibiotic treatment for asymptomatic bacteriuria is not indicated. Antibiotic prophylaxis, DMSA scanning, and MCUG are not recommended as routine investigations for all children following the first episode of uncomplicated UTI [7].

Prevention of Recurrence

General preventive measures include ensuring adequate water intake, avoiding constipation, encouraging regular and complete bladder emptying, and maintaining good perineal hygiene. Antibiotic prophylaxis is indicated for infants and young children with complicated UTI or recurrent UTI associated with structural abnormalities [10].

Table 2: Antibiotic Treatment for UTI in Children [6,8]

Clinical Setting	First-Line	Alternatives / Notes	Duration
Lower UTI (Cystitis)	Oral Co-amoxiclav 30 mg/kg/dose 8 hourly OR Cefalexin 12.5–25 mg/kg/dose 8 hourly OR Cefuroxime 12.5 mg/kg/dose 12 hourly	Trimethoprim 4 mg/kg/dose 12 hourly (if >6 weeks) OR Co-trimoxazole 24 mg/kg/dose 12 hourly	7 days
Upper UTI / Pyelonephritis – mild to moderate	Oral Co-amoxiclav 12.5 mg/kg/dose 8 hourly OR Oral Cefuroxime 12.5 mg/kg/dose 12 hourly OR Cefixime 8 mg/kg/day in 2 doses	If resistant organism, use according to culture and sensitivity	10-14 days
Severe UTI / Pyelonephritis – requiring IV	IV Co-amoxiclav 30 mg/kg/dose 8 hourly OR IV Cefotaxime 50 mg/kg/dose 8 hourly OR IV Ceftriaxone 50–75 mg/kg/day OD	IV Amikacin 7.5 mg/kg/dose 12 hourly or 15 mg/kg OD (if cephalosporin resistant)	IV 48–72 hrs then step down to oral to complete 10–14 days
Neonate (<3 months) - Pyelonephritis – requiring IV	IV Cefotaxime 50 mg/kg/dose 8 hourly ± Amikacin 7.5 mg/kg/dose 12 hourly or 15 mg/kg/day	Avoid ceftriaxone in neonates	IV 5-7 days then step down to oral to complete 14 days
Prophylaxis (recurrent/complicated UTI)	Trimethoprim 2 mg/kg OD (night) OR Co-trimoxazole 12–24 mg/kg OD (night) OR Nitrofurantoin 1 mg/kg OD (night, if >3 months) OR Cefalexin 12.5 mg/kg OD (night) OR Nalidixic acid 15 mg/kg/dose morning and night (if >3 months)	Usually continued for 6–24 months; reassess periodically	—

OD: Once daily

Follow-Up (7)

Children with evidence of structural anomalies of the kidney, ureter, or bladder require regular assessment. Those with significant renal parenchymal defects should have their height, weight, blood pressure, and urinary protein monitored on an ongoing basis. Children with a history of recurrent or atypical/complicated UTIs should be referred to a paediatric nephrologist for further evaluation.

Case Scenario 1

"Neurogenic Bladder and Vesicoureteral Reflux in a Child with Repaired Myelomeningocele"

Patient Presentation:

A 3-year-old girl with a history of ruptured myelomeningocele repair on day 3 of life presented with high-grade fever, vomiting, and vague abdominal pain for 5 days. There were three previous similar episodes treated in the community with oral antibiotics. She also had gross motor developmental delay and chronic constipation requiring intermittent laxatives since one year of age.

Examination:

Ill-looking, febrile, haemodynamically stable.

Abdominal examination revealed a distended bladder, palpable faecal masses, and right renal angle tenderness.

Investigations:

• **Blood tests:** Neutrophilic leukocytosis, elevated CRP (110 mg/L), normal renal function, sterile blood culture.

• **Urinalysis:** Numerous pus cells; urine culture grew *Escherichia coli* (>10^5 CFU/mL).

• **Ultrasound KUB:** Bilateral hydronephrosis, hydroureters, and right pyelonephritis.

• **MCUG:** Bilateral Grade III vesicoureteric reflux with trabeculated, thick-walled bladder.

• **Tc-99m DMSA:** Right kidney upper pole cortical scarring; left kidney normal.

Management:

Child was started on intravenous Cefotaxime (50 mg/kg every 8 hours) for 10 days with good response. She was discharged on Co-trimoxazole prophylaxis and regular laxatives. MRI spine, physiotherapy, occupational therapy, and referrals to neurology and neurosurgery were arranged. Further follow-up at the nephrology clinic included assessment for the need for clean intermittent catheterization (CIC).

Key Learning Points

• Children with repaired myelomeningocele are at high risk of neurogenic bladder and recurrent UTIs.

• Early urological assessment and imaging are essential to detect complications such as VUR and cortical scarring.

• Long-term multidisciplinary care (nephrology, neurology, urology, physiotherapy) is vital to prevent progressive renal damage.

Case Scenario 2

"Posterior Urethral Valve Presenting with Recurrent Urinary Tract Infection and Failure to Thrive in an Infant"

Patient Presentation:

A six-month-old boy with a background history of failure to thrive since the late neonatal period presented with a four-day history of high-grade fever, irritability, vomiting, and poor feeding. A similar episode occurred at three months of age, treated with oral antibiotics at an outpatient clinic. The mother also reported a poor urine stream since birth.

Examination:

The child was ill-looking and febrile with abdominal distension. Anthropometry revealed severe malnutrition (weight < -3 SD, length between -2 and -3 SD, weight-for-length < -3 SD).

Investigations:

• **Blood tests:** Neutrophilic leukocytosis, CRP 130 mg/L, creatinine 90 µmol/L.

• **VBG:** Normal anion gap metabolic acidosis.

• **Urinalysis:** Catheterized sample - field full of pus cells.

• **Urine culture:** Failed due to unsuccessful in-and-out catheter sampling prior to antibiotics.

• **Ultrasound KUB:** Distended bladder with thickened wall.

