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## Perioperative and Periinterventional Antibiotic Prophylaxis in Urology: Key Recommendations from the German Interdisciplinary AWMF S3 Clinical Practice Guideline

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# Perioperative and Periinterventional Antibiotic Prophylaxis in Urology: Key Recommendations from the German Interdisciplinary AWMF S3 Clinical Practice Guideline

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**Short Title:** Perioperative Antibiotic Prophylaxis in Urology (AWMF S3 Guideline)

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## Abstract

Perioperative and periinterventional antibiotic prophylaxis remains fundamental to infection prevention in surgical and interventional urology, yet its overuse and unjustified prolongation continue to drive antimicrobial resistance and expose patients to avoidable harm. The newly finalized German interdisciplinary AWMF S3 Clinical Practice Guideline establishes an evidence-based, risk-adapted, and stewardship-oriented framework that redefines antibiotic prophylaxis as a rigorously justified and time-limited intervention. This manuscript distills the urology-specific recommendations and contrasts them with the 2025 EAU Guidelines on Urological Infections, emphasizing alignment, procedural nuance, and practical relevance. The AWMF S3 framework mandates strict indication, intravenous administration 30 to 60 minutes before incision, single-dose prophylaxis for most clean and clean-contaminated procedures, and redosing only when pharmacokinetically warranted, with discontinuation at wound closure as a universal standard. Within urology, resistance-adapted prophylaxis with rectal antisepsis is recommended for transrectal prostate biopsy, whereas transperineal biopsy may be safely performed without antibiotics in low-risk patients with sterile urine and proper antisepsis. Prophylaxis confers no consistent benefit for ureterorenoscopy or cystoscopy in sterile urine, but remains indicated for percutaneous nephrolithotomy, transurethral resection of the prostate, and major open or laparoscopic procedures such as radical prostatectomy and cystectomy, where broad-spectrum single-dose coverage with intraoperative redosing may be required in prolonged surgery. Across all procedures, the AWMF S3 and EAU 2025 recommendations show high concordance, differing primarily in granularity and evidence grading. A risk-adapted, single-dose strategy unites patient safety with antimicrobial stewardship and positions urology as a model discipline for rational, quality-assured infection prevention in modern surgery.

**Keywords:** antibiotic prophylaxis, urology, AWMF S3 guideline, EAU Guidelines, antimicrobial stewardship, prostate biopsy, ureterorenoscopy, percutaneous nephrolitholapaxy, radical cystectomy, infection prevention

## Introduction

Postoperative and postinterventional infections rank among the most clinically significant complications in contemporary medicine, increasing morbidity, mortality, hospital stay, and healthcare costs [1–3]. These infections often necessitate additional courses of broad-spectrum or reserve antibiotics, which further accelerate the emergence of antimicrobial resistance (AMR) [1–3]. National surveillance data from Germany demonstrate that, despite measurable progress, perioperative antibiotic prophylaxis (PAP) still offers substantial potential for optimization [4–6]. A considerable proportion of inpatient antibiotic prescriptions are administered as prophylaxis, and unnecessary extensions beyond a single dose or a 24-hour limit remain frequent [4–6]. Such prolonged regimens confer no additional clinical benefit but increase selective pressure and facilitate the spread of multidrug-resistant organisms [7,8]. **Figure 1** illustrates the stewardship balance between clinical benefit and potential harm, emphasizing that inappropriate prolongation beyond evidence-based limits heightens resistance risk without improving outcomes.

The global magnitude of this challenge has been strikingly highlighted by recent large-scale analyses. A comprehensive assessment encompassing more than 470 million patient records revealed that, in 2019 alone, approximately 4.95 million deaths were associated with bacterial AMR, of which 1.27 million were directly attributable [9]. This disease burden equals that of human immunodeficiency virus (HIV) infection and malaria combined and underscores the urgency of sustainable antimicrobial stewardship.

Against this backdrop, the interdisciplinary AWMF S3 Clinical Practice Guideline on perioperative and periinterventional antibiotic prophylaxis, finalized in 2024, marks a milestone in evidence-based infection prevention [10]. Beyond providing an evidence-based framework for indication, agent selection, dosage, and timing, the guideline introduces both a conceptual and cultural paradigm shift in perioperative prophylaxis. It defines a strict, risk-adapted indication, mandates discontinuation of prophylaxis at the end of surgery or intervention, and promotes a single-dose standard, with redosing restricted to clearly justified pharmacokinetic circumstances. These recommendations are embedded into standardized clinical workflows through the integration of quality indicators and institutional Standard Operating Procedures (SOPs). Importantly, the guideline's interdisciplinary structure ensures applicability across surgical disciplines and includes a dedicated chapter addressing operative and interventional urology [10].

At the same time, global analyses indicate that current strategies to curb AMR remain insufficient to arrest its ongoing expansion. Particularly in resource-limited settings, but increasingly worldwide, effective implementation of antimicrobial stewardship programs and infection control measures is imperative to slow resistance emergence [11]. Urology occupies a central position in this transformation, given its wide spectrum of invasive diagnostic and therapeutic procedures, each carrying a measurable infection risk [12]. The evolving European guideline landscape, particularly the 2025 edition of the EAU (European Association of Urology) Guidelines on Urological Infections, provides an essential international reference framework against which the German AWMF S3 recommendations can be positioned and critically appraised [10,13,14].

The objective of this article is to systematically present the urology-specific recommendations of the German interdisciplinary AWMF S3 Clinical Practice Guideline, contextualize them within the contemporary European framework, and delineate their implications for clinical urological practice in Germany.

## Guideline Development and Methodological Framework

The German AWMF S3 Clinical Practice Guideline on Perioperative and Periinterventional Antibiotic Prophylaxis was developed in accordance with the methodological standards of the AWMF framework, representing the highest level of evidence synthesis and consensus building in German clinical guideline development [10]. The process followed a systematic interdisciplinary approach integrating structured literature searches, comprehensive evidence appraisal, and a multistage moderated consensus procedure involving all relevant surgical, anesthesiological, and infectious disease societies.

Clinical questions were formulated using the PICOS framework (Population, Intervention, Comparator, Outcome, Study design) to ensure precise, comparable evidence generation across defined clinical scenarios, including urological interventions [15]. Evidence appraisal adhered to the GRADE methodology (Grading of Recommendations, Assessment, Development, and Evaluation) [16]. Certainty of evidence was assessed based on study quality, consistency, directness, precision, and risk of publication bias. Each recommendation was categorized by level of obligation ("shall," "should," or "may") to reflect the intended strength of clinical implementation [17]. The degree of consensus among participating societies was systematically documented and categorized as "strong consensus" ( $\geq 95\%$  agreement), "consensus" (75–95%), or "majority consensus" (50–75%) [17]. In areas with limited or uncertain evidence, structured expert consensus statements were formulated to ensure clinical applicability and preserve decision-making guidance (**Table 1**).

