



**INDIAN HEALTH SERVICE**  
**National Pharmacy and Therapeutics Committee**  
**Formulary Brief: Diabetic Foot Ulcers**  
**-October 2023-**



**Background:**

The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) was provided a clinical review of the management of diabetic foot ulcers (DFU). Medications listed on the IHS National Core Formulary relevant to this condition include moisturizers (both cream- and petroleum-based) and the antibiotics amoxicillin-clavulanic acid, cephalexin, ciprofloxacin, clindamycin, doxycycline, and trimethoprim-sulfamethoxazole, as well as the antifungals clotrimazole and fluconazole. Following this review, the NPTC made **no modifications** to the National Core Formulary.

**Discussion:**

Risk of DFU, amputation, and mortality is higher in people who live in rural areas and in a lower socioeconomic status. African Americans and American Indians, compared with Caucasians, have a two-fold increased risk of amputation after diagnosis of DFU. Up to 20 percent of patients hospitalized with DFU will undergo lower extremity amputation. In 2018, there were 6.1 lower extremity amputations per 1,000 adults aged 18 years or older with diagnosed diabetes (154,000 lower extremity amputations). This is up from 4.9 lower extremity amputations per 1,000 adults aged 18 years or older with diagnosed diabetes in 2016. Among people with diabetes who have had a lower extremity amputation, between 19% to 53% will have an amputation of the opposite extremity within 5 years. The lifetime risk of a foot ulcer for patients with diabetes (type 1 or 2) is up to 34 percent. Patients with DFU have a 2.5-fold increased risk of death compared with diabetic patients without foot ulcers. Approximately one-half of all DFU will become infected. Infection can lead to further complications including sepsis, gangrene, amputation, and death. Even after an ulcer has healed, proper foot care is important as more than one-half of healed ulcers recur within five years. DFU are associated with a five-year mortality ranging between 30-50%, with the most common causes of death from cardiovascular disease and infection.<sup>1-3</sup>

Neuropathy is especially problematic for patients with DFU. Over 80% of diabetic patients with foot ulcers have concomitant neuropathy. Furthermore, nearly half of people with diabetic peripheral neuropathy may not be symptomatic. Neuropathy can result in insensitivity and, as a result, mild trauma from ill-fitting shoes, burns, or other sources which can be unnoticed, untreated, and progress to DFU. Neuropathy can also result in deformed feet. Loss of protective sensation, foot deformities, and limited joint mobility can lead to abnormal biomechanical loading of the foot, which produces high mechanical stress, and ultimately causes callus formation. Calluses then lead to a further increase in the loading of the foot which can create a blister and eventually cause skin ulceration.<sup>1,3,4</sup>

People diagnosed with both diabetes and peripheral vascular disease have a higher risk of amputation. Up to 50% of patients with DFU also have peripheral vascular disease.<sup>1,4</sup>

In 2019, the International Working Group of the Diabetic Foot (IWGDF) published comprehensive guidelines on the prevention and treatment of DFU. The guidelines highlight the importance of foot exams by patients, caregivers, and health professionals, education for patients and caregivers, the importance of proper foot wear, offloading pressure, revascularization therapy, diabetes and other co-morbidity management, and local ulcer care including sharp debridement, among other recommendations.<sup>4</sup> (Table 1)

<b>Prevention</b>	<b>Treatment</b>
1. Identifying the at-risk foot	1. Pressure offloading and ulcer protection
2. Regularly inspecting and examining the at-risk foot	2. Restoration of tissue perfusion
3. Educating patients, family & healthcare professionals	3. Treatment of infection
4. Ensuring routine wearing of appropriate footwear	4. Metabolic control and treatment of co-morbidities
5. Treating risk factors for ulceration	5. Local ulcer care
	6. Education for patients and relatives

One of the important components of prevention and treatment of DFU is classifying or staging the DFU. A common methodology for staging DFU is known as the Wagner method. Ulcers are graded as follows: Grade 1: Superficial ulcer – Skin and subcutaneous tissue only; Grade 2: Deep ulcer to tendon, muscle, joint capsule, or bone; Grade 3: Deep ulcer with abscess, osteomyelitis, or tendinitis; Grade 4: Partial foot gangrene; Grade 5: Whole foot gangrene.

The University of Texas system expands on the Wagner classification method by providing both a grading and staging system. DFU are graded as follows: Grade 0: Pre- or post-ulcerative; Grade 1: Full-thickness ulcer not involving tendon, capsule, or bone; Grade 2: Tendon or capsular involvement without bone palpable; Grade 3: Probes to bone. DFU are staged as follows: A: Non-infected; B: Infected; C: Ischemic; D: Infected and ischemic.<sup>5</sup>

DFU can also be classified utilizing the Threatened Limb Classification: WIFI (Wound/Ischemia/Foot Infection). This method provides a more quantitative assessment of peripheral artery disease in addition to grading the wound and staging the infection. Scores are assigned on the following bases: none (0), mild (1), moderate (2), and severe basis (3). This methodology helps identify relative importance of the various factors at any given time, provides an assessment of likelihood of amputation at one year, and the stage of limb threat determines potential need for admission and revascularization.<sup>5</sup>

In October 2023, the IWGDF in collaboration of The Infectious Disease Society of America (IDSA) published guidelines on the diagnosis and treatment of diabetic foot infections. The authors recommend that the diagnosis of a diabetic foot infection be clinically based on the presence of local or systemic signs and symptoms of inflammation. If clinical diagnosis is unclear, biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), or procalcitonin (PCT) can be considered to help with the determination of the diagnosis. Providers should not use foot temperature or quantitative microbial analysis to diagnose. Providers should consider hospitalizing all persons with diabetic foot infection who have either a severe foot infection or a moderate infection associated with key relevant morbidities. If possible, tissue cultures should be utilized to determine the causative pathogen. The authors recommend using conventional microbiology techniques over molecular techniques for the first-line identification of pathogens from tissue samples. A combination of methods can be used to rule out osteomyelitis. These include probe-to-bone test, plain X-rays, and ESR, CRP, or PCT. If it is still unclear whether or not the patient has osteomyelitis, magnetic resonance imaging can be performed. Neither topical nor systemic antibiotics should be used to prevent infections for uninfected DFU. Patients with mild infections (ulcers not deeper than the fascia) should receive appropriately targeted antibiotic treatment for gram-positive cocci. Patients with an infected ulcer which extends into deeper tissues should receive initial therapy for gram-positive cocci and gram-negative rods. Providers should not empirically treat *Pseudomonas aeruginosa* unless the patient has had a positive *Pseudomonas aeruginosa* culture from the affected site in the past few weeks. Anaerobic coverage should be added if there is ischemia, necrosis, or gas formation. The authors recommend against using adjunctive granulocyte colony-stimulating factor treatment, topical antiseptics, silver preparations, honey, bacteriophage therapy, or negative-pressure wound therapy for the treatment of diabetic foot infections. Additionally, they recommend against using topical antibiotics in combination with systemic antibiotics for treating either soft-tissue infections or osteomyelitis.<sup>6</sup>

### Findings:

Diabetic foot ulcers cause significant morbidity and mortality. American Indian and Alaska Native patients are at high risk for developing diabetic foot ulcers complications. Diabetic foot ulcers require a multifaceted and vigilant approach to prevention and treatment. Recent guidelines from the IWGDF and IDSA provide guidance on the appropriate prevention and management of diabetic foot ulcers to include treatment of infection. For information including education on diabetes foot care, diabetic foot ulcer management, foot exam best practices, footwear selection, please visit [Clinical Resources | Division of Diabetes Treatment and Prevention \(DDTP\) \(ihs.gov\)](#).

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*If you have any questions regarding this document, please contact the NPTC at [IHSNPTC1@ihs.gov](mailto:IHSNPTC1@ihs.gov). For more information about the NPTC, please visit the [NPTC website](#).*

### References:

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