• **MCUG:** Bilateral Grade III vesicoureteral reflux, hydroureter, hydronephrosis, trabeculated bladder, and dilated posterior urethra consistent with posterior urethral valve (PUV).

Management:

• Urinary catheterization following surgical referral.

• Intravenous Cefotaxime 50 mg/kg every 8 hours for 10 days followed by oral antibiotics for 4 days to complete a total of 14 days of antibiotics with good clinical response.

• Managed as UTI complicated with obstructive uropathy.

• Renal function normalized following catheterization.

• Nutritional rehabilitation initiated.

• Referred to paediatric surgical team for posterior urethral valve ablation.

• Discharged with planned follow-up at nephrology and surgical clinics.

Key Learning Points

• Posterior urethral valve should be suspected in male infants with poor urine stream, recurrent UTIs, and growth failure.

• Early diagnosis and surgical intervention are crucial to prevent irreversible renal damage.

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Self-Assessment Questions - Management of Urinary Tract Infections in Children

Question 1

Which of the following statements are True (T) or False (F) regarding UTI in children?

a) In children aged <2 years, a bag urine sample is acceptable for urine culture.
b) Positive urinalysis is considered >5 WBC/HPF in uncentrifuged urine sample.
c Urine sample should be transported to the lab within two hours of collection
d) Infants are known to present as failure to thrive.
e) Prevention of constipation is crucial in preventing recurrent UTI.

Answers – F, F, T, T, T

Question 2

Which of the following statements are True (T) or False (F) regarding UTI in children?

a) Performing routine urine cultures in an asymptomatic child during clinic follow-up is recommended.
b) Antibiotic prophylaxis is recommended in all children less than 6 months of age following the first episode of uncomplicated UTI.
c) Ultrasound scan KUB should be performed after first episode of upper UTI/pyelonephritis.
d) Infants <3 months with upper UTI/pyelonephritis need initial treatment with intravenous antibiotics.
e) Ceftriaxone is recommended to be used as second-line treatment in neonates.

Answers – F, F, T, T, F

Question 3

A two-month-old baby boy, second-born to healthy non-consanguineous parents (one healthy sibling), presented to OPD with a history of fever, poor feeding, and irritability for 2 days.

Examination findings:

- Temperature: 102°F (axillary), ill-looking
- Pulse rate: 124/min
- Capillary refill time: <3 sec
- Respiratory rate: 30/min
- Lungs: Clear
- Abdomen: Distended, bowel sounds present

Anthropometry:

- Weight: -2SD to -3SD
- Length: -1SD to -2SD
- Weight/Length: -2SD to -3SD

Investigations:

- WBC: 23 × 10^9/L
- Hb: 10.9 mg/dL
- Platelets: 230 × 10^3/L
- CRP: 240 mg/dL
- UFR: Moderately field full pus cells, field full red cells
- Urine and blood cultures: Pending
- Ultrasound KUB: Awaiting

Which of the following is the most appropriate step in management?

a) Oral antibiotics as outpatient therapy may be effective in the initial management of this condition.
b) In-out catheter sample for culture and ABST must be attempted before initiating antibiotic therapy if clean catch mid-stream urine sample is difficult.
c) DMSA scan must be arranged within 3 month on discharge.
d) Absence of intermittent urine stream in the history excludes the possibility of posterior urethral valve in this child.
e) Urine culture must be repeated after completion of IV antibiotics.

Answer- B

Evidence-Based Approach to Constipation: Diagnosis, Management, and Specialist Referral

Introduction

Constipation is a prevalent gastrointestinal issue, affecting about 15% of the global population [1]. Functional constipation (FC), defined by the Rome IV criteria, is a gastrointestinal disorder characterized by chronic symptoms lasting at least 6 months, with criteria met for the previous 3 months. Diagnosis includes 2 or more of the following symptoms in ≥25% of bowel movements: straining, lumpy or hard stools (Bristol Stool Form Scale types 1-2), incomplete evacuation, anorectal obstruction, or manual maneuvers for defecation. Additional criteria include fewer than three spontaneous bowel movements per week and rare loose stools without laxatives. FC is differentiated from irritable bowel syndrome (IBS) by the lack of predominant abdominal pain. Opioid-induced constipation (OIC) is excluded from FC diagnosis for research but may coexist clinically [2].

While NHS England generally encourages self-care for simple, short-term constipation, clinicians must remain proactive in identifying and addressing cases with complex underlying causes or chronic presentations [3]. The initial management strategy should prioritize non-pharmacological interventions. When necessary, a stepped approach to pharmacological therapy can be implemented. A key component of effective management is recognizing and addressing any secondary causes, which may include systemic conditions or side effects from medication [1].

Diagnostic Approach

The diagnosis of chronic idiopathic constipation primarily relies on clinical evaluation through detailed history-taking and physical examination. Clinicians should gather comprehensive information on bowel frequency, stool consistency (utilizing the Bristol Stool Scale), straining, sensations of incomplete evacuation, use of digital maneuvers, and the duration of symptoms.

Physical examinations should include an abdominal assessment, visual inspection of the perianal region, and a digital rectal examination (DRE). This examination is crucial for assessing anal sphincter tone, the content of the rectal vault, and identifying any masses, hemorrhoids, or fissures.

Clinicians should be vigilant for red flag symptoms (Table 1). These symptoms necessitate urgent specialist referral and potential colonoscopy to rule out malignancy [4].

Table 1. Alarming Features Requiring Referral

Red Flag Symptoms for Urgent Specialist Referral/Colonoscopy
Rectal bleeding
Unexplained weight loss
Severe abdominal pain
Nocturnal symptoms
Anorexia
Tenesmus
New-onset constipation in patients over 50 years of age

For patients suspected of having defecatory dysfunction or obstructed defecation syndrome (ODS), characterized by excessive straining, prolonged defecation time, sensations of incomplete evacuation, or reliance on digital maneuvers. Clinicians should consider specialized testing such as anorectal manometry and balloon expulsion testing.