Implementation is supported by quality indicators encompassing structural, process, and outcome dimensions. These indicators include documentation of timely antibiotic administration within 30 to 60 minutes before incision, appropriate dosage and intraoperative redosing criteria, and consistent discontinuation of prophylaxis at the end of the procedure [10]. They serve both as internal benchmarks and as measurable targets for quality assurance across surgical disciplines.

## Evidence Base and International Reference Framework

The recommendations were developed within the context of established international reference standards. Across all participating disciplines, 135 PICO questions were addressed, resulting in 94 evidence-based recommendations and 41 expert consensus statements [10]. For each evidence-based statement, a systematic literature search was conducted, and the highest available level of evidence was critically appraised before assigning the corresponding recommendation grade. The complete methodological process, including search strategies, inclusion criteria, and consensus protocols, is detailed in the methodological appendix of the guideline. To ensure international alignment and contextual relevance, the 2025 EAU Guidelines on Urological Infections served as the principal European reference framework [14]. The current EAU document, representing an updated version of the 2024 edition, employs a structured methodology with predefined update intervals, transparent documentation of chapter revisions, and systematic literature searches across major databases [13,14]. Relevant sections addressing perioperative and periinterventional prophylaxis were methodologically cross-referenced and validated. Both the appraisal of evidence and the derivation of recommendation strength follow standardized, reproducible procedures that facilitate comparability between the AWMF S3 and EAU 2025 guidelines. A structured methodological comparison between both documents is provided in **Supplementary Table 1**. The comparative interpretation of these two frameworks is addressed exclusively within the Discussion section of this manuscript [10,13,14].

Additionally, two recent meta-analyses on transperineal prostate biopsy, both published after the finalization of the AWMF S3 guideline, were incorporated as post-publication evidence [18,19]. Each meta-analysis followed a predefined protocol, applied multi-database search strategies, and assessed evidence certainty according to GRADE. Their results are discussed solely within the Discussion to critically reflect the AWMF S3 recommendations in light of emerging evidence.

The presentation of data in the Results section remains strictly descriptive, while interpretative contextualization, including comparative discussion with the EAU 2025 guideline and recent post-guideline evidence, is confined to the Discussion.

## Core Guideline Recommendations for Perioperative and Periinterventional Antibiotic Prophylaxis

### Indication

The AWMF S3 Clinical Practice Guideline defines a strict, risk-adapted indication for perioperative antibiotic prophylaxis. Prophylaxis is warranted only when relevant microbial exposure of the surgical field is anticipated or when the patient belongs to a clearly defined high-risk group. The indication arises from the interaction between procedure-related contamination risk, technical characteristics, and patient-specific factors such as immunosuppression or an elevated ASA score.

**Consensus and grade:** strong consensus; evidence based. Avoidance of unnecessary antibiotic administration constitutes a central tenet of antimicrobial stewardship.

### Antibiotic Selection and Dosage

Antibiotic selection should be guided by the expected microbial spectrum of the operative field. The chosen agent must be bactericidal, cost effective, and associated with a low incidence of adverse reactions. Local resistance patterns and prior antibiotic exposure must be considered, particularly regarding methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and multidrug-resistant Gram-negative bacteria (MRGN).

**Consensus and grade:** broad consensus; evidence based. Final selection should occur within the framework of the institutional Antimicrobial Stewardship Program.

### Timing of Administration

The initial dose must be administered intravenously 30 to 60 minutes before incision to ensure sufficient tissue concentrations at the time of potential microbial exposure. For vancomycin or other infusion-based regimens requiring longer administration times, an interval of up to 120 minutes before incision is acceptable.

Cephalosporins may be administered as a short infusion or intravenous bolus. The prophylactic window extends from the start of anesthesia induction until the end of the surgical procedure.

**Consensus and grade:** evidence-based recommendation with strong consensus. Implementation through standardized institutional protocols, structured workflow integration, and continuous process and outcome monitoring is mandatory. **Figure 2** illustrates the recommended administration timeline, including the intravenous initiation window and intraoperative redosing thresholds.

### Duration and Redosing

A single-dose regimen constitutes the standard of care. Redosing is indicated only when the duration of surgery exceeds twice the elimination half-life of the administered antibiotic or when substantial intraoperative blood loss (>1500 mL) occurs. Prophylaxis must be discontinued at wound closure. Any continuation beyond this point constitutes therapeutic antibiotic use rather than prophylaxis and is strongly discouraged.

**Consensus and grade:** recommendation grade A; evidence level 2; consensus strength 100%.

### Quality Management

The AWMF S3 guideline mandates institutional Standard Operating Procedures (SOPs), checklists, and regular internal audits. Timely intravenous administration, accurate dosing and redosing, and complete documentation of all prophylactic measures are defined as quality indicators subject to continuous institutional review.

**Consensus and grade:** recommendation grade A; consensus strength 100%.

**Table 2** summarizes the general principles and their binding character within the framework of the AWMF S3 guideline.

## **Urology-Specific Guideline Recommendations**

The AWMF S3 Clinical Practice Guideline integrates the urological perspective through a dedicated chapter that addresses PICOS-based questions derived from high-frequency urological procedures. In total, nine PICOS questions were formulated. One remained without recommendation, two received a “may,” three a “should,” and three a “shall” classification, reflecting increasing levels of clinical obligation.

### **Prostate Biopsy**

**Transrectal Biopsy (TRB):** Transrectal prostate biopsy traverses a heavily colonized rectal segment and carries a measurable risk of infectious complications, including sepsis. Both the AWMF S3 and the EAU Guidelines support antimicrobial prophylaxis for TRB and emphasize that adding rectal antisepsis with povidone-iodine significantly reduces infection rates. Fluoroquinolones are no longer approved for this indication in Europe. In clinical practice, prophylaxis should therefore be resistance adapted, ideally guided by prebiopsy rectal swab cultures, and use non-fluoroquinolone options or combinations aligned with local resistance epidemiology.

**Implication:** When TRB is unavoidable, administer a non-fluoroquinolone, resistance-adapted prophylaxis together with immediate preprocedural rectal antisepsis using povidone-iodine. **Consensus and grade:** strong consensus; evidence based.

**Transperineal Biopsy (TPB):** The AWMF S3 Guideline defines TPB as a procedure for which antibiotic prophylaxis may be omitted under strictly defined conditions, supported by 100 percent consensus. Omission is acceptable only when no risk factors for infection are present, urinary tract infection has been excluded, and meticulous perineal antisepsis with chlorhexidine or octenidine / phenoxyethanol is ensured. In patients at increased risk, a single intravenous dose of cefuroxime, cefazolin, or ampicillin-sulbactam administered 30 minutes before the procedure may be considered.

