Anthem

Medical Policy

Subject: Silver-based Products for Wound and Soft Tissue Applications
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Description/Scope

This document addresses the use of antimicrobial silver wound dressings, (for example, Acticoat, Actisorb™, and Silversorb®). Such products have been proposed for the treatment of wounds and soft tissue.

Note: For information regarding the use of other soft-tissue, bone and fat grafting products, please see:

- MED.00132 Adipose-derived Regenerative Cell Therapy and Soft Tissue Augmentation Procedures
- SURG.00011 Allogeneic, Xenographic, Synthetic, Bioengineered, and Composite Products for Wound Healing and Soft Tissue Grafting
- TRANS.00035 Therapeutic use of Stem Cells, Blood and Bone Marrow Products

Position Statement

Investigational and Not Medically Necessary:

Antimicrobial silver wound dressings, (for example, Acticoat, Actisorb, and Silversorb) are considered**investigational and not medically necessary** for all applications.

Rationale

Antimicrobial silver wound dressings (e.g., Acticoat, Actisorb, AQUACEL® AG, Silversorb and Urgotul® Silver) have not been sufficiently evaluated in the peer-reviewed literature. It is not possible to determine their efficacy as a dressing to facilitate wound care because of the limited availability of clinical data. A nonrandomized, non-blinded non-inferiority study by Harding and colleagues published in 2011 compared AQUACEL AG (n=145) to Urgotul Silver (n=136). The results of the study indicate non-inferiority, within a pre-determined non-inferiority margin of -15%. However, it should be noted that the use of either of these products is not well studied in comparison to standard treatment. A study by Biffi and others from 2012 did just that, comparing AQUACEL AG (n=58) in a blinded and randomized manner to standard care (n=54). The authors reported no significant differences between groups with regard to the overall rate of surgical site infections (experimental group, 15.5% vs. controls, 20.4%; p=0.451).

Another non-blinded, RCT involved 24 subjects with diabetic foot ulcers who received treatment with collagen/oxidized regenerated cellulose/silver (COS group) compared to 15 subjects who received standard treatment (Gottrup, 2013). The authors reported that more wounds in the COS group reached 50% wound closure by week 4 (79% [19/24]) compared to the control group (43% [6/14]), (p=0.035). At each time point recorded, there was a higher proportion of improved wounds in the COS group compared with the control group, and the differences were significant at week 4, week 8, and week 10 (p=0.035, p=0.018, p=0.046, respectively). At the end of the study, 91% of wounds in the collagen/ORC/silver treatment group were either healed or showed a reduction in wound size of at least 50% compared to 69% of wounds in the control group. However, this difference was not found to be significant. The number of subjects withdrawing from the study due to wound infection was significantly higher in the control group (31% [4/13]) vs. the COS group (0% [0/23]) (p=0.012). No adverse events were reported to be related to the use of COS. Given this data, further investigation with greater numbers of subjects in a larger number of centers and in different phases of wound care is needed.

In 2015, Ozaki and others published the results of a large RCT involving 500 subjects with lower extremity vascular surgery wounds assigned to post-operative treatment with standard gauze dressing or Acticoat dressing (n=250 per group). The intent-to-treat analysis indicated that there was no significant difference between groups with regard to wound complication rates. The authors concluded that the use of Acticoat provided no benefit with regard to wound complications.

In 2017, Li and colleagues published the findings of a meta-analysis involving nine RCTs including 2196 subjects with surgical wounds. They reported that silver-containing dressings did not effectively prevent the incidence of surgical site infections (RR=0.92), superficial surgical site infections (RR=0.67), or deep surgical site infections (RR=0.78). They also commented that the quality of the available evidence was “very low” and further high-quality studies are needed.

Struik and others (2018) reported the results of an RCT comparing AQUACEL Ag vs. standard care for post-operative wound care in 230 women who underwent breast cancer surgery. A total of 106 subjects received treatment with AQUACEL and 124 received standard care. The authors reported that 7 AQUACEL subjects (6.6%) developed surgical site infections vs. 16 control subjects (12.9%) (RR, 0.51; p=0.112; adjusted OR, 0.49; p=0.135). An ad hoc exploratory subgroup analysis of subjects undergoing breast conserving surgery resulted in surgical site infection rates of 1.8% in the AQUACEL group vs. 10.8% in controls (adjusted OR, 0.15; p=0.087). The AQUACEL group had fewer dressing changes within 48 hours (adjusted OR, 0.12; p<0.001) and fewer re-operations (0% vs. 3.2%, p=0.062). They concluded that the use of AQUACEL did not result in improvements in the primary outcome of the study, surgical site infections.

Connery and others reported the results of a blinded RCT of women undergoing cesarean delivery and treated with either standard gauze dressing (n=330) or Silver Nylon dressing (n=330). They reported that there were no significant differences between groups with regard to the primary outcome, superficial surgical site infection, at 1 and 6 weeks post-op (p=0.096). They concluded that silver nylon dressing was not more effective than gauze for the treatment of post-cesarean delivery wound recovery.

A retrospective review was conducted involving 78 children with mid-dermal torso burns treated with either Acticoat (n=64, 82%) or Biobrane (n=14, 18%) (Selvarajah, 2019). Between 10-14 days, 56% of subjects in the Acticoat group had their burns spontaneously healed without the need of skin graft surgery vs. 71% in of subjects in the Biobrane group. Days to complete healing was reported to be 13 days in the Acticoat group vs. 17 days in the Biobrane group, although this was not statistically significant (p=0.3). The authors also reported that subjects managed with the Biobrane dressing required more operative sessions under general anesthesia, a longer hospital stay, more clinic visits and a higher number of positive wound swab colonization with heavy growth when compared to Acticoat group subjects. They concluded, “Acticoat reduced healing time, decreased the requirements for a general anesthesia,

reduced inpatient hospital stay and risk of infection." These results are impaired by the retrospective methodology, as well as lack of blinding, small number of subjects in the Biobrane group vs. the Acticoat group, and other issues.

Lafontaine (2023) reported the results of an unblinded RCT involving 118 subjects undergoing treatment for diabetic foot ulcers who underwent treatment with either Acticoat dressing (n=63) or dressing without sliver (n=55). The primary outcome, percent of ulcers healed by 12 weeks, was 75% in the control group vs. 69% in the Acticoat group (p=0.49). The percentage of subjects with all ulcers healed was 69% in the control group vs. 60% in the Acticoat group (p=0.32). Regression modeling, adjusting for peripheral arterial disease, infection, and ulcer size at randomization, indicated that the silver was not a factor in healing at 12 weeks (p=0.53). Additionally, the authors reported no significant differences between groups with regard to progression to osteomyelitis (12% for the control group vs. 9% for the Acticoat group, p=0.61), progression to amputation (8% vs. 5%, respectively, p=0.55), new infection following randomization (17% vs. 13%, respectively, p=0.52), or requirement of antibiotics (61% vs. 69%, p=0.33).

Overall, there is a lack of credible scientific evidence published in peer-reviewed medical literature which permits reasonable conclusions concerning the effect of silver dressings for the treatment of wounds. High-quality evidence addressing this issue derived from adequately-powered, well-designed and conducted double-blind RCTs is needed to establish whether or not this treatment method provides results in net health benefit compared to standard of care.

Background/Overview

The skin is the largest organ of the body. It is composed of two layers, the epidermis and the dermis, and provides functions critical to survival. The skin acts as a protective barrier to fluid losses and dehydration and it protects against infection and injury by providing a barrier to repel bacteria and other organisms. The skin provides sensory contact with our environment that tells us whether we are feeling light touch, pressure, pain, heat, or cold. Damage to the skin that is extensive or prolonged may interfere with these functions or with those of other body systems and may become life threatening in some circumstances.

The treatment of burns and wounds that have failed to heal despite conservative measures, referred to as chronic wounds, pose a significant burden on the population in terms of pain, disability, and decreased quality of life. Chronic wounds may be due to the effects of diabetes, venous insufficiency to the extremities, pressure due to prolonged periods in the same body position, and other types of skin injuries. They can be difficult to treat and may require treatment with various coverings, such as skin graft or other materials to prevent infection, maintain an environment conducive to healing, or provide a medium for re-growth of new skin. Antimicrobial silver wound dressings (e.g., Acticoat, Actisorb, Silversorb) involve a synthetic layer of nylon, rayon etc. coated with silver nanocrystals. It has been proposed that such coatings act as a barrier to infectious agents and kill bacteria before they are able to reach the wound.

Definitions

Antimicrobial silver wound dressing (e.g., Acticoat, Actisorb, and Silversorb): A technology proposed to prevent wound adhesion, limit nosocomial (hospital) infections, control bacterial growth, and facilitate burn wound care through a silver-coated dressing material. It consists of layers of a silver-coated synthetic mesh.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
For the following procedure codes or when the code describes a procedure or product indicated in the Position Statement section as investigational and not medically necessary.

HCPCS

A4649	Surgical supply, miscellaneous [no specific code for antimicrobial silver wound dressings (e.g., Acticoat, Actisorb, AQUACEL Ag, Promogran Prisma, Silversorb, Urgotul Silver)]

ICD-10 Diagnosis

	All diagnoses

References

Peer Reviewed Publications:

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2. Brown M, Dalziel SR, Herd E, et al. A randomized controlled study of silver-based burns dressing in a pediatric emergency department. J Burn Care Res. 2016; 37(4):e340-347.
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5. Guthrie J, Potter R. Clinical acceptability of a dressing with matrix technology: a multisite evaluation of acute and chronic wounds. J Wound Care. 2016; 5(8):465-469.
6. Harding K, Gottrup F, Jawień A, et al. A prospective, multi-centre, randomised, open label, parallel, comparative study to evaluate effects of AQUACEL® Ag and Urgotul® Silver dressing on healing of chronic venous leg ulcers. Int Wound J. 2012; 9(3):285-294.
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dermal torso burns. Int J Burns Trauma. 2019; 9(4):82-87.
11. Struik GM, Vrijland WW, Birnie E, Klem TMAL. A randomized controlled trial on the effect of a silver carboxymethylcellulose dressing on surgical site infections after breast cancer surgery. PLoS One. 2018; 13(5):e0195715.
12. Tredget EE, Shankowsky HA, Groeneveld A, Burrell R. A matched-pair, randomized study evaluating the efficacy and safety of Acticoat silver-coated dressing for the treatment of burn wounds. J Burn Care Rehabil. 1998; 19(6):531-537.
13. Yin HQ, Langford R, Burrell RE. Comparative evaluation of the antimicrobial activity of ACTICOAT antimicrobial barrier dressing. J Burn Care Rehabil. 1999; 20(3):195-200.

Government Agency, Medical Society, and Other Authoritative Publications:

1. Dumville JC, Gray TA, Walter CJ, et al. Dressings for the prevention of surgical site infection. Cochrane Database Syst Rev. 2016;(12):CD003091.
2. Norman G, Christie J, Liu Z, et al. Antiseptics for burns. Cochrane Database Syst Rev. 2017;(7):CD011821.
3. Norman G, Dumville JC, Moore ZE, et al. Antibiotics and antiseptics for pressure ulcers. Cochrane Database Syst Rev. 2016;(4):CD011586.
4. Norman G, Westby MJ, Rithalia AD, et al. Dressings and topical agents for treating venous leg ulcers. Cochrane Database Syst Rev. 2018;(6):CD012583.
5. O'Donnell TF Jr, Passman MA, Marston WA, et al.; Society for Vascular Surgery; American Venous Forum. Management of venous leg ulcers: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg. 2014; 60(2 Suppl):3S-59S.
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Websites for Additional Information

1. National Library of Medicine (NIH). Burns. Reviewed April 18, 2016. Available at: http://www.nlm.nih.gov/medlineplus/burns.html. Accessed on November 14, 2023.

Index

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	11/09/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Rationale, References, and Index sections.
Reviewed	11/10/2022	MPTAC review.
Revised	11/11/2021	MPTAC review. Revised title: *Silver-based Productions for Wound and Soft Tissue Applications*. Content for Autologous Skin-, Blood- or Bone Marrow-derived Products for Wound and Soft Tissue Applications moved to TRANS.00035. Content for Bioengineered autologous skin-derived products (for example, SkinTE, MyOwn Skin) moved to SURG.00011. Updated Description, Rationale, Background/Overview, Definitions, References, Websites, and Index sections. Updated Coding section; removed Q4200, Q4226 now addressed in SURG.00011, removed 0232T, 0481T, 20999 and G0460 now addressed in TRANS.00035.
Reviewed	05/13/2021	MPTAC review. Updated Rationale, References and Websites sections.
Revised	05/14/2020	MPTAC review. Title changed to Silver-based Products and Autologous Skin-, Blood- or Bone Marrow-derived Products for Wound and Soft Tissue Applications. Content related to autologous adipose-derived regenerative cell therapy (for example, Lipogems) removed from this document and addressed in MED.00132 Adipose-derived Regenerative Cell Therapy and Soft Tissue Augmentation Procedures. Updated Rationale, Background/Overview, Definitions, Websites for Additional Information and Index sections. Updated Coding section; removed 0489T, 0490T, 0565T, 0566T and S9055.
Revised	11/07/2019	MPTAC review. Removed MN and INV and NMN statements regarding recombinant human platelet-derived growth factor (becaplermin [Regranex]). Updated Description, Rationale, Background, Definitions, and Coding sections; removed HCPCS code S0157.
Revised	08/22/2019	MPTAC review. Revised document title. Revised INV and NMN statement regarding Bioengineered autologous skin-derived products. Added new INV and NMN statements addressing Autologous adipose-derived regenerative cell therapy and Use of autologous protein solution. Updated Description, Rationale, Definitions, References, and Index sections. Updated Coding section with 10/01/2019 HCPCS changes to add Q4226, 01/01/2020 CPT changes to add 0565T and 0566T, also added CPT 0481T, 0489T, 0490T.
Revised	01/24/2019	MPTAC review. Added new INV and NMN statement addressing bioengineered autologous skin-derived products. Updated Description, Rationale, and References sections. Updated Coding section; added HCPCS code Q4200.
Reviewed	01/25/2018	MPTAC review. The document header wording updated from “Current Effective Date” to “Publish Date.” Updated Rationale, References, and Index sections.

Reviewed	02/02/2017	MPTAC review. Updated formatting in Position Statement section. Updated Rationale, References, and Index sections.
Revised	02/04/2016	MPTAC review. Added Aurix to Investigational and Not Medically Necessary statement. Removed Safeblood from document. Updated Rationale, Coding and References sections. Removed ICD-9 codes from Coding section.
Reviewed	02/05/2015	MPTAC review. Added clarification that 'autologous conditioned plasma' is a type of PRP. Updated Rationale and References sections.
Revised	02/13/2014	MPTAC review. Added investigational and not medically necessary statement addressing bone marrow aspirate concentrate. Updated Rationale, Coding and References sections.
Reviewed	05/09/2013	MPTAC review. No change to position statement. Updated Rationale and References sections. Updated Coding section with 07/01/2013 HCPCS changes.
New	05/10/2012	MPTAC initial document development.

Applicable to Commercial HMO members in California: When a medical policy states a procedure or treatment is investigational, PMGs should not approve or deny the request. Instead, please fax the request to Anthem Blue Cross Grievance and Appeals at fax # 818-234-2767 or 818-234-3824. For questions, call G&A at 1-800-365-0609 and ask to speak with the Investigational Review Nurse.

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.