In cases of refractory constipation, colonic transit studies using radiopaque markers may assist in distinguishing between slow transit constipation and normal transit accompanied by defecatory dysfunction. Additionally, defecography (either fluoroscopic or MRI-based) can be advantageous for identifying structural pelvic floor abnormalities in complicated scenarios (Table 2) [5].

Table2. Diagnostic Investigations

Investigations	Indications
Anorectal manometry	Defecatory dysfunction Obstructed defecation syndrome (ODS)
Balloon expulsion test	Defecatory dysfunction Obstructed defecation syndrome (ODS)
Colonic transit studies	Refractory constipation
Defecography	Pelvic floor abnormalities

Non-Pharmacological Management

The foundation of effective management of constipation lies in a holistic approach that

emphasizes lifestyle modification across three main areas: dietary changes, defecatory habits, and general lifestyle adjustments.

Dietary Modifications:

• Aim to gradually increase dietary fiber intake to about 20-35g per day. This can be achieved by incorporating a variety of fruits, vegetables, legumes, and whole grains into the meals.

• It is crucial to pair this increased fiber intake with adequate hydration, consuming at least 1.5 liters of water daily. This helps maintain optimal stool consistency and mitigates issues that may arise from fiber supplementation. If necessary, consider using bulk-forming laxatives to help reach the target fiber goal [1].

Defecatory Modifications:

• Educating patients about the gastrocolic reflex can enhance their defecatory habits. Encourage attempts to have bowel movements during peak colonic motility times, particularly within two hours of waking and 30 minutes after meals.

• Correcting defecation posture can significantly improve bowel emptying. Using a footstool to achieve a squat-like position can reduce the anorectal angle, easing stool passage.

• Implementing habit training, with scheduled toileting attempts twice daily, has shown benefits, particularly for those with physical challenges.

General Lifestyle Recommendations:

• Incorporate regular physical activity that fits the patient's abilities, aiming for at least 150-200 minutes of moderate aerobic exercise weekly [1].

• Review and address any medications contributing to constipation, such as opioids and anticholinergics, especially in elderly patients who may face multiple risk factors like decreased mobility and polypharmacy.

• Understand that temporary constipation due to lifestyle changes (e.g., travel or post-surgery) typically responds well to these conservative measures.

Pharmacological Management

When lifestyle changes are insufficient, employing a stepwise pharmacological approach based on the severity of symptoms is the key (Table 3,4).

• Mild Constipation:

Mild constipation is defined as 3 or fewer bowel movements per week and may be accompanied by hard, dry or lumpy stools, excessive straining or a sensation of incomplete evacuation responding to lifestyle modifications ± bulk-forming agents [4,5]. Stool softeners (e.g., docusate sodium) are beneficial when minimizing straining is necessary.

Table 3. Mild constipation Treatment

Treatment Recommendation	Recommended Agents	Evidence Summary
First-line therapy	Bulk-forming laxatives (e.g., ispaghula husk, methylcellulose)	Bulk-forming laxatives are recommended as first-line therapy because they are safe and effective in increasing fecal bulk and improving bowel movements.
Second-line therapy	Osmotic laxatives (e.g., Polyethylene glycol(PEG), Lactulose)	Consider osmotic laxatives if symptoms are inadequately controlled with bulk-forming agents. PEG is generally preferred over lactulose due to better tolerability and effectiveness.

• Moderate Constipation:

Symptoms that last and require medical assessment, particularly when they have persisted more than three weeks, are very uncomfortable or are accompanied by warning signs such as abdominal pain or change in stool caliber [4,5].

Prescription medications, such as selective 5-HT4 agonists (prucalopride), can be beneficial. These agents enhance intestinal fluid secretion and reduce abdominal discomfort, particularly for patients with constipation-predominant irritable bowel syndrome [5].

• Severe Cases:

For situations like fecal impaction, immediate manual disimpaction may be required, followed by colonic evacuation using high-volume PEG solutions or enemas. It is essential to implement maintenance therapy with osmotic agents to prevent recurrence.

Opioid-Induced Constipation (OIC):

• Utilize a combination of osmotic (like PEG) and stimulant laxatives for OIC. For cases that are refractory, consider specialist options such as peripherally acting μ-opioid receptor antagonists (naloxegol) or selective 5-HT4 agonists under supervision to restore gut motility [4].

Table 4. Classification of Laxatives

Class	Mechanism	Indication	Adverse effects
Bulk-forming	Absorb water in the intestine and increase stool bulk	Mild constipation	Bloating, flatulence, abdominal distension
Osmotic laxative	Raise osmotic pressure in the intestinal lumen, drawing water into the bowel to soften stool and stimulate bowel movements	Persistent constipation	Diarrhea Abdominal cramps, bloating, dehydration
Stimulant laxative	Stimulate enteric nerves to increase intestinal motility and promote secretion of water and electrolytes into colon	Opioid-induced constipation	Abdominal cramps, diarrhea, nausea, electrolyte imbalance
Stool softeners	Soften stool	Avoid straining	Mild abdominal cramps
Selective 5-HT4 Agonist (Prokinetic Agents)	Stimulate 5-HT4 receptors in the enteric nervous system, enhancing colonic peristalsis and accelerating gastrointestinal transit	Refractory constipation	Headache abdominal pain, dizziness

This structured approach allows for tailored management of constipation while acknowledging that patients with obstructive defecation syndrome (ODS) may require specialized interventions.

Management of Obstructed Defecation Syndrome (ODS)

Obstructed Defecation Syndrome (ODS) can significantly impact patients' quality of life, and effective management begins with a thorough evaluation. For individuals suspected of ODS, anorectal manometry (ARM) plays a vital role in assessing anorectal function [1].

Recent findings in Sri Lanka highlight that nearly 50% of ODS patients exhibit dyssynergic defecation Type 1, characterized by paradoxical contractions, especially among men over 50. This evidence emphasizes the necessity of physiological evaluation, particularly in challenging cases.

