Indian Health Service
National Pharmacy and Therapeutics Committee
Formulary Brief: *Nutritional Supplements in Wound Healing*
-February 2016-

Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) reviewed nutritional supplements in wound healing at the February 2016 NPTC meeting. Vitamin C and zinc were the focus of the review which included the role and use of each supplement in promotion of wound healing, a review and generalization of pertinent literature reviews, analyses and findings and a determination if any changes were warranted to the current National Core Formulary (NCF). As a result of the NPTC clinical review, **no changes were made to the NCF** relating to nutritional supplements in wound healing.

Discussion:
Roughly 2% of the United States (US) suffers from chronic non-healing wounds and approximately 3 million Americans suffer from pressure ulcers. It is estimated that US healthcare costs devoted to wound care is greater than $50 billion annually. On average, the time to heal a chronic wound is 15 weeks with an average cost of $3300 - $9300 per wound. Those who suffer from pressure ulcers requiring hospitalization accrue costs of greater than $20,000 per hospitalization.

Those with comorbidities such as diabetes, cardiovascular disease, peripheral vascular disease and obesity often have more wound healing issues. Additionally, those who are at increasing age, frail, have a history of wounds, multiple comorbid disease states or malnutrition are at risk for poor wound healing. The role of vitamin C and zinc is multifactorial in the wound healing process. Vitamin C is an essential cofactor for collagen and protein synthesis of bones, skin, capillary walls and connective tissue as well as providing enhanced neutrophil function and angiogenesis which aide in its wound healing functions. Zinc functions to aide in the wound healing process by supporting collagen and protein synthesis, membrane stability and clot formation.

Much of the data surrounding the use of vitamin C and zinc in wound healing is a result of multiple, concomitant nutritional interventions in patients with noted existing nutritional deficiencies. No studies were found that examined vitamin C alone. However, a 2012 Cochrane review of six small trials was examined looking at the effects of oral zinc for arterial or venous leg ulcers and found no significant difference with zinc supplementation compared to placebo (RR 1.22, 95% CI: 0.88–1.68). Another small study examined the effects of topical zinc oxide for acute open wounds and found significant decreases in both *Staphylococcus aureus* infections ($p<0.05$) and post-op antibiotic use ($p<0.005$). The study also showed a decrease in median healing time (54 days vs. 62 days) but this was not significant ($p=0.32$).

When looking at combined nutritional interventions, specifically vitamin C and zinc for wound healing, many studies and reviews found unclear benefits to vitamin and mineral supplementation, unless patients had confirmed or suspected nutritional deficiencies. A 2014 Cochrane review of 23 studies and a meta-analysis found no clear evidence for the use of nutritional supplementation in pressure ulcers (RR 0.86; 95% CI: 0.73–1.00).

Both the US and European pressure ulcer guidelines focus on multifactorial care for the management of pressure ulcers. Much of treatment is focused on appropriate wound assessment and evaluation, proper cleaning and debridement, effective topical wound products, nutritional assessment and supplementation, pain management and adjunctive therapy. The US guidelines discuss the need for nutritional supplementation if indicated but state the preferred source is through diet. European guidelines do not mention supplementation with specific minerals and trace elements. Additional guidelines for pressure, venous, diabetic and arterial ulcers only note the use of nutritional supplementation for pressure ulcers. These guidelines specifically note that vitamin and mineral supplementation should only be given if deficiencies are confirmed or suspected and use of zinc supplementation was not found to be beneficial in venous leg ulcers.

Findings:
Benefits to chronic wound healing and ulcer treatment appear to result from a thorough nutritional assessment. The use of caloric, protein, vitamin and mineral supplementation should be considered if confirmed or suspected deficiencies exist. It is apparent that vitamin C and zinc appear to be important pathophysiologically for wound healing but there is insufficient evidence to support the individual supplementation of each routinely.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

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