The meta-analysis by Wolff et al., encompassing more than 12,000 men, demonstrated no statistically significant reduction in rare infectious outcomes such as urinary tract infection, fever, sepsis, or rehospitalization when prophylaxis was administered [18]. These findings support the omission of antibiotic prophylaxis within an antimicrobial stewardship framework. Although the included studies were heterogeneous and event rates were low, the direction of effect remained consistent across all subgroups. Consistent with these observations, Stangl et al., in a meta-analysis of ten randomized controlled trials including 4,188 participants, demonstrated that transperineal prostate biopsy was associated with substantially lower odds of infection-related hospitalization compared with the transrectal approach (odds ratio 0.23; 95% confidence interval 0.10 to 0.54), as well as a significantly reduced incidence of postprocedural fever (odds ratio 0.68; 95% confidence interval 0.52 to 0.89) [19].

The EAU Guidelines confirm the superior infection-safety profile of TPB compared with TRB and cite randomized controlled trials and large cohort studies showing low infection rates irrespective of prophylaxis use. The EAU panel acknowledges that omission of prophylaxis may be feasible but withholds a formal recommendation pending the results of ongoing randomized trials.

#### **Summary of recommendations:**

- **AWMF S3:** Omission of prophylaxis during TPB is acceptable when no risk factors are present, urinary tract infection is excluded, and antisepsis is adequate; consensus 100 percent; very low quality of evidence but consistent findings.
- **EAU 2025:** TPB is safer than TRB regarding infection risk; omission of prophylaxis appears feasible, pending validation in ongoing randomized trials.

**Figure 3** illustrates the decision algorithm for biopsy route and prophylactic approach.

### **Endourological Procedures**

**Ureterorenoscopy (URS):** The EAU Guidelines report no proven benefit of antibiotic prophylaxis in reducing postoperative urinary tract infections following ureterorenoscopy, although a minor reduction in bacteriuria may occur. The AWMF S3 Guideline allows for a risk-adapted single-dose prophylaxis in patients with elevated infection risk, such as those with positive urine cultures prior to intervention, obstructive uropathy, or immunosuppression. When indicated, the prophylactic regimen should follow the general AWMF S3 principles regarding timing, spectrum, and duration.

**Consensus and grade:** recommendation grade B; strong consensus.

**Extracorporeal Shock Wave Lithotripsy (ESWL):** Two meta-analyses found no clinical benefit of antibiotic prophylaxis in patients with sterile urine undergoing ESWL. Accordingly, both the AWMF S3 and the EAU Guidelines do not recommend routine prophylaxis for ESWL. Antibiotic administration is reserved for patients with bacteriuria or infected stones.

**Consensus and grade:** strong consensus; evidence based.

**Cystoscopy:** Evidence from meta-analyses remains inconsistent. The AWMF S3 Guideline does not recommend routine prophylaxis for diagnostic or therapeutic cystoscopy. However, selective use may be justified in defined high-risk constellations, such as immunosuppression, prosthetic devices, or prior infection history. The EAU Guidelines similarly find no significant benefit in preventing symptomatic infection and restrict prophylaxis to comparable high-risk situations.

**Consensus and grade:** recommendation grade B; broad consensus.

**Percutaneous Nephrolithotomy (PNL / PCNL):** Randomized controlled trials and meta-analyses consistently demonstrate a significant reduction in postoperative infectious complications with antibiotic prophylaxis for percutaneous nephrolithotomy. Two randomized trials confirmed that a single pre-incision dose is sufficient in patients with sterile urine. Both the AWMF S3 and the EAU Guidelines recommend single-dose prophylaxis, with antibiotic selection and timing aligned to the general AWMF S3 framework.

**Consensus and grade:** recommendation grade A; strong consensus.

**Transurethral Resection of the Prostate (TURP):** Systematic reviews and meta-analyses show that perioperative antibiotic prophylaxis significantly reduces infectious complications following TURP. Both the AWMF S3 and the EAU Guidelines recommend preoperative prophylaxis, typically with a single intravenous dose administered 30 to 60 minutes before incision.

**Consensus and grade:** recommendation grade A; strong consensus.

**Transurethral Resection of the Bladder (TURB):** For TURB, the AWMF S3 Guideline provides a weak recommendation for prophylaxis limited to high-risk patients, including those with preexisting bacteriuria, recurrent urinary tract infections, or immunosuppression. The EAU Guidelines likewise restrict prophylaxis to these specific risk groups and discourage its routine use in low-risk settings.

**Consensus and grade:** recommendation grade B; broad consensus.

**Table 3** summarizes the evidence-based recommendations for major endourological and transurethral procedures according to the AWMF S3 and EAU 2025 frameworks.

### **Open and Laparoscopic Urological Surgery**

The AWMF S3 Clinical Practice Guideline formulates distinct recommendations for open and laparoscopic urological procedures, reflecting procedure-specific risk profiles and available evidence. Across all interventions, the general AWMF S3 principles apply: single-dose administration, field-specific antibiotic selection, intraoperative redosing only for procedures exceeding twice the antibiotic's half-life or involving blood loss greater than 1500 mL, and termination of prophylaxis at wound closure. These standards apply unless specific patient or procedural risk factors justify deviation.

### **Radical Prostatectomy**

Evidence from randomized controlled trials and meta-analyses demonstrates no benefit of multi-day antibiotic regimens over a single pre-incision dose for infection prevention following radical prostatectomy. Both the AWMF S3 and the EAU 2025 Guidelines therefore recommend a single-dose prophylaxis administered 30 to 60 minutes before incision, typically with a second-generation cephalosporin or an aminopenicillin-β-lactamase inhibitor combination. Prophylaxis should not extend beyond 24 hours in uncomplicated cases.

**Consensus and grade:** recommendation grade A; strong consensus.

These findings reinforce the AWMF S3 principle of antimicrobial stewardship by limiting antibiotic exposure without compromising patient safety.

### **Radical Cystectomy**

Radical cystectomy represents a high-risk procedure for infectious complications due to extended operative duration, bowel anastomosis, and potential contamination of the urinary and gastrointestinal tracts. The AWMF S3 Guideline recommends broad-spectrum empiric prophylaxis initiated intravenously 30 to 60 minutes before incision, with intraoperative redosing based on procedure length and intraoperative blood loss. Recommended regimens include a cephalosporin (second or third generation) combined with metronidazole, or an aminopenicillin-β-lactamase inhibitor combination.

Postoperative continuation beyond wound closure is not routinely indicated and should be reserved for specific high-risk situations, such as intraoperative bowel leakage or overt contamination.

The EAU Guidelines provide a concordant recommendation, emphasizing timely pre-incision administration and avoidance of prolonged postoperative courses.

**Consensus and grade:** recommendation grade A; strong consensus.

#### **Renal Surgery (Partial and Radical Nephrectomy)**

For open or laparoscopic renal surgery, including both partial and radical nephrectomy, the AWMF S3 Guideline supports single-dose prophylaxis using a second-generation cephalosporin or equivalent agent, administered intravenously 30 to 60 minutes before incision. Routine redosing or postoperative continuation is not recommended unless the procedure exceeds expected duration thresholds or involves substantial blood loss.