Biofeedback therapy stands out as the most effective treatment approach for ODS, as traditional pharmacological treatments often fall short [5]. Referral to a specialized colorectal center is critical to access this non-pharmacological method.

Surgical Management for Refractory Cases

Surgery is reserved for a specific group of patients with chronic, treatment-resistant constipation who meet stringent criteria. The primary surgical option is a colectomy with ileorectal anastomosis, which is suitable for patients with confirmed slow colonic transit times and absent defecatory dyssynergia [5]. Surgery should only be considered after all non-surgical therapies, such as laxatives and biofeedback, have been thoroughly attempted and proven ineffective.

Prevention and Patient Education

Preventive measures for constipation align closely with the management strategies discussed, focusing on healthy lifestyle changes. Adequate fiber intake (20-35 g/day), sufficient hydration (at least 1.5 liters of water daily), and regular exercise are essential [1]. Patients should aim for symptom relief rather than being fixated on daily bowel movements, as natural patterns can vary significantly.

Gradual fiber intake increases can help minimize bloating, while consistent toileting habits, preferably after meals or in the morning, can enhance natural colonic activity. Keeping a bowel diary can assist in tracking symptoms and responses to treatment, promoting adherence and better outcomes.

For patients on opioids, initiating prophylactic laxatives (such as PEG or stimulant laxatives) at the beginning of therapy can prevent constipation. If the use of laxatives is no longer necessary, they should be tapered gradually rather than stopped abruptly to avoid rebound constipation. Providing patient education material, such as leaflets and digital resources, can reinforce these strategies effectively.

Conclusion

Effectively managing chronic constipation necessitates a comprehensive strategy starting with dietary and lifestyle changes for all patients. A systematic approach should be employed, beginning with osmotic laxatives when necessary, and progressing to stimulant laxatives if symptoms persist. It is vital for clinicians to identify and address any secondary factors contributing to constipation and to rule out differential diagnoses.

Particular attention should be given to medications that may exacerbate constipation, such as opioids and anticholinergics. This is especially important for elderly patients, who often face multiple risk factors such as reduced mobility and polypharmacy. In cases of persistent constipation where controllable factors or alarm symptoms are absent, secretagogue therapy could offer benefits [4].

Fecal impaction requires immediate action, starting with manual disimpaction, followed by effective colonic evacuation and an appropriate maintenance plan. For patients who continue to experience symptoms despite ongoing treatment, or who present with red flag signs or suspected defecatory dysfunction, a thorough re-evaluation and potential referral to a specialist are recommended.

It's also essential for clinicians to recognize that transient constipation due to lifestyle changes, such as travel or recovery from surgery, generally responds well to conservative measures. By adopting a tailored, patient-centered approach, healthcare providers can enhance treatment outcomes while minimizing the risk of complications (Figure1). This holistic perspective not only addresses the immediate symptoms but also promotes overall gastrointestinal health and well-being.

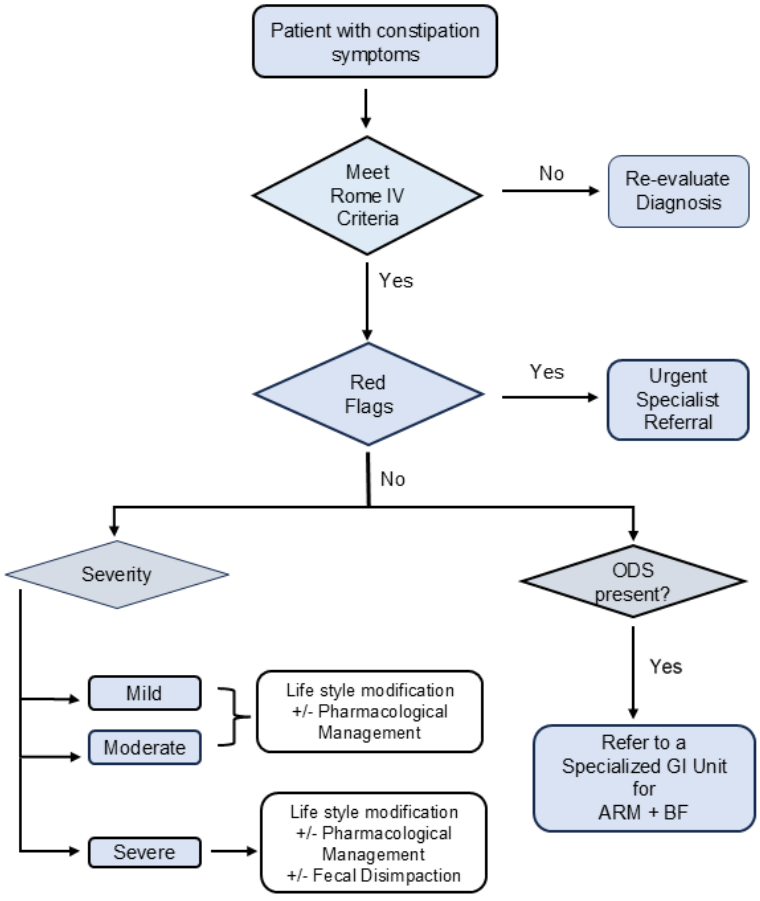

Figure 1: Clinical Decision Pathway for Chronic Constipation: From Diagnosis to Specialist Referral

Summary:

Constipation is a common gastrointestinal complaint with varying etiologies, ranging from lifestyle-related factors to functional and secondary causes. This article provides an evidence-based overview of the diagnosis and management of constipation in adults, focusing on differentiating between mild and refractory cases. It highlights the role of lifestyle interventions, pharmacological options, and the criteria for specialist referral. To enhance practical

understanding, three case scenarios are included to illustrate the stepwise management strategies for both mild and severe constipation.

Case Scenarios

Case 1: Mild Constipation Responsive to Lifestyle and Bulk-Forming Agents

Patient: A 28-year-old female teacher presents with a 3-month history of infrequent bowel movements, straining, and hard stools. She has fewer than three spontaneous bowel movements per week, with no red flag symptoms or alarm features.

Evaluation:

• Bristol Stool Type 2-3

• No weight loss or rectal bleeding

• Digital rectal examination normal

• Diagnosis: Functional constipation (Rome IV criteria)

Management:

The patient was managed with a stepwise, non-pharmacologic approach:

• Counseled on dietary modifications including gradual increase in fiber intake to 20–25 g/day using whole grains, fruits, and vegetables. (Practically advised increasing dietary fiber by aiming for 4-5 portions of fruits and vegetables daily, in line with local dietary habits. This included having a fruit like a banana, apple, or slice of papaw after each main meal (breakfast, lunch, and dinner) and 1–2 portions of vegetables, such as 3 tablespoons of cooked vegetables or 1 cup of "mallum" (finely shredded greens), during the main meal. Whole grains were recommended as a replacement for white rice or plain flour, with the note that fiber intake should be balanced with calorie control, especially in overweight individuals.)

• Advised to maintain adequate hydration. (1.5-2 L/day of fluid intake.)

• Educated on proper toileting posture using a footstool to facilitate anorectal angle relaxation.

• Recommended regular, unhurried toilet time, preferably after meals to utilize the gastrocolic reflex.

• Then initiated ispaghula husk (bulk-forming laxative) with gradual titration based on tolerance and response as the pharmacological approach.

• Encouraged to engage in moderate physical activity, such as brisk walking. (30 minutes, 5 days/week)

Outcome - At 4-week follow-up, the patient reported improved bowel frequency and stool consistency, with no need for escalation of therapy.

Case 2: A Male with Refractory Severe Constipation with Slow Transit

History: A 50-year-old male with a history of diabetes and osteoarthritis presents with chronic constipation for over six months. He has fewer than one bowel movement per week, despite using over-the-counter laxatives. He complains of excessive straining, a sensation of incomplete evacuation, and occasional fecal incontinence. There are no red flag symptoms. His medications include amitriptyline and calcium supplements.

Examination: Digital rectal examination showed decreased anal tone and no masses. No signs of fecal impaction.

Investigations:

• Colonoscopy (done six months prior) was normal.

• Referred for anorectal manometry, which ruled out dyssynergia.

• A colonic transit study using radio-opaque markers showed delayed colonic transit.

• CBC was normal.

• Thyroid Functional Test was normal.

• Serum Calcium mildly elevated

• HbA1c 8.4%

Management:

A pharmacologic escalation was undertaken after addressing potential contributing factors:

• Medication review identified amitriptyline and calcium supplements as potential constipating agents; deprescribing was initiated.

• Slow-transit constipation found to be likely caused by poor glycemic control (high HbA1c). The patient was referred for diabetes treatment optimization, which included modifying antidiabetic medication and strengthening dietary and lifestyle changes to enhance glycemic control.

• Started on polyethylene glycol (PEG) 17 g daily, titrated up to 34 g/day based on stool frequency and consistency.

• Due to suboptimal response, prucalopride 2 mg once daily (a selective 5-HT4 receptor agonist) was added to enhance colonic transit.

• Reinforced lifestyle interventions including scheduled toileting, adequate dietary intake of fibre

& fluid intake, and daily light physical activity as in Case scenario 1.

• The patient was advised on long-term safety and titration of osmotic laxatives as needed.

• Significant clinical improvement was observed at 6 weeks, with regular, soft bowel movements and reduced straining.

Outcome: After six weeks, the patient reported significant symptom relief with regular soft bowel movements and minimal need for straining with optimization of diabetes management.

Case 3: Severe Constipation with Dyssynergic Defecation

Patient: A 62-year-old male with diabetes and hypertension presents with chronic constipation for over 6 months. He experiences excessive straining, a sensation of incomplete evacuation, and uses digital maneuvers for removal of faeces. Laxatives have provided minimal relief.

Evaluation:

• Normal colonoscopy 1 year ago

• DRE: paradoxical contraction of the anal sphincter

• Referred to a specialized GI Unit.

• Anorectal manometry revealed dyssynergic defecation Type 1

• Balloon expulsion test was abnormal

• CBC was normal.

• Thyroid Functional Test were normal

• Serum Calcium mildly elevated.

• HbA1C 7%

• Diagnosis: Severe constipation with dyssynergic defecation.

Management:

A multidisciplinary, targeted approach was adopted:

• Initiated bowel cleansing with high-dose PEG to reduce fecal load and improve baseline transit.

• Prescribed glycerine suppositories as needed.

• Referred for biofeedback therapy, the evidence-based treatment of choice for dyssynergic defecation.

• The patient completed 6 sessions over 8 weeks focused on correcting paradoxical anal contraction and improving pelvic floor coordination.

• Lifestyle and dietary advice reinforced as Case Scenario 1.

• Advised on squat-like toileting posture and timed defecation.

• The glycemic control was satisfactory in this patient. In order to maintain glycaemic objectives, the current diabetic regimen was maintained with regular diabetes follow-up and reinforcement of dietary recommendations.

• Follow-up at 3 months showed marked symptomatic improvement with normalized defecation dynamics and reduced reliance on manual maneuvers.

Outcome: After 3 months of biofeedback therapy, the patient achieved symptomatic relief with normalized defecation dynamics and reduced need for digital maneuvers.

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Self-Assessment Questions

Evidence-Based Approach to Constipation: Diagnosis, Management, and Specialist

Question 1

A 56-year-old lady has recurrent constipation despite increasing dietary fibre, maintaining adequate hydration and taking ispaghula husk for six weeks. She continues to have fewer than three bowel movements per week with hard stools.

Which pharmacological agent should be added next, and why?

Answer - Add an osmotic laxative, preferably polyethylene glycol (PEG). Because PEG improves stool water content, increases the frequency of bowel movements, and is generally more tolerated than lactulose, it is advised when bulk-forming drugs are unable to adequately control symptoms.

Question 2

A 61-year-old man complains of excessive straining, prolonged time spent on the toilet, a sensation of incomplete evacuation and the need to use his fingers to assist defecation. Colonoscopy performed one year earlier was normal.

Which investigations would be most appropriate to confirm the underlying diagnosis?

Answer- A defecatory disorder or obstructed defecation syndrome (ODS) is suggested by the clinical picture. To assess anorectal coordination and detect dyssynergic defecation, the most appropriate investigations are balloon expulsion tests and anorectal manometry.

Question 3

Which investigation is most useful in differentiating slow-transit constipation from defecatory dysfunction?

Answer - Radiopaque marker-based colonic transit studies are helpful in distinguishing between normal-transit constipation linked to defecatory dysfunction and slow-transit constipation.

Question 4

How should opioid-induced constipation be managed?

Answer - Management includes the use of osmotic laxatives, often combined with stimulant laxatives. Patients with refractory symptoms may benefit from peripherally acting μ-opioid receptor antagonists such as naloxegol or selective 5-HT4 agonists such as prucalopride under specialist supervision.

Question 5

A 65-year-old woman reports chronic constipation with excessive straining and a sensation of incomplete evacuation. Digital rectal examination demonstrates paradoxical contraction of the anal sphincter during attempted defecation.

What is the most likely diagnosis, and what is the most effective treatment?

Answer - The most likely diagnosis is dyssynergic defecation. The most effective treatment is biofeedback therapy, which retrains pelvic floor coordination and is superior to conventional laxative therapy for this condition.

Sodium Valproate in Women of Childbearing Potential: A Continuing Medication Safety Challenge

Introduction

Sodium valproate is a broad-spectrum antiseizure medication that is also used in the management of bipolar affective disorder and the prophylaxis of migraine. Despite its excellent efficacy, particularly in generalized epilepsies, valproate is one of the most teratogenic medicines currently in clinical use. Exposure during pregnancy is associated with a substantially increased risk of major congenital malformations and neurodevelopmental disorders in exposed children [1,2].

Consequently, the use of valproate in women of childbearing potential has become a major medication safety concern worldwide, resulting in prescribing restrictions, pregnancy prevention programmes, and recommendations regarding contraception, pre-pregnancy counselling, and specialist supervision. Given its continued use in Sri Lanka, it is important that healthcare professionals understand the risks associated with valproate and adopt strategies to minimise harm while ensuring appropriate disease control.

Why is valproate important?

Despite the well-established risks associated with its use during pregnancy, sodium valproate remains an important medicine in clinical practice because, for some patients, it is the most effective treatment option available. It is a broad-spectrum antiseizure medication that is particularly effective in genetic generalized epilepsy (previously termed idiopathic generalized epilepsy), a developmental epilepsy syndrome that commonly begins in childhood or adolescence [1]. Evidence from the SANAD study demonstrated that valproate was superior to several newer antiseizure medications in terms of overall treatment success and seizure control in patients with generalized epilepsies [3]. Consequently, while the risks associated with valproate exposure during pregnancy are substantial, the medicine continues to have an important role in clinical practice, making safe prescribing and appropriate patient counselling essential [1].

What are the risks?

Major congenital malformations

Sodium valproate is one of the most teratogenic medicines currently used in clinical practice. Exposure during pregnancy is associated with a substantially increased risk of major congenital malformations, with studies consistently demonstrating a two- to three-fold increase in risk compared with the general population. The overall risk of major congenital malformations among exposed pregnancies is approximately 11%, in comparison to an estimated 2% of unexposed infants. The risk increases further with higher maternal doses and when valproate is used in combination with other antiseizure medications [1,4].

Neural tube defects, particularly spina bifida, are among the most characteristic congenital abnormalities associated with valproate exposure and occur in approximately 1-2% of exposed pregnancies. Other reported malformations include congenital heart defects, cleft lip and palate, craniofacial abnormalities, limb defects, and urogenital abnormalities such as hypospadias. Importantly, the risk appears to be dose-dependent, with markedly higher rates of malformations reported at daily doses exceeding 1000–1500 mg [4].

Neurodevelopmental disorders

In addition to structural birth defects, prenatal exposure to valproate is associated with long-term neurodevelopmental impairment. Prospective studies have demonstrated lower cognitive performance and reduced intelligence quotient (IQ) scores in children exposed to valproate in utero compared with children exposed to other antiseizure medications. These adverse effects appear to be dose-dependent and may occur even in the absence of major congenital malformations [5,6].

Prenatal exposure to valproate is associated with an increased risk of adverse neurodevelopmental outcomes. Studies suggest that up to 30-40% of exposed children may experience developmental difficulties, including delayed speech and language development, learning difficulties, and reduced cognitive performance. In addition, an increased risk of neurodevelopmental disorders such as autism spectrum disorder and attention-deficit/hyperactivity disorder (ADHD) has been reported. A large population-based study reported an approximately five-fold increase in the risk of autism spectrum disorder among children exposed to valproate during pregnancy. Emerging evidence suggests that the risk of adverse neurodevelopmental outcomes may be

further increased with higher maternal doses and polytherapy [6-9].

Recognition of these risks has led to major international restrictions on the use of valproate in women of childbearing potential and underscores the importance of careful risk-benefit assessment before prescribing.

Valproate Pregnancy Prevention Programme (PPP)

In response to the well-established teratogenic and neurodevelopmental risks associated with valproate exposure during pregnancy, the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) introduced a Pregnancy Prevention Programme (PPP) for women and girls of childbearing potential receiving valproate. The programme was designed to minimise the risk of unplanned pregnancy and ensure that patients are fully informed of the potential risks before and during treatment [10].

The key components of the PPP include specialist initiation and supervision of treatment, counselling regarding the risks of valproate use during pregnancy, use of effective contraception, provision of written educational materials, documentation of informed decision-making, and regular review of the ongoing need for treatment. In the UK, patients receiving valproate are required to undergo at least an annual specialist review and complete a risk acknowledgement process to confirm their understanding of the potential risks [10,11].

Although a formal PPP has not been implemented in Sri Lanka, the principles of risk communication, effective contraception, specialist review, and documented shared decision-making should be incorporated into routine clinical practice.

Practical recommendations for clinicians

Given the substantial risks associated with in utero valproate exposure, valproate should be avoided in women of childbearing potential whenever equally effective alternative therapies are available. This is particularly relevant in focal epilepsies, where several alternative antiseizure medications with comparable efficacy are available [12-14].

Although valproate should be avoided whenever suitable alternatives are available, there are certain epilepsy syndromes, particularly some generalized epilepsies, in which seizure control may be difficult to achieve with alternative medications. In these situations, treatment decisions should be individualized following a careful assessment of the risks and benefits. Valproate should only be considered when alternative treatments are ineffective, not tolerated, or otherwise unsuitable [12].

Valproate is contraindicated for migraine prophylaxis during pregnancy because the potential risks outweigh the benefits. In women with epilepsy or bipolar disorder, valproate should only be used during pregnancy when alternative treatments are ineffective, not tolerated, or otherwise unsuitable [13,15].

When valproate is considered necessary, monotherapy should be used whenever possible and the lowest effective dose prescribed. The risk of major congenital malformations and neurodevelopmental disorders is dose-dependent, with lower risks observed at lower doses. Therefore, clinicians should aim to use the lowest dose that achieves acceptable seizure control and, where feasible, maintain doses below 500-600 mg/day [12,16,17].

Women of childbearing potential receiving valproate should be counselled regarding the risks associated with treatment during pregnancy and advised to use effective contraception throughout treatment. Ideally, treatment should be reviewed before conception occurs. Women planning pregnancy should undergo specialist review to determine whether treatment withdrawal or a switch to a safer alternative is possible. Any medication changes should be completed and their effectiveness assessed before conception [12-14].

Folic acid supplementation should be recommended to all women of childbearing potential receiving antiseizure medications. Women taking valproate are generally advised to receive high-dose folic acid supplementation before conception and during early pregnancy because of the increased risk of neural tube defects. Although folic acid supplementation may not completely prevent valproate-associated foetal abnormalities, it remains an important component of preconception care [12-14].

Women should be informed that prenatal screening can identify many structural foetal abnormalities but cannot reliably predict neurodevelopmental impairment in exposed children [12].

If pregnancy occurs while taking valproate, treatment should not be discontinued abruptly. Uncontrolled seizures may pose significant risks to both the mother and foetus. Urgent specialist neurologist review should be arranged to determine the safest management strategy, and decisions

regarding dose reduction, treatment continuation, or medication changes should be individualized based on the patient's epilepsy syndrome and seizure control [12-14].

Regular review of treatment, documentation of counselling, and shared decision-making are essential to minimise foetal risks while maintaining adequate control of epilepsy [12-14].

Table 1. Risk minimisation strategies for women of childbearing potential receiving valproate

Clinical scenario	Recommended action
Woman of childbearing potential requiring antiseizure medication	Consider alternatives to valproate whenever suitable and effective options are available.
Focal epilepsy	Avoid valproate where possible, as several alternative antiseizure medications with comparable efficacy are available.
Generalized epilepsy	Consider valproate only when alternative treatments are ineffective, not tolerated, or unsuitable. Carefully weigh the benefits of seizure control against potential foetal risks.
Woman receiving valproate and not planning pregnancy	Ensure effective contraception, provide counselling regarding teratogenic risks, and review treatment regularly.
Woman planning pregnancy	Arrange a review by a specialist neurologist before conception. Consider treatment withdrawal (if appropriate) or switching to a safer alternative before pregnancy occurs.
Valproate treatment considered necessary	Use monotherapy whenever possible and prescribe the lowest effective dose.
Woman receiving valproate who becomes pregnant	Do not stop valproate abruptly. Arrange urgent review by a specialist neurologist.
All women of childbearing potential receiving valproate	Prescribe folic acid supplementation and provide counselling regarding pregnancy-related risks.

Conclusion

The teratogenic and neurodevelopmental risks associated with valproate are among the most well-established adverse effects of any medicine used in routine clinical practice. While valproate continues to have an important role in the management of selected patients, particularly those with generalized epilepsies that are difficult to control with alternative therapies, its use in women of childbearing potential requires careful consideration. Safe prescribing practices, effective contraception, preconception counselling, and regular specialist review are essential to minimise preventable harm. Ultimately, informed shared decision-making between clinicians and patients remains the cornerstone of safe valproate therapy.

Key medication safety messages

• Valproate should be avoided in women of childbearing potential whenever suitable alternatives exist.

• The risk of major congenital malformations is approximately 11%.

• Neural tube defects occur in approximately 1-2% of exposed pregnancies.

• Up to 30-40% of exposed children may experience developmental difficulties.

• Risks increase with higher doses and polytherapy.

• Effective contraception and pre-pregnancy counselling are essential.

• Valproate should not be discontinued abruptly if pregnancy occurs.

• Regular specialist review and shared decision-making are critical.

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Regulatory News from the National Medicines Regulatory Authority (NMRA)

Ceftazidime/Avibactam

Available strength

Ceftazidime 2 g / Avibactam 0.5 g

Dosage form

Powder for concentrate for solution for intravenous infusion.

Pharmacotherapeutic group

Antibacterials for systemic use, cephalosporins and β-lactamase inhibitors.

ATC code

J01DD52

Pharmacodynamics

Ceftazidime is a third-generation cephalosporin antibacterial agent that exerts bactericidal activity by inhibiting bacterial cell wall synthesis through binding to penicillin-binding proteins (PBPs), resulting in bacterial cell lysis and death.

Avibactam is a non-β-lactam β-lactamase inhibitor that protects ceftazidime from hydrolysis by certain β-lactamases. It inhibits Ambler class A β-lactamases, including extended-spectrum β-lactamases (ESBLs) and *Klebsiella pneumoniae* carbapenemase (KPC), class C β-lactamases (AmpC), and selected class D β-lactamases such as OXA-48. By inhibiting these enzymes, avibactam restores the activity of ceftazidime against many resistant Gram-negative organisms.

Ceftazidime/avibactam is active against many Enterobacteraes and *Pseudomonas aeruginosa* isolates producing susceptible β-lactamases. However, it is not active against organisms producing metallo-β-lactamases (MBLs) such as New Delhi metallo-β-lactamase (NDM), Verona integron-encoded metallo-β-lactamase (VIM), and imipenemase (IMP).

Pharmacokinetic properties

Absorption

Ceftazidime/avibactam is administered intravenously and therefore has a bioavailability of 100%.

Distribution

The plasma protein binding of ceftazidime and avibactam is low, approximately 10% and 8%, respectively.

Both agents distribute well into extracellular fluid and achieve therapeutic concentrations in many tissues, including the lungs, peritoneal fluid, bone, and urine. Penetration across an intact blood-brain barrier is limited; however, therapeutic concentrations of ceftazidime can be achieved in the cerebrospinal fluid when the meninges are inflamed. Data on the penetration of avibactam into the cerebrospinal fluid are limited.

The volume of distribution at steady state is approximately 17 L for ceftazidime and 22 L for avibactam.

Metabolism

Ceftazidime undergoes minimal metabolism in humans. Avibactam is not significantly metabolized and is excreted largely unchanged.

Elimination

Both ceftazidime and avibactam are primarily eliminated unchanged by renal excretion. The elimination half-life of both agents is approximately 2-3 hours in individuals with normal renal function.

As both components are predominantly eliminated by the kidneys, dose adjustment is required in patients with renal impairment to avoid drug accumulation and toxicity.

Indications and dosage

Ceftazidime/avibactam is indicated in adults and paediatric patients aged 3 months and older for the treatment of complicated intra-abdominal infections (in combination with metronidazole), complicated urinary tract infections including pyelonephritis, hospital-acquired pneumonia including ventilator-associated pneumonia, and bacteraemia associated with these infections. It is also indicated for the treatment of infections caused by aerobic Gram-negative organisms in patients with limited treatment options.

The recommended dosage in adults with normal renal function is 2 g ceftazidime/0.5 g avibactam administered by intravenous infusion every 8 hours. Dose adjustment is required in patients with renal impairment.

Table 1: Recommended treatment duration

Indication	Duration
Complicated intra-abdominal infection (cIAI)	5–14 days
Complicated urinary tract infection (cUTI), including pyelonephritis	5–10 days
Hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)	7–14 days
Infections caused by aerobic Gram-negative organisms in patients with limited treatment options	According to the site and severity of infection, microbiological findings, and clinical response

The duration of treatment should be individualized based on the patient's clinical condition, source control, microbiological results, and response to therapy.

Renal dose adjustment

Dose adjustment is required when creatinine clearance (CrCl) is ≤50 mL/min.

Table 2: Renal dose adjustment

Creatinine clearance (mL/min)	Recommended dose
>50	2 g/0.5 g every 8 hours
31–50	1 g/0.25 g every 8 hours
16–30	0.75 g/0.1875 g every 12 hours
6–15	0.75 g/0.1875 g every 24 hours
≤5	0.75 g/0.1875 g every 48 hours

Contraindications

Hypersensitivity to ceftazidime, avibactam, or any of the excipients.

Hypersensitivity to cephalosporin antibiotics.

History of severe hypersensitivity reactions (e.g. anaphylaxis, severe cutaneous adverse reactions) to any other β-lactam antibacterial agent, including penicillins, monobactams, or carbapenems.

Special warnings and Cautions

Serious hypersensitivity reactions and anaphylaxis.

Clostridium difficile-associated diarrhea.

Development of resistant organisms during therapy.

Use only when susceptibility is demonstrated or strongly suspected.

Renal impairment - Neurological adverse effects including encephalopathy and seizures, are more in patients with renal dysfunction.

Positive direct Coombs test which may result in interference with the cross matching and/or drug induced hemolytic aneamia.

Sodium content should be considered in patients requiring sodium restriction.

Adverse effects

Common

Nausea

Diarrhea

Positive Coombs test

Vomiting

Elevated liver enzymes

Uncommon

Rash

Headache

Dizziness

Candidiasis

Thrombocytosis

Serious

Anaphylaxis

Seizures

Clostridium difficile-associated diarrhea

Medicine interactions

No clinically significant cytochrome P450-mediated drug interactions are expected with ceftazidime/avibactam.

Concomitant administration with nephrotoxic agents, such as aminoglycosides, may increase the risk of renal impairment and warrants monitoring of renal function.

Probenecid inhibits the renal tubular secretion of avibactam, resulting in increased avibactam exposure, and concomitant use is not recommended.

Renal function should be monitored when ceftazidime/avibactam is administered with other potentially nephrotoxic medicines.

Use in special populations

Pregnancy

There are limited data on the use of ceftazidime/avibactam in pregnant women. Animal studies do not indicate direct or indirect harmful effects at clinically relevant exposures. Ceftazidime/avibactam should be used during pregnancy only if the expected benefit outweighs the potential risk to the fetus.

References

Summary of Product Characteristics/Data Sheet approved by NMRA.

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Lactation

Ceftazidime is excreted into human breast milk in small quantities. It is unknown whether avibactam is excreted into human milk. A risk to the breastfed infant cannot be excluded; therefore, caution should be exercised when administering ceftazidime/avibactam to breastfeeding women.

Fertility

There are no human data on the effects of ceftazidime/avibactam on fertility. Animal studies have not demonstrated clinically relevant adverse effects on male or female fertility.

Effects on ability to drive and use machines

Ceftazidime/avibactam may have a minor influence on the ability to drive and use machines. Neurological adverse reactions, including dizziness, have been reported and may affect the ability to perform such activities.