National PBM Drug Monograph
Papain-Urea (Accuzyme®) and
Papain-Urea-Chlorophyllin Copper Complex Sodium (Panafil®)
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Introduction

The FDA released a document to provide guidance to sponsors, who develop products used in the management of chronic cutaneous ulcers (e.g., venous stasis, diabetic foot, and pressure ulcers) or burns. Recommendations identify labeling claims, outcome measures, and trial design. The incidence of complete wound closure is cited as the most desired outcome measure. *Complete wound closure* is defined as skin closure without drainage or dressing requirements. Additional outcome measures considered clinically significant include accelerated wound closure (time to complete closure) and improved quality of healing (cosmetic and durability).[1] The clinical trials outlined in the monograph will highlight these efficacy outcome measures.

The authors of the FDA Guidance highlight the principle that wounds differ pathophysiologically, suggesting it is impossible to extrapolate the results of a clinical trial evaluating patients with one wound type to patients with a different wound type. In other words, if a product increases the incidence of complete wound closure in pressure ulcers, the results of the trial cannot be generalized to patients with other wound types.[1] The published data for Papain-Urea (Accuzyme®) and Papain-Urea Chlorophyllin Copper Complex Sodium (Panafil®) is available only in the pressure (decubitus) ulcer management.

Care of ulcers involves the debridement of necrotic tissue, cleansing of the wound, and the application of a dressing, which maintains a continuously moist ulcer bed with the surrounding tissue intact skin dry. The debridement methods vary depending on the patient's condition and the associated goals. Various methods may be utilized during the course of caring for the pressure ulcer.[2]

Chemical debridement is the application of a topical agent (enzymatic or nonenzymatic), which chemically disrupts or digests devitalized extracellular material present in the wound. Most of the research in the field of chemical debridement has focused on the use of enzymes with protelytic action, namely Collagenase. Theoretically, the combination of chemical agents, which are nonenzymatic and enzymatic, rather than a single enzyme preparation may offer additional efficacy in the debridement process. Papain-Urea is the combination of a proteolyic enzyme (papain) and a chemical agent, which denatures nonviable protein (urea).[3, 6, 7, 8] Papain-Urea Chlorophyllin Copper Complex Sodium is the proteolytic enzyme (papain), chemical activator (urea), and non-specific inhibitor of wound digestion products (chlorophyllin copper complex sodium).[4, 5, 9] **The monograph will summarize the evidence for the effectiveness of two enzymatic debridement agents, Papain-Urea (Accuzyme®) and Papain-Urea Chlorophyllin Copper Complex Sodium (Panafil®).**

Product Description

Each gram of Accuzyme® enzymatic debriding ointment contains Papain (8.3×10^5 USP units of activity) and 100 mg Urea USP in a hydrophilic ointment base composed of purified water, USP; emulsifying wax, NF; glycerin, USP; isopropyl palmitate, NF; potassium phosphate monobasic, NF; fragrance; methylparaben, NF and propylparaben, NF. It is a water-soluble product that should be stored at temperatures 46-59°F and exposure to temperatures above 90°F for prolonged periods should be avoided.[3]

Each gram of Panafil® enzymatic debriding ointment contains Papain (not less than 521,700 USP units of activity) and 100 mg Urea USP, and 5 mg Chlorophyllin Copper Complex Sodium in a hydrophilic ointment base composed of purified water USP; Propylene Glycol, USP; White Petroleum, USP; Stearyl Alcohol NF; Polyoxyl 40 Stearate, NF; Sorbitan Monostearate, NF; Boric Acid, NF; Chlorobutanol (Anhydrous), NF as a preservative; Sodium Borate, NF. It is a water-soluble product that should be stored at controlled room temperature (59°-89°F).[4]

Panafil® spray contains Papain (not less than 521,700 USP units of activity) and 100 mg Urea USP, and 5 mg Chlorophyllin Copper Complex Sodium in a hydrophilic ointment base composed of purified water USP, Glycerin, USP, Cetearyl Alcohol & Ceteth-20 Phosphate & Dicetyl Phosphate; Mineral Oil, USP; Lactose, (Anhydrous); sodium Hydroxide, NF; Methylparaben, NF; Propylparaben, NF. Store upright at controlled room temperature (68-77°F). [5]

Each gram of Kovia® enzymatic debriding ointment contains Papain (8.3×10^5 USP units of activity) and 100mg urea in a hydrophilic ointment base composed of purified water, isopropyl palmitate, glycerin, promulgen G, potassium phosphate monobasic, fragrance, methylparaben and propyl paraben. Store in a cool place.[6]

Each gram of Ethezyme 830™ enzymatic debriding ointment contains Papain (8.3×10^5 USP units of activity) and 100 mg Urea in an ointment base composed of purified water, USP, emulsifying wax, NF, fragrance, glycerin, USP, isopropyl palmitate, NF, methylparaben, NF, Polyoxyl 40 sterate, NF, potassium phosphate monobasic, USP, and propylparaben, NF and tocopherols, mixed. Store in a cool place.[7]

Each gram of Gladase® enzymatic debriding ointment contains Papain (8.3×10^5 USP units of activity) and 100mg Urea. This is then combined in an ointment base composed of purified water, emulsifying wax, glycerin, isopropyl palmitate, potassium phosphate monobasic, fragrance, methylparaben, and propylparaben. Store in a cool place.[8]

Each gram of Ziox™ debriding-healing ointment contains Papain USP (not less than 521,700 USP units per gram of ointment), 100 mg Urea USP, and 5 mg Chlorophyllin Copper Complex Sodium USP in a hydrophilic base of purified water, Propylene Glycol, USP, White Petrolatum, USP, Stearyl Alcohol, Sorbitan Monostearate, Polyoxyl 40 Stearate, Boric Acid, Sodium Borate and Chlorobutanol (Anhydrous). It is a water-soluble product that should be stored at controlled room temperature (59°-89°F).[9]

Pharmacology/Pharmacokinetics

Papain, is active over a pH range of 3 to 12. It is relatively ineffective when used alone as a debriding agent and requires the presence of activators to stimulate its digestive potency. The combination of papain and urea promotes two supplemental chemical actions. First, it exposes by solvent action, the activators of papain. Secondly, it denatures the nonviable protein matter in lesions; thereby rendering it more susceptible to enzymatic digestion. The combination of papain and urea has been shown in pharmacologic studies to result in twice as much digestive activity as papain alone.[10]

Chlorophyllin Copper Complex Sodium is postulated as promoting healthy granulations, controlling local inflammation and reducing wound odors.[10] Specifically, Chlorophyllin Copper Complex Sodium inhibits the hemagglutinating and inflammatory properties of protein degradation products in the wound, including the products of enzymatic digestion.[11, 12] The manufacturers state the inclusion of Chlorophyllin Copper Complex Sodium in Panafil® and Ziox™ allows its continuous use for as long as desired to help produce and then maintain a clean wound base and to promote healing.[4, 5, 9]

FDA Approved Indications and Off-label Uses

Papain-Urea products were available before 1962, thus the FDA exempted these topical products from the Drug Efficacy Study Implementation (DESI). Therapeutic equivalence information is not available for Papain-Urea and Papain-Urea-Chlorophyllin Copper Complex Sodium because these products were not approved through a New Drug Application (NDA). Equivalence ratings can only be assigned when there is a NDA, which the generic proves bioequivalence.[13]

Papain-Urea and Papain-Urea-Chlorophyllin Copper Complex Sodium are suggested by the manufacturer for debridement of necrotic tissue and liquefication of slough in acute and chronic lesions such as diabetic ulcers, pressure ulcers, varicose ulcers, infected wounds, postoperative wounds, traumatic wounds, burns, carbuncles, and pilonidal cyst wounds. [3, 4, 5, 6, 7, 8, 9]

Current VA National Formulary Status

Non Formulary

Dosage and Administration

Cleansing the wound with a wound cleanser or saline is the initial step in preparing the wound for Papain-Urea or Papain-Urea Chlorophyllin Copper Complex Sodium. It is important to avoid cleansing with hydrogen peroxide solution as it may inactivate the papain.[3, 4, 5, 6, 7, 8, 9]

Papain-Urea or Papain-Urea Chlorophyllin Copper Complex Sodium should be applied directly to the wound and covered with an appropriate dressing that is secured into place. Application daily or twice daily is preferred. Longer intervals between re-dressings (two or three days) have proved satisfactory. Papain-Urea Chlorophyllin Copper Complex Sodium Spray may be applied under pressure dressings. To remove accumulation of liquefied necrotic material, the wound should be irrigated at each redressing.[3, 4, 5, 6, 7, 8, 9]

Instructions for Using Papain-Urea Chlorophyllin Copper Complex Sodium Spray [5]***:***

Prime Container: Upon initial use only, the user will need to prime the non-aerosol spray pump. Begin first time use by holding the spray upright directly over the wound, and prime the pump 6-8 times.

Once the pump has been primed, hold the spray bottle approximately 2" – 3" from the wound and use even, firm, and consistent pressure to dispense the product. When sprayed from the appropriate distance of 2" – 3", the spray should appear in a nickel-sized diameter.

Completely cover the wound site with the spray. The wound should not be visible under the product. Cover wound with appropriate dressing of choice (saline-moistened gauze or semi-occlusive dressings are appropriate), and secure in place.

Papain-Urea Chlorophyllin Copper Complex Sodium Spray is designed to be used at an angle; however, as the product is dispensed, it may be necessary to hold the spray in an upright position to achieve a full pump.

Adverse Effects

Papain-Urea is generally well tolerated and non-irritating. A small percentage of patients may experience a transient "burning" sensation upon applying Papain-Urea. The profuse exudate from enzymatic digestion may occasionally irritate the skin. More frequent dressing changes will alleviate such discomfort until amount of exudate decreases.[3, 4, 5, 6, 7, 8, 9]

Precautions/Contraindications

Papain-Urea is contraindicated in patients who have shown sensitivity to papain or any other components of this preparation. [3, 6, 7, 8]

Adverse Events (Safety Data)

Papain-Urea Chlorophyllin Copper Complex Sodium Spray is generally well tolerated and nonirritating. A small percentage of patients may experience a transient "burning" sensation on application of the spray. Occasionally, the profuse exudates resulting from enzymatic digestion may cause irritation. In such cases, more frequent dressing changes until the exudate diminishes will alleviate discomfort.[3, 4, 5, 6, 7, 8, 9]

Drug Interactions

Hydrogen peroxide solution may inactivate the papain. Precautions to avoid hydrogen peroxide during the wound cleansing process are included in the manufacturer's labeling instructions.[3, 4, 5, 6, 7, 8, 9]

The salts of heavy metals such as lead, silver, and mercury may inactivate papain. Therefore, contact with topical medications containing these metals should be avoided on the wound treated with Papain-Urea.[3, 4, 5, 6, 7, 8, 9]

Clinical Trials

The wound care literature contains few published, comparative clinical trials. The clinical trial section of this monograph contains one published, comparative trial evaluating Papain-Urea (Accuzyme®) and Collagenase (Santyl®) for the treatment of pressure ulcers.[14] Additionally, the monograph contains two published, case series reports evaluating Papain-Urea Chlorophyllin Copper Complex Sodium (Panafil®) for the treatment of pressure ulcers.[15, 16] Abstracts and anecdotal testimonials were not included according to established PBM Drug Monograph Template.

Pressure Ulcer Comparative Trial [14]:

Citation	Alvarez O. Chemical Debridement of Pressure Ulcers: A Prospective, Randomized, Comparative Trial of Collagenase and Papain-Urea Formulations. Wounds 2000; 12(2):15-25.
Study Goals	Primary Efficacy Endpoints • Resolution of necrotic tissue by both clinical evaluation and surface area • Time to complete granulation by clinical assessment • Overall wound score by clinical assessment Secondary Endpoints • Incidence and time to 50% granulation by 4 weeks and ulcer healing • Bacterial burden of wound (quantitative microbiology of wound)
Methods	**Study Design** Randomized, prospective, three center, parallel group, 4-week comparative trial • 21 patients included (10 in the Collagenase group and 11 in the Papain-Urea group) **Screening Phase – 2 weeks** • Wound and devitalized tissue were assessed and measured. • Wound cleansing included a normal saline wash followed by application of a nonadherent primary dressing with moist to moist saline gauze, once daily or as needed. • No other topical agents were used during the screening phase **Treatment Phase – 4 weeks** • Randomized to a treatment group if the target pressure ulcer and area of necrosis were stable (<20% change) or improving (decreased in size) • Efficacy endpoints were evaluated at –2, 0 (randomization), 2, 3, and 4 weeks • Wound bacterial burden was determined prior to treatment, at week 1, 4 weeks and when wound was free of devitalized tissue • Same dressing technique was used throughout study Data Analysis • Percent reduction in size and necrotic tissue were compared for the two treatment groups using the t-test of independent samples • Incidence of 50% granulation was performed with Mann Whitney Rank Sum Test • Debridement and healing rates were performed with the gross cumulative life table method • Comparisons between rates of debridement discontinuation for the Collagenase and Papain-Urea were performed with the Z test. • Statistical significance was considered to be $p < 0.05$ Inclusion Criteria • Wound over a bony prominence in a mobility-compromised individual caused by pressure, shear friction or excessive moisture • Full thickness or partial thickness and may involve bone or muscle • A wound in need of debridement (opinion of investigator) • Nonviable tissue attached to base of wound • Wounds on feet had an ankle brachial index >0.75 or a normal pulse volume recording to exclude arterial disease Exclusion Criteria • Clinical symptoms of infection, cellulitis, osteomyelitis, inadequate nutrition, or uncontrolled diabetes • Clinically significant medical conditions that would impair wound healing inclusive of renal, hepatic, hematologic, neurologic, or immunological disease • Patients receiving corticosteroids, immunosuppressive agents, radiation or chemotherapy within one month prior to study entry

Results

Baseline Demographics

	Collagenase (n = 10)	Papain-Urea (n = 11)
Median Age (years)	80	84
Age Range (years)	77-86	53-90
Ulcer Area (mean, mm^2)	878.1	1062.5
Ulcer Area (range, mm^2)	175-3150	125-3025
Necrotic Tissue Size (mean, mm^2)	806.8	758.9
Necrotic Tissue Size (range, mm^2)	175-3150	125-1825

Debridement of Slough vs. Eschar (%)

	Collagenase	Papain-Urea	p value
Slough			
Week 3	32.7	73.4	Not reported
Week 4	34.0	93.3	
Eschar			
Week 3	46.7	90.8	
Week 4	43.1	98.5	

Reduction in Ulcer Size (%)

	Collagenase	Papain-Urea	p value
Week 1	5.8 +/-17.4	1.9+/-7.6	Not reported
Week 2	19.9+/-29.2	23.7+/-25.8	
Week 3	27.3+/-28.5	34.8+/-25.2	
Week 4	33.9+/-26.17	55.4+/-33.5	

Debridement of Necrotic Tissue by Clinical Evaluation

Scoring System for Necrotic Tissue Percentage:

76-100%	51-75%	26-50%	11-25%	1-10%	none
1	**2**	**3**	**4**	**5**	**6**

Average Score	Collagenase	Papain-Urea	p value
Week 1	2.0	1.9	Not reported
Week 2	2.0	3.9	
Week 3	2.0	4.5	
Week 4	1.3	5.5	

Percent Reduction of Necrotic Tissue from Baseline by Planimetry

	Collagenase	Papain-Urea	p value
Week 3	37.3	86.5	< 0.05
Week 4	35.8	95.4	< 0.01

Overall Wound Response to Treatment by Clinical Assessment

(Assessing granulation, edema, erythema, induration, undermining, odor, exudates type and epithelialization)

Scoring System for Overall Response:

Wound Deteriorated	No Change	Minimal Change	Average Improvement	Significant Improvement	Necrotic Tissue Resolved
0	**1**	**2**	**3**	**4**	**5**

	Collagenase	Papain-Urea	p value
Week 4	1.1	4.5	<0.01

	Amount of Granulation **Scoring System for Granulation Percentage:** None 0% **1** — Pink/dull <25% wound filled **2** — Bright beefy red 25-74% wound filled **3** — Bright beefy red 75-100% wound filled **4** **Average Score** / **Collagenase** / **Papain-Urea** / **p value** Baseline: 1.8 / 1.5 / Not reported Week 1: 1.7 / 3.2 Week 2: 1.5 / 3.5 Week 3: 1.7 / 3.6 Week 4: 2.5 / 3.8 • Linear regression analysis from this data suggested the mean time to 50% granulation was 6.8 days for Papain-Urea and greater than 28 days for Collagenase. **Bacterial burden of wound** • No statistically significant differences in the quantity of resident bacteria between treatment regimens.
Conclusions	• No significant differences exist in the rate of ulcer healing or in bacterial burden of the pressure ulcers treated with either Papain-Urea or Collagenase. • Papain-Urea significantly reduced the area of necrotic tissue at 4-weeks as measured by planimetry in comparison to Collagenase in pressure ulcers requiring conservative debridement. • Pressure ulcers treated with Papain-Urea had a greater degree of granulation than those treated with Collagenase at weekly periods during a 4-week assessment.
Critique	**Limitations** • Small sample size (21 patients) • Study was not blinded to the investigators or patients • *Complete wound closure*, the most useful measure, was not included as a primary efficacy endpoint. • While both products had the same rate of ulcer healing and controlled bacterial burden of the pressure ulcers, the incidence of complete healing was not reported. • Results did not address the primary efficacy endpoint of time to complete granulation. • Reduced area of necrotic tissue and increased granulation measurements are not considered to be acceptable wound healing claims because the clinical benefit of statistically significant differences has not been established. • Although pressure ulcers treated with Papain-Urea had a greater degree of granulation than those treated with Collagenase, authors acknowledged the inability to determine whether the increased granulation tissue production resulted from Papain-Urea or the improved visibility after debridement. • Baseline characteristics in the Papain-Urea group may have favored reduction in necrosis. For example, average necrotic tissue size / average ulcer area was 71% for Papain-Urea and 92% for Collagenase. • Clinical benefit of wound closure was not assessed after the 4-week period; thus, the durability of the effect and the surveillance of adverse effects of the product were not measured. • Collagenase application did not include the use of a topical antibiotic powder as recommended in the package insert. Even though infected wounds were excluded, the authors acknowledge the possibility the topical antibiotic may lower a wound's bacterial burden and subsequently affect the healing process. • Generalizability to the VA population may be limited given the exclusion criteria. • Supported by HEALTHPOINT®

Pressure Ulcer Case Series Reports: [15, 16]

Citation	Miller E. Decubitus Ulcers Treated with Papain-Urea Chlorophyllin Ointment. New York J Med: 1956;May:1446-7.
Study Goals	Primary Efficacy Endpoints • Completed healing or partial healing • Rate of complete healing
Methods	**Study Design** Case series comparing efficacy and safety of Papain-Urea Chlorophyllin (N=24) and Papain-Urea (N=15) Wound cleansing included a normal saline wash followed by application of a nonadherent primary dressing, once daily or as needed. In more resistant cases, a schedule of twice-daily changes was used. Data Analysis • Statistical analysis was not included. Inclusion Criteria • Wound over a bony prominence caused by pressure, shear • Wound resistant to previous therapy Exclusion Criteria • Not specified
Results	**Baseline Demographics** — **PU CCS & PU** (n = 39) Mean Age (years): 70 **Efficacy** — **PU CCS** (n = 24) / **PU** (n = 15) Complete Healing: 23 / 0 Partial Healing: 1 / 0 Rate of Healing Within 3 weeks: 1 Between 3 – 4 weeks: 12 Between 4 – 5 weeks: 5 Between 8 – 12 weeks: 5 **Safety** Irritation: 0 / missing data Local Inflammatory reactions: 0 / 15
Conclusions	• Twenty-three patients with decubitis ulcers, previously resistant to therapy, were completely healed within three months of Papain-Urea Chlorophyllin Copper Complex Sodium therapy. • Patients using Papain-Urea Chlorophyllin Copper Complex Sodium did not experience irritation. • All fifteen patients receiving Papain-Urea discontinued therapy due to local inflammatory reactions within one to three days.
Critique	**Limitations** • Case series design was utilized. • Small sample size (39 patients). • Baseline characteristics in the two groups were not provided. • Generalizability to the VA population is questionable given the exclusion criteria were not specified. • Efficacy results did not specify how complete or partial healing was assessed or defined. • Clinical benefit of wound closure was not assessed after the treatment period; thus, the durability of the effect and the surveillance of adverse effects of the product were not measured. • The concentration of Papain-Urea was not specified. Discontinuation rates related to local inflammatory reactions are difficult to extrapolate to the current branded Papain-Urea (Accuzyme®). • Supported by Rystan Company®

Citation	Morrison J and Casali J. Continuous Proteolytic Therapy for Decubitus Ulcers. Am J Surg:1957;93:446-8.
Study Goals	Primary Efficacy Endpoints • Completed healing or partial healing
Methods	**Study Design** Case series comparing efficacy of Papain-Urea Chlorophyllin (N=30) Data Analysis • Statistical analysis was not included. Inclusion Criteria • Wound over a bony prominence caused by pressure, shear • Wound resistant to previous topical therapy • Patients age between 50 to 80 years Exclusion Criteria • Not specified
Results	**Baseline Demographics –**Not specified **Efficacy** **PU CCS** (n = 30) Complete Healing 27
Conclusions	• Twenty-seven of 30 patients with decubitis ulcers, previously resistant to topical therapy, were completely healed within two to six weeks of Papain-Urea Chlorophyllin. • Complete debridement was accomplished within three to five days. • Patients who did not respond to therapy were described as having extensive necrotic involvement and greater than 80 years old.
Critique	**Limitations** • Case series design was utilized. • Small sample size (30 patients) • Baseline characteristics in the two groups were not provided. • Generalizability to the VA population is questionable given baseline patient demographics, baseline ulcer data, and exclusion criteria were not specified. • Efficacy results did not specify how complete or partial healing was assessed or defined. • Clinical benefit of wound closure was not assessed after the treatment period; thus, the durability of the effect and the surveillance of adverse effects of the product were not measured. • Descriptions of complete debridement, extensive necrotic involvement, and previous topical therapy were not specified. • Supported by Rystan Company®

Acquisition Cost

Chemical Debriding Agents	Size	Cost
Papain-Urea (Accuzyme®) Ointment	30 gram	$ 30.40
Papain-Urea Chlorophyllin (Panafil®) Ointment	30 gram	$ 52.82
Papain-Urea Chlorophyllin (Panafil®) Spray	33 mL	$ 52.82

Self-Proclaimed Generic Papain-Urea Products	Size	Cost
Papain-Urea (Kovia™) Ointment	30 gram	$ 12.74
Papain-Urea (Ethezyme®) Ointment	30 gram	$ 21.83
Papain-Urea (Gladase®) Ointment	30 gram	$ 38.57
Papain-Urea Chlorophyllin (Ziox™) Ointment	30 gram	$ 21.40

Conclusions

Relevant clinical literature for Papain-Urea (Accuzyme®) is limited to one clinical trial evaluating twenty-one patients with pressure ulcers for four weeks of therapy. [14] While both Papain-Urea (Accuzyme®) and Collagenase (Santyl®) had the same rate of ulcer healing and controlled bacterial burden of the pressure ulcers, the incidence of complete healing was not reported as an efficacy measure. Several design considerations coupled with the absence of complete healing rates do not allow differentiation in efficacy between Papain-Urea (Accuzyme®) and Collagenase (Santyl®).

Two case-series reports evaluated patients treated with Papain-Urea Chlorophyllin (Panafil®) for the treatment of pressure ulcers. Miller's evaluation of thirty-nine patients who were treated with either Papain-Urea Chlorophyllin (Panafil®) or Papain-Urea suggests efficacy in the Papain-Urea Chlorophyllin (Panafil®) group. Twenty-three of twenty-four patients were completely healed within three months of Papain-Urea Chlorophyllin Copper Complex Sodium therapy. However, efficacy results did not specify how complete or partial healing was assessed or defined. Clinical benefit of wound closure was not assessed after the treatment period; thus, the durability of the effect and the surveillance of adverse effects of the product were not measured. Patients using Papain-Urea Chlorophyllin Copper Complex Sodium did not experience irritation. In contrast, all fifteen patients receiving Papain-Urea discontinued therapy due to local inflammatory reactions within one to three days. The concentration of Papain-Urea was not specified. Discontinuation rates related to local inflammatory reactions are difficult to extrapolate to the current branded Papain-Urea (Accuzyme®).[15] Morrison and Casali's evaluation of thirty patients who were treated with Papain-Urea Chlorophyllin (Panafil®) suggests efficacy in terms of reported healing rates. It is important to recognize that efficacy results did not specify how complete or partial healing was assessed or defined. In addition, clinical benefit of wound closure was not assessed after the treatment period; thus, the durability of the effect and the surveillance of adverse effects of the product were not measured. The generalizability to the VA population is questionable given baseline patient demographics, baseline ulcer data, and exclusion criteria were not specified.[16]

Recommendations

Papain-Urea and Papain-Urea Chlorophyllin Copper Complex Sodium offer characteristics that are beneficial in a population being treated for pressure ulcers. The data published suggest some improvement in pressure ulcer healing. Based on modest clinical evidence, recommendations include adding Papain-Urea and Papain-Urea Chlorophyllin Copper Complex Sodium as ingredient-specific entities to the VANF. VISNs may identify the preferred product(s) to be dispensed.

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