Formulary Clinical Review
32 PPM Silver Hydrogel Antibacterial Wound Dressing Gel
(SilvrSTAT® — American Biotechnology Labs, LLC; Alpine, Utah)
84:04.16 Miscellaneous Local Anti-Infectives

Edgar R. Gonzalez, PharmD, FASHP, FASCP
Associate Professor of Neuroscience
Department of Neuroscience
Marshall University School of Medicine
Huntington, West Virginia
&
Secretary, Pharmacy & Therapeutics Committee
Clinical Pharmacy Manager
Cabell Huntington Hospital, Inc.

Huntington, West Virginia

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Executive Summary

Introduction: SilvrSTAT® is a proprietary formulation of silver (nano-silver at 0.01 micron in purified water) admixed with propylene glycol, triethanolamine, and emulsified with carbomer to yield a hydrosol antibacterial wound dressing gel that contains 32 part per million (ppm) molecular silver (American Biotechnology Labs, LLC; Alpine, Utah). SilvrSTAT® is FDA cleared for the treatment of 1st and 2nd degree burns, wounds including pressure, stasis and diabetic ulcers, lacerations, surgical incision sites, device insertion sites , and graft and donor sites. SilvrSTAT is the only silver FDA cleared to inhibit wounds infected with methicillin-resistant *Staphylococcus Aureus* (MRSA) and vancomycin-resistant *Enterococci* (VRE). Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

Pharmacology: SilvrSTAT® represents a major break through in wound dressings by incorporating metallic, nanocrystalline silver particles suspended in a highly purified gel within a flexible, three-dimensional fabric. This patented multivalent molecular structure gives SilvrSTAT® sustained biocidal activity. The multivalent silver oxide molecule is missing several electrons in its outer shell so it repeatedly "steals electrons" from bacteria and simultaneously "spins off" electrons gained from lyzed bacteria. This gives SilvrSTAT® the unique ability among silver dressings to give continuous killing of microbes; whereas all other cationic silver dressings stop killing once all silver cations are neutralized. Lastly, nanocrystalline silver binds aqueous molecules from wound exudates to yield a silver wound dressing that is both more stable and bioavailable than conventional silver wound dressings. These properties are not observed with either ionic or micronized silver.

Clinical Efficacy: SilvrSTAT® exerts three effects of silver (i.e., antimicrobial, pro-healing, and anti-inflammatory effects) that positively affect wound healing and clinical efficacy. SilvrSTAT® kills a broad range of viruses, fungi, and bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE), and multi-drug resistant organisms (MDROs). SilvrSTAT® demonstrates superior bacteria kill times versus other currently available silver products approved for use in wound management. In-vitro comparison of Kill-time curves for SilvrSTAT® and silver sulfadiazine cream (10,000 ppm) document a clinically relevant advantage for SilvrSTAT® for eradication of MDROs. Treatment with SilvrSTAT® reduces the frequency of MRSA-related decubitus ulcers in the long term care setting. SilvrSTAT® produced successful closure of 95% and 100% of treated wounds at 1 and 5 weeks of treatment, respectively. SilvrSTAT® expedites wound healing by reducing inflammation and activating stem cells to reduce MRSA-related decubitus ulcers by 40%. Furthermore, SilvrSTAT® reduced the cost of treatment by $18.07 per ulcer per day.

Adverse Drug Reactions / Drug Interactions: SilvrSTAT® is intended for external use only. If condition persists or worsens, medical attention may be required. There are no known or reasonably suspected adverse reactions associated with the use of SilvrSTAT®. SilvrSTAT® contains a low concentration of nanocrystalline metallic particles of silver and does not pose a risk for argyria. The silver particles in SilvrSTAT® have a neutral charge and will not interact with sodium chloride in normal saline to precipitate silver as insoluble silver chloride. Wounds may be cleansed with normal saline and then rinsed with a neutral solution without affecting the activity of SilvrSTAT®. However, papain containing wound dressings may be inactivated by silver-containing wound dressing and should not be used concomitantly.

Dosage and Administration: Apply approximately 15 gm of SilvrSTAT® directly to the affected area and cover with an appropriate dressing. For burns, SilvrSTAT® should be applied to the affected area and allowed to dry. SilvrSTAT® Wound Dressing Gel should be changed every 24 hours, but frequency will depend on type and condition of wound.

Clinical Recommendations: SilvrSTAT® should be recommended for formulary inclusion because it offers numerous unique and distinct, patented characteristics when compared to currently available silver wound dressings:

1. Pure, crystalline, metallic silver approximately 5 to 7 nanometers in size.
2. Each nanoparticle of silver is covered by an Ag_40_4 - Ag^2 oxide charged coating.
3. The silver oxide coating separates the nanocrystalline silver particles by 2 to 3 nanometers and allows them to attract electrons individually.
4. The nanoparticles resonate at the frequency of ultraviolet light that kills microbes and explains the catalytic action that sustains the biocidal action of SilvrSTAT® after the silver oxide coating strips away.
5. Produces rapid and continuous bactericidal activity; unlike conventional wound dressings that become inactive once all silver cations are neutralized.
6. Only silver wound dressing FDA-cleared to inhibit MRSA and VRE
7. Low 32 ppm silver concentration and will not stain the skin or pose a risk for argyria
8. No known or expected adverse events
9. Hydrogel formulation may facilitate autolytic debridement of necrotic tissue
10. Contains no sulfa or alcohol
11. Non-flammable
12. May be used with hyperbaric oxygen therapy

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Introduction

SilvrSTAT® is a proprietary formulation of silver (nano-silver at 0.01 micron in purified water) admixed with propylene glycol, triethanolamine, and emulsified with carbomer to yield a hydrogel antibacterial wound dressing gel that contains 32 part per million (ppm) molecular silver (American Biotechnology Labs, LLC; Alpine, Utah).[1] SilvrSTAT® Ag_4O_4 complex allows rapid antibacterial activity at extremely low concentrations of silver. The transparent, water-based, gel improves visualization of the wound, is non-flammable and contains no alcohol, alginate, or sulfa moieties that can impair granulation tissue and surrounding skin.[1]

SilvrSTAT® is a major break through in silver wound dressing products. SilvrSTAT® incorporates metallic, nanocrystalline silver within a three-dimensional fabric that kills a broad range of viruses, fungi and bacteria including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococci* (VRE), and multi-drug resistant organisms (MDROs) (Table 1).[1] SilvrSTAT® is FDA cleared for the treatment of 1st and 2nd degree burns, wounds including pressure, stasis and diabetic ulcers, lacerations, surgical incision sites, device insertion sites , and graft and donor sites. SilvrSTAT is the only silver FDA cleared to inhibit wounds infected with methicillin-resistant *Staphylococcus Aureus* (MRSA) and vancomycin-resistant *Enterococci* (VRE). Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

Table 1. Kill Time Curves with SilvrSTAT®[1]

Organism	Exposure Interval	Avg. Control Titer (CFU/ml)	Percent Reduction	Log Reduction
MRSA	1 HR	1.9×10^6	>99.99	>4.98
	24 HR	1.9×10^6	>99.99	>4.98
P. Aeruginosa	1 HR	2.1×10^6	>99.99905	>5.02
	24 HR	2.1×10^6	>99.99905	>5.02
VRE	1 HR	1.9×10^6	>99.56	2.35
	24 HR	1.9×10^6	>99.99	>5.38

Bacteria	Not less than 1.0 log reduction from the initial calculated count at 7 days, not less than 3.0 log reduction from the initial count at 14 days, and no increase from the 14 days count at 28 days
Yeast & Molds	No increase from the initial calculated count at 7,14, and 28 days

Experimental models of biofilms suggest that silver may reduce bacterial adhesion and destabilize the biofilm matrix, as well as kill bacteria within the matrix and increase susceptibility of bacteria to antibiotics.[2] Nanocrystalline silver is effective for prophylaxis given its rapid and broad spectrum efficacy.[2] The Food and Drug Administration (FDA) has cleared SilvrSTAT® for the treatment of various wound infections; including MRSA and VRE .[1]

Table 2. FDA-cleared indications for SilvrSTAT®[1]

- Management of 1st and 2nd degree burns
- Management of stasis ulcers, pressure ulcers, and diabetic ulcers
- Lacerations, abrasions, skin tears
- Surgical incision sites
- Device insertion site wounds
- Graft wounds, donor sites
- MRSA, VRE

Wound Infections and the Antimicrobial