The EAU Guidelines similarly recommend a single pre-incision dose for nephrectomy procedures, emphasizing the lack of evidence supporting extended antibiotic courses.

Consensus and grade: recommendation grade B; strong consensus.

#### **Special Considerations**

In transplant-related or intensive-care settings, or in patients with colonization by multidrug-resistant organisms (MRSA, VRE, or MRGN), antibiotic prophylaxis must be individualized. The AWMF S3 Guideline recommends interdisciplinary consultation with infectious disease specialists and resistance-adapted regimens, including dose adjustments for obesity and renal impairment.

**Consensus and grade:** recommendation grade B; expert consensus.

**Table 4** provides detailed intraoperative redosing criteria, pharmacokinetic thresholds, and antibiotic selection for these major urological procedures, while **Supplementary Table 2** outlines patient-specific adaptations and resistance management strategies.

### **Catheter-Associated Interventions**

Both the AWMF S3 and the EAU Guidelines emphasize that antibiotic prophylaxis is not indicated for routine catheter-associated interventions. This applies to indwelling catheter replacement, suprapubic catheter exchange, and intermittent self-catheterization, provided that aseptic technique and sterile equipment are ensured. The cornerstone of infection prevention is strict adherence to procedural hygiene, including hand disinfection, sterile lubricant use, and avoidance of unnecessary catheterization.

**Consensus and grade:** expert consensus; evidence level 4.

### **Minor Urological Procedures**

For minor urological interventions, such as diagnostic cystography, retrograde pyelography, or minor procedures on the external genitalia, the available evidence remains insufficient to either support or refute the use of antibiotic prophylaxis. The AWMF S3 Guideline therefore classifies this domain as “no recommendation possible”, reflecting the lack of controlled studies and the generally low infection risk associated with these interventions. In clinical practice, adherence to aseptic principles and individualized risk assessment remains the most prudent approach.

**Consensus and grade:** no recommendation; evidence level 4.

**Table 3** summarizes all major urological procedures, including endourological, laparoscopic, and open surgeries such as radical cystectomy, according to the AWMF S3 and EAU 2025 recommendation frameworks.

**Table 4** provides detailed intraoperative redosing criteria, duration thresholds, and pharmacokinetic considerations for complex procedures, while **Supplementary Table 2** outlines patient- and pathogen-specific adaptations, including dose modification in obesity, immunosuppression, or colonization with multidrug-resistant organisms.

A structured overview of evidence levels, study quality, and consensus strength across all evaluated urological procedures is presented in **Supplementary Table 3**.

## Discussion

### Synthesis: Patient Safety and Antimicrobial Stewardship as Complementary Goals

The AWMF S3 Clinical Practice Guideline establishes a framework in which patient safety and antimicrobial stewardship reinforce rather than oppose each other. By emphasizing precise indication and a single-dose strategy, the guideline aligns evidence-based medicine with prudent antibiotic use. Extending prophylaxis beyond wound closure does not improve outcomes but heightens selective pressure and fosters antimicrobial resistance. The integration of Standard Operating Procedures, checklists, and internal audits provides a measurable structure for adherence and transparency. Recommendation grade A, evidence level 2, and unanimous consensus for single-dose use with narrowly defined redosing scenarios underscore the binding nature of these principles.

### Urology as a Model for Evidence-Based Prophylaxis Limitation

Urology exemplifies the paradigm shift toward rational antibiotic use. The transperineal prostate biopsy, now recognized as a procedure with exceptionally low infection risk, illustrates this transition. When urinary infection is excluded and antisepsis is adequate, omission of antibiotic prophylaxis is both safe and evidence based. The meta-analyses by Wolff et al. and Stangl et al. corroborate this finding [18,19], and the EAU-Guidelines adopt a cautiously aligned position. Together, these data demonstrate how specialty-specific evidence can meaningfully advance global antimicrobial stewardship [20,21].

### International Alignment and Procedural Nuance

The AWMF S3 and EAU 2025 Guidelines are broadly aligned yet differ in granularity and implementation context. Both endorse a single-dose regimen for clean and clean-contaminated procedures. The AWMF S3 framework, however, provides more detailed procedural differentiation and explicitly embeds its recommendations within institutional stewardship programs. Percutaneous nephrolithotomy and transurethral resection of the prostate are supported by clear evidence for prophylaxis, whereas ureterorenoscopy, cystoscopy, and extracorporeal shock wave lithotripsy require individualized assessment. This alignment harmonizes European standards while preserving flexibility for local adaptation.

## Clinical Implementation and Stewardship Integration

Translation into clinical practice depends on structured pathways and interdisciplinary oversight. Leadership, continuous education, audit and feedback cycles, and transparent documentation form the backbone of a sustainable stewardship culture (policy brief: see **Supplementary material**).

From both infectious disease and urological perspectives, the transperineal route should become the default approach for prostate biopsy, minimizing infection risk and antibiotic exposure [22,23]. Transrectal biopsy should be reserved for exceptional circumstances and accompanied by rigorous infection control measures.

Endourological procedures demand risk-adapted decision-making, with prophylaxis restricted to patients at elevated risk. In open, laparoscopic, or robotic surgery, best practice consists of a single intravenous dose given thirty to sixty minutes before incision, with redosing only for prolonged duration or significant blood loss, and discontinuation at wound closure.

## Limitations and Research Gaps

Despite broad interdisciplinary consensus, the strength of evidence varies across procedures. For transrectal biopsy, additional randomized trials would refine confidence in optimal non-fluoroquinolone regimens, although current evidence remains directionally consistent.

Radical cystectomy continues to present an evidence gap; recent studies have explored extended prophylaxis for up to three days or additional dosing at the time of stent removal [24–29]. Berkut et al. observed lower thirty-day infection rates after prolonged meropenem prophylaxis [25,28], whereas Rich et al. reported fewer wound infections when ampicillin/sulbactam, gentamicin, and fluconazole were combined [29]. In contrast, Thurnheer et al. demonstrated that twenty-four hours of prophylaxis was not inferior to prolonged courses at stent removal [26]. According to the AWMF S3 definitions, regimens extending beyond twenty-four hours constitute pre-emptive therapy rather than prophylaxis [10]. However, the evidence base is evolving. A recent randomized controlled trial by Hussein et al. found that thirty days of postoperative prophylaxis with nitrofurantoin or trimethoprim-sulfamethoxazole after robot-assisted radical cystectomy significantly reduced ninety-day urinary tract infections, infection-related readmissions, and overall costs without increasing adverse events [30]. These findings illustrate how current clinical research is expanding the practical range of so-called prophylactic strategies beyond the conventional twenty-four-hour definition. The ongoing REINFORCE trial is expected to clarify whether individualized prophylaxis at ureteral stent removal further reduces infection risk [24].

Other domains with limited evidence include elective scrotal and inguinal surgery, transurethral resection of bladder tumors (TURB), radical prostatectomy, and reconstructive surgery such as buccal mucosa graft urethroplasty. For these interventions, randomized controlled trials are scarce, and existing data remain underpowered or inconsistent. In a cohort of 178 patients undergoing elective scrotal or inguinal procedures, the surgical site infection rate was threefold higher without prophylaxis (12 percent vs 4 percent), though not statistically significant ( $p = 0.058$ ) [31]. Further prospective trials are warranted to delineate true effect sizes [32]. Beyond urology, a systematic review and network meta-analysis published in *JAMA Surgery* found that antiseptic wound irrigation may reduce surgical site infection rates [33]. Although not specific to urology, intraoperative antiseptic irrigation may represent a pragmatic adjunct for selected procedures. For complex constellations such as immunosuppression or colonization with multidrug-resistant organisms, prospective data remain scarce.

Importantly, fluoroquinolones have no role in contemporary urological prophylaxis. The updated EAU Guidelines, supported by a joint editorial with the European Medicines Agency in *European Urology*, call unequivocally for their discontinuation owing to serious adverse effects and insufficient efficacy evidence [14,34]. Future studies should therefore focus on resistance-adapted alternatives, short-course prophylaxis validation, and implementation science approaches to strengthen real-world adherence.

## Conclusions

Perioperative antibiotic prophylaxis in urology should be reserved for procedures with meaningful microbial exposure or for patients at elevated infection risk, ideally within a structured institutional stewardship framework. The default regimen is a single intravenous dose administered thirty to sixty minutes before incision, with redosing limited to prolonged operations or substantial blood loss and discontinuation at wound closure. These parameters reflect recommendation grade A, evidence level 2, and unanimous consensus.

Antibiotic choice must be bactericidal, procedure specific, and tailored to local resistance profiles, balancing efficacy, tolerability, and cost. For transperineal biopsy, omission of prophylaxis is appropriate when urinary tract infection is excluded and antisepsis is reliable; a single-dose regimen remains an option for high-risk patients. Transrectal biopsy requires a non-fluoroquinolone, resistance-adapted regimen combined with rectal antisepsis. Endourological procedures should follow a differentiated, risk-oriented strategy—single-dose prophylaxis for percutaneous nephrolithotomy and TURP, selective prophylaxis for TURB, ureterorenoscopy, and extracorporeal shock wave lithotripsy.

Sustained quality and patient safety depend on rigorous implementation of SOPs, internal audits, and comprehensive documentation throughout the perioperative course. By uniting evidence-based medicine and antimicrobial stewardship, urology provides a model discipline for harmonizing infection prevention with responsible antibiotic use across surgical specialties.

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## Conflicts of Interest

K. Hauner and M. May served as official representatives of the German Society of Urology (registered association, e.V.) (DGU) in the working group responsible for the AWMF S3 Clinical Practice Guideline on Perioperative and Periinterventional Antibiotic Prophylaxis. G. Bonkat, F. Wagenlehner, and J. Kranz are members of the panel that developed the European Association of Urology (EAU) Guidelines on Urological Infections. M. May and F.M.E. Wagenlehner were members of the journal's Editorial Board at the time of submission. The remaining authors have no conflicts of interest to declare. All authors declare that they have no financial or personal relationships that could inappropriately influence or bias the content of this manuscript.

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## Author Contributions

*K. Hauner, J. Kranz, and M. May* drafted the manuscript, while *M. May* conceived the study and designed its overall structure. *K. Hauner and M. May* contributed to the methodological synthesis of the AWMF S3 guideline and supported the integration of evidence tables. *J. Kranz, F. Wagenlehner, and G. Bonkat* contributed to the comparative analysis and contextual interpretation of the EAU 2025 guideline framework. *G. Magistro and S. Hansen* provided critical review and clinical validation of the urological content. All authors contributed to the critical revision of the manuscript for important intellectual content and approved the final version for submission. Accordingly, the authors confirm that no generative AI tools were used in the conceptualization, writing, or editorial refinement of this manuscript.

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## Figure Legends

### Figure 1. The Stewardship Balance: Benefit versus Harm in Perioperative Prophylaxis

The stewardship balance model integrates patient safety and antimicrobial stewardship into a single framework. Optimal perioperative antibiotic use occurs at equilibrium, where the benefits of infection prevention are preserved without promoting resistance or adverse drug effects. The concept translates the AWMF S3 and EAU recommendations into a visual metaphor of rational restraint. The leftward tilt corresponds to underprotection, while the rightward tilt reflects antibiotic overexposure and loss of ecological integrity.

### Figure 2. Timing of Perioperative Antibiotic Prophylaxis and Redosing

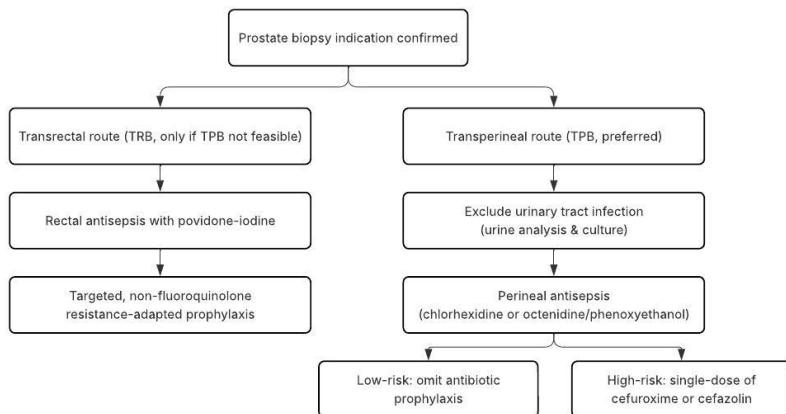
Timing scheme for perioperative antibiotic prophylaxis according to the AWMF S3 Guideline and aligned EAU recommendations. The initial dose is administered 30 to 60 minutes before incision. Redosing is restricted to pharmacokinetic need or substantial blood loss. Prophylaxis is stopped at wound closure. Any administration beyond this point constitutes treatment rather than prophylaxis.

### Figure 3. Decision Algorithm for Prostate Biopsy and Antibiotic Prophylaxis

Decision algorithm for prostate biopsy and antibiotic prophylaxis. The flowchart outlines the recommended pathways following the confirmation of an indication for prostate biopsy. The preferred approach is transperineal biopsy (TPB), beginning with exclusion of urinary tract infection via urinalysis, culture, and assessment of risk factors, followed by perineal antisepsis using chlorhexidine or octenidine/phenoxyethanol. Based on patient risk stratification, either omission of antibiotics (low risk) or a single dose of cefuroxime, cefazolin, or ampicillin/sulbactam (30 to 60 minutes prior to biopsy) is advised. Alternatively, if TPB is not feasible, the transrectal route (TRB) may be considered, with rectal antisepsis using povidone-iodine and targeted, non-fluoroquinolone, resistance-adapted antibiotic prophylaxis. This algorithm emphasizes clinical decision-making aimed at minimizing infectious complications.

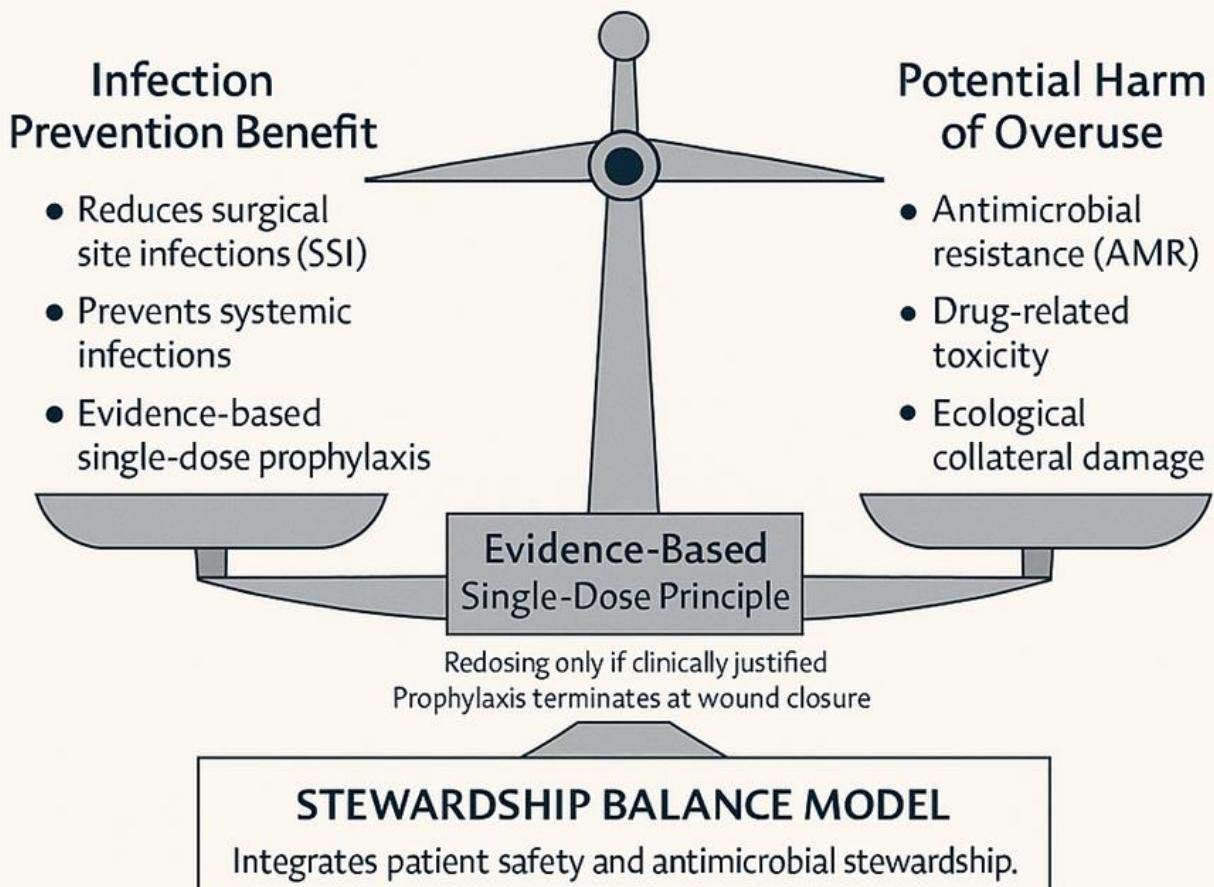
Legend: *Low-risk patients* are defined as those with sterile urine, no diabetes mellitus, no immunosuppression, no indwelling catheter for longer than 14 days, and no recent urinary tract infection. *High-risk patients* are those with one or more of the above factors.

**Decision Algorithm for Prostate Biopsy and Antibiotic Prophylaxis**

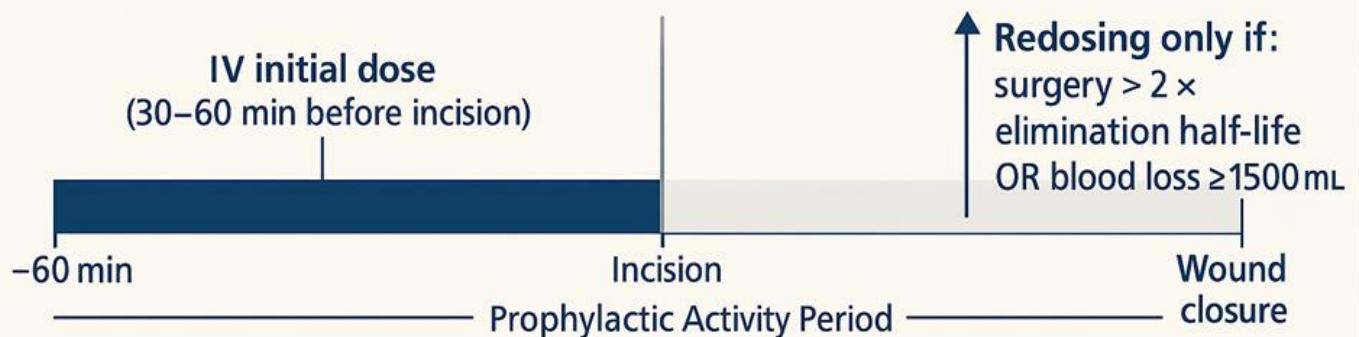


# THE STEWARDSHIP BALANCE

## Benefit vs. Harm in Perioperative Antibiotic Prophylaxis



## TIMING OF PERIOPERATIVE ANTIBIOTIC PROPHYLAXIS AND REDOSING



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**Table 1. Framework for Guideline Development, Evidence Appraisal, and Consensus Formation**

Methodological structure of the interdisciplinary AWMF S3 Clinical Practice Guideline on Perioperative and Periinterventional Antibiotic Prophylaxis summarizing the principal evidence evaluation and consensus processes applied to all surgical and urological recommendations. Comparative reference: EAU-Guidelines on Urological Infections 2025, Chapter 2 (Methodology). Both frameworks are based on structured question formulation, systematic evidence synthesis, and transparent consensus documentation.

**Abbreviations:** AMR, antimicrobial resistance, ASA, American Society of Anesthesiologists, AWMF, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, EAU, European Association of Urology, GRADE, Grading of Recommendations Assessment Development and Evaluation, LE, level of evidence, PICO(S), population intervention comparator outcome (plus study design), RKI, Robert Koch Institute, SOP, Standard Operating Procedure, TURP, transurethral resection of the prostate.

| Domain                       | AWMF S3 Methodology (2024)  | EAU-Guideline Reference (2025)  | Corresponding Application in Urology   |
|------------------------------|---|---|--|
| Framework                    | AWMF S3 highest methodological level; interdisciplinary, cross-specialty process coordinated by the AWMF and the Robert Koch Institute (RKI).   | Structured methodology coordinated by the EAU-Guidelines Office; updated annually with defined literature timeframes. | Enables harmonization of perioperative prophylaxis recommendations across urological subspecialties. |
| Question formulation         | PICOS format (Population, Intervention, Comparator, Outcome, Study design).   | PICO format (Population, Intervention, Comparator, Outcome).  | Provides comparability of questions addressing biopsy, TURP, or cystectomy prophylaxis.              |
| Evidence assessment          | GRADE (Grading of Recommendations, Assessment, Development and Evaluation); quality rated by study design, consistency, precision, directness, and risk of bias.                              | GRADE-derived framework using Levels of Evidence (LE 1–4) and Grades of Recommendation (A–C).                         | Harmonized interpretation of evidence certainty for urology-specific statements.                     |
| Consensus process            | Multistage, moderated consensus under AWMF supervision; quantitative thresholds: <i>strong consensus</i> $\geq 95\%$ , <i>consensus</i> $\geq 75\%$ , <i>majority consensus</i> $\geq 50\%$ . | Expert-panel consensus within each chapter including multidisciplinary validation.                                    | Ensures transparent, quantifiable agreement in urology-related recommendations.                      |
| Recommendation strength      | Three levels: <i>shall</i> (mandatory), <i>should</i> (recommended), <i>may</i> (optional).   | Three levels: <i>strong</i> , <i>weak</i> , <i>expert opinion</i> .   | Defines clinical imperatives within urological decision-making.                                      |
| Evidence vs. consensus ratio | 94 evidence-based / 41 expert-consensus recommendations (total 135 PICOS questions).  | Not centrally quantified but reported per chapter.  | Reflects the balance between evidence and expert guidance for urological procedures.                 |
| Quality indicators           | Structure-, process-, and outcome-based metrics: documentation of timing, dosage, redosing criteria, and termination of prophylaxis.  | Implementation indicators in development within the EAU framework.  | Facilitates benchmarking and continuous quality improvement across urological centers.               |

**Table 2. Core Principles of Perioperative Antibiotic Prophylaxis According to the AWMF S3 and EAU-Guidelines**

General evidence-based and consensus-based principles governing perioperative and periinterventional antibiotic prophylaxis. The table contrasts the AWMF S3 (2025) and EAU (2025) frameworks and outlines their implementation relevance in urological surgery and interventional procedures. All statements are verified against recommendation strength, consensus level, and clinical applicability.

**Abbreviations:** ABS, antibiotic stewardship, AMR, antimicrobial resistance, ASA, American Society of Anesthesiologists, AWMF, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, EAU, European Association of Urology, IV, intravenous, MRGN, multidrug resistant gram-negative bacteria, MRSA, methicillin resistant *Staphylococcus aureus*, SOP, Standard Operating Procedure, VRE, vancomycin resistant enterococci.

| Principle                          | AWMF S3 Guideline (2024)   | EAU-Guideline (2025)  | Implementation in Urology   |
|------------------------------------|--|---|---|
| Indication                         | Strict, risk-adapted indication only when relevant microbial exposure or high patient risk exists; based on procedure characteristics and individual factors (e.g., immunosuppression, high ASA score). <i>Strong consensus, evidence-based.</i> | Indication limited to procedures with proven infection risk or high-risk constellations. <i>Evidence-based recommendation.</i>        | Defines prophylaxis for selected high-risk interventions; mandates omission when no demonstrable benefit. |
| Antibiotic selection               | Choose bactericidal, cost-effective agents with low adverse-effect potential; guided by expected microbial spectrum, prior antibiotic exposure, and local resistance data (MRSA, VRE, MRGN). <i>Broad consensus, evidence-based.</i>             | Empirical selection according to procedure type and local resistance; stewardship alignment emphasised. <i>Strong recommendation.</i> | Promotes pathogen-oriented, resistance-adapted prophylaxis, embedded within ABS programs.                 |
| Dosage and route                   | Standardized single intravenous (IV) administration at defined doses; adapted to patient weight, renal function, and drug pharmacokinetics. <i>Consensus ≥ 95%.</i>  | Single pre-incision IV dose in most procedures; dosage per pharmacokinetics. <i>Strong recommendation.</i>                            | IV route obligatory; oral regimens discouraged except where explicitly validated.                         |
| Timing                             | Administer 30–60 minutes before incision; up to 120 minutes for long-infusion agents (e.g., vancomycin). <i>Evidence-based recommendation, strong consensus.</i>   | IV administration 30–60 minutes before incision; re-dose if procedure exceeds 2 × half-life or significant blood loss.                | Unified perioperative timing standard across surgical disciplines.  |
| Duration and redosing              | Single-shot is standard; redose only if surgery exceeds 2 × half-life or > 1500 mL blood loss; discontinue at wound closure. <i>Grade A, evidence level 2, 100% consensus.</i>   | Discontinue at wound closure; no postoperative continuation unless infection suspected.   | Ends prophylaxis at closure; prevents treatment masquerading as prophylaxis.                              |
| Stewardship and quality management | Mandatory institutional SOPs, checklists, internal audits, and continuous ABS oversight; documentation of timing, dosage, redosing, and discontinuation. <i>Grade A, 100% consensus.</i>   | Strong alignment with antimicrobial stewardship principles; regular audit cycles encouraged.  | Integrates prophylaxis into structured infection-control and quality-improvement systems.                 |
| Postoperative continuation         | Explicitly not recommended; any postoperative antibiotic constitutes therapy, not prophylaxis. <i>Grade A, evidence level 2.</i>   | Same principle affirmed; strong recommendation to stop after closure.   | Eliminates unnecessary postoperative exposure.  |

**Table 3. Urology-Specific Procedures: Comparative Recommendations of the AWMF S3 and EAU-Guidelines**

Comparative synthesis of prophylactic recommendations for common urological interventions, structured by procedure type. The table contrasts the indication, recommendation strength, and consensus level of the AWMF S3 (2025) and EAU (2025) guidelines. All statements are based on verified evidence categories within both frameworks.

**Abbreviations:** ABS, antibiotic stewardship, AMR, antimicrobial resistance, ASA, American Society of Anesthesiologists, AWMF, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, EAU, European Association of Urology, ESWL, extracorporeal shock wave lithotripsy, IV, intravenous, MRSA, methicillin resistant *Staphylococcus aureus*, PCNL, percutaneous nephrolithotomy, PNL, percutaneous nephrolithotomy, RCT, randomized controlled trial, SOP, Standard Operating Procedure, TPB, transperineal biopsy, TRB, transrectal biopsy, TURB, transurethral resection of the bladder, TURP, transurethral resection of the prostate, URS, ureterorenoscopy, VRE, vancomycin resistant enterococci.

| Procedure  | AWMF S3 Guideline (2024)  | EAU-Guideline (2025)   | Clinical Implication and Alignment   |
|--|---|--|--|
| Transrectal prostate biopsy (TRB)                        | Antibiotic prophylaxis mandatory; non-fluoroquinolone, locally resistance-adapted regimen; combine with rectal antisepsis using povidone-iodine. <i>Consensus 100%</i> .            | Prophylaxis recommended; rectal antisepsis obligatory; fluoroquinolones not approved.            | Alignment on prophylaxis and antisepsis; divergence on drug selection flexibility.                                   |
| Transperineal prostate biopsy (TPB)                      | Prophylaxis may be omitted if urinary infection is excluded and antisepsis adequate; single IV dose for high-risk patients only. <i>Consensus 100%, very low evidence quality</i> . | Prophylaxis omission considered feasible; strong infection safety profile; pending further RCTs. | Alignment on omission under controlled conditions; stewardship milestone.  |
| Ureterorenoscopy (URS)                                   | Risk-adapted single-shot prophylaxis permitted; omit in low-risk patients. <i>Consensus 90%</i> .   | No routine benefit for prophylaxis in reducing symptomatic infections.                           | Alignment on selective, risk-based prophylaxis.  |
| Extracorporeal shock wave lithotripsy (ESWL)             | No prophylaxis recommended in patients without bacteriuria. <i>Strong consensus</i> .   | No prophylaxis in absence of bacteriuria.  | Full concordance.  |
| Cystoscopy (diagnostic)                                  | No routine prophylaxis; consider in high-risk constellations. <i>Weak recommendation, expert consensus</i> .  | No proven benefit; high-risk patients only.  | Complete agreement.  |
| Percutaneous nephrolithotomy (PNL/PCNL)                  | Prophylaxis recommended; single-shot sufficient. <i>Evidence level 2, grade A</i> .   | Single pre-procedural dose recommended; evidence consistent.                                     | Alignment on single-shot standard.   |
| Transurethral resection of the prostate (TURP)           | Prophylaxis required; single IV dose pre-incision. <i>Evidence-based, grade A</i> .   | Same recommendation; single-dose approach.   | Full alignment.  |
| Transurethral resection of the bladder (TURB)            | Prophylaxis only for high-risk patients (e.g., immunosuppression, bacteriuria, long procedure time). <i>Weak recommendation, consensus 90%</i> .                                    | Restrict prophylaxis to high-risk subgroups (immunosuppression, bacteriuria).                    | Prophylaxis may be considered in patients with bacteriuria or relevant immunosuppression; routine use not recommend. |
| Radical prostatectomy / cystectomy / partial nephrectomy | Single-shot prophylaxis; redose if prolonged time or >1500 mL blood loss; stop at wound closure. <i>Grade A, 100% consensus</i> .   | Single pre-incision dose; re-dose as indicated; no postoperative extension.                      | Full alignment on duration and discontinuation principles.   |

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**Table 4. Procedure-Specific Redosing Criteria and Duration Thresholds in Major Urological Surgery**

Both the AWMF S<sub>3</sub> and EAU-Guidelines converge on a single shot paradigm supported by robust consensus and moderate-quality evidence. Across all major urological procedures, extending prophylaxis beyond wound closure yields no measurable reduction in infectious complications and increases the risk of resistance development. The AWMF S<sub>3</sub> guideline operationalizes this principle through explicit redosing criteria tied to procedure duration and blood loss, thereby translating stewardship principles into actionable surgical standards. Its strength lies in enforceable clarity, measurable quality indicators, and interdisciplinary applicability across open, laparoscopic, and robotic approaches.

**Abbreviations:** AWMF, Association of the Scientific Medical Societies in Germany; EAU, European Association of Urology; IV, intravenous; MRGN, multidrug-resistant gram-negative bacteria; MRSA, methicillin-resistant *Staphylococcus aureus*; RPLND, retroperitoneal lymph node dissection; S<sub>3</sub>, evidence- and consensus-based German guideline; VRE, vancomycin-resistant enterococci.

| Procedure Type   | Primary Antibiotic Prophylaxis  | Indication for Redosing                                      | Maximum Recommended Duration   | AWMF S <sub>3</sub> Recommendation   | EAU-Guideline Alignment   |
|--|---|--|--------------------------------|--|---|
| Radical prostatectomy (open, laparoscopic, robotic)                      | Cefuroxime 1.5 g IV (pre-incision); alternative: cefazolin 2 g IV                             | Surgery > 3 h or blood loss > 1500 mL                        | Discontinue at wound closure   | <i>Shall</i> (Grade A, evidence 2, 100% consensus)   | Concordant; single-shot regimen preferred   |
| Radical cystectomy (with urinary diversion)                              | Broad-spectrum cephalosporin (e.g., cefotaxime 2 g IV + metronidazole 500 mg IV pre-incision) | Surgery > 3 h or major blood loss; repeat after 2 half-lives | Limit total duration to ≤ 24 h | Limit total duration to ≤ 24 h in cases with bowel or urinary diversion; discontinue at wound closure whenever feasible. | Prefer single-dose regimen; redose only if surgery exceeds 3 h or major blood loss; no postoperative extension. |
| Partial nephrectomy (open/laparoscopic/robotic)                          | Cefuroxime 1.5 g IV (pre-incision)  | Redose if duration > 3 h or blood loss > 1500 mL             | Stop at wound closure          | <i>Should</i> (Grade B, evidence 3, consensus > 90%)   | Concordant; same criteria   |
| Radical nephrectomy / nephroureterectomy                                 | Cefuroxime 1.5 g IV (pre-incision)  | Duration > 3 h or high intraoperative contamination          | Discontinue at wound closure   | <i>Shall</i> (Grade A, consensus 95%)  | Concordant  |
| Retroperitoneal lymph node dissection (RPLND)                            | Cefazolin 2 g IV (pre-incision)   | Surgery > 3 h or excessive tissue trauma                     | Stop at wound closure          | <i>Should</i> (Grade B, consensus > 90%)   | No specific deviation   |
| Reconstructive surgery (e.g., urethroplasty)                             | Cefazolin 2 g IV (pre-incision)   | Only if duration > 2 half-lives                              | Limit to ≤ 24 h                | <i>Should</i> (Grade B, consensus > 90%)   | Concordant; same limit  |
| Complex scrotal/inguinal surgery (e.g., hydrocelectomy, varicocelectomy) | Cefuroxime 1.5 g IV (pre-incision)  | Rarely indicated   | Stop at wound closure          | <i>May</i> (Grade 0, low evidence)   | Concordant; low evidence base   |