



Opinion and Recommendation Statement of Treatment of Urinary Tract Infection

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Urinary Tract Infections (UTIs) belong to some of the most common bacterial infections, affecting 150 million people each year worldwide [1-3]. Although they predominantly impact the female population, UTIs also represent a significant cause of morbidity in male infants and older men. Around 20-30% of women with an acute UTI will experience recurrence through relapse or reinfection [4]. Based on the recommendations of various national and international guidelines, UTIs are primarily treated with antibiotics [5,6]. This treatment approach applies to acute and recurrent infections, and although some guidelines have been expanded to include the use of non-antibiotic treatments [7,8] whose value in tackling UTIs is supported by practical experience, they are yet to find sufficient prominence in healthcare. Indeed, antibiotics are applied hastily and much too frequently in the treatment of uncomplicated UTIs. Beyond increasing the burden of treatment side effects for patients, this excessive use of antibiotics contributes to developing antibiotic resistance, a major global issue with serious healthcare consequences.

Antimicrobial resistance represents a partial or complete loss of susceptibility toward antimicrobial treatments such as antibiotics. Emerging and steady increase of resistant microbes poses a threat for the effective treatment of infectious diseases, which is particularly concerning in light of limited therapeutic options and declining development of innovative antibiotics as well as the higher risk of complications or a poorer outcome linked to infections with antimicrobial-resistant microorganisms [9-12]. *Escherichia coli*, the most common pathogen associated with UTIs, shows varying resistance to different antibiotics used for the treatment of UTIs and has been described as increasingly developing multidrug resistance in Europe [1,13-16]. Within the European Union, antibiotic resistance is linked to estimated 33,000

yearly fatalities and 1.5 billion € yearly costs due to healthcare needs and productivity loss [17]. Although antimicrobial resistance varies across European countries, it notably correlates with the use of antimicrobial treatments [10,13,18]. Furthermore, UTIs have been reported among the most common reasons for antibiotic use in Europe, sharing the same percentage as the flu, and superseded only by sore throat and bronchitis [19]. Our own recent analysis of market research data also indicates substantial use of antibiotics in Europe, notably affected by UTI-related prescriptions [3]. We therefore strongly believe that the use of antibiotics in healthcare, including the treatment of UTIs, warrants strict caution and should be reserved for cases where such treatment is necessary. In all other cases, based on diagnostic indications and physician assessment, non-antibiotic alternatives should be considered, such as in the case of acute, simple UTIs or the prophylaxis of recurrent UTIs.

Various non-antibiotic alternatives with a comparatively lower burden of predominantly mild side effects are available for UTI treatment, with cranberries, probiotics, D-mannose, estrogens and immunostimulants among the most studied in the context of recurrent UTIs [2,4,10,20,21]. D-mannose is a sugar physiologically present within the human body and has been shown to be protective against recurrent UTIs while also indicating good prospects for possible use in the treatment of acute UTIs [22-24]. Most alternative treatments are readily available in pharmacies and easy to use. Beyond their role in the safe and effective treatment of UTIs, such alternatives help tackle the issue of antibiotic resistance while also reducing the burden of side effects otherwise occurring due to antibiotic treatment, such as microbial dysbiosis which can facilitate other health issues. However, for successful integration of non-antibiotic treatments in the UTI therapy regime, different stakeholders of the healthcare system need to be more aware of

their use cases and benefits.

In light of the abovementioned issues, we strongly recommend a multifaceted approach to raising awareness and promoting appropriate use of non-antibiotic treatments. Patients should be educated on relevant aspects of disease and treatment, so they can make informed decisions on self-treatment options. With developing knowledge on predisposing factors for UTIs, it is important to approach patients known to be at risk as well as newly identified potential risk groups such as young women on low-dose contraceptives or women with urogenital atrophy. Pharmacists and physicians, particularly of the fields most commonly consulted by UTI patients, such as general practitioners, urologists and gynecologists, need to be informed on the existence, benefits and use cases of non-antibiotic treatments, especially in countries with OTC antibiotics. Simple and fast tools should be utilized to obtain accurate diagnosis and avoid unnecessary prescription of antibiotics in everyday practice. In order to ensure appropriate information is disseminated in a consistent manner, suitable channels need to be employed to effectively communicate existing knowledge on alternatives to antibiotics.

Reconsidering current practices in the treatment of UTIs is urgently needed, as it would not only improve patient care, but also represent an important step in tackling antibiotic resistance. Each healthcare professional has the power to contribute to this change of practice. We therefore respectfully share our opinion and recommendation in the hope that you also will become an agent of change and join the global initiative of saving antibiotics for a better healthcare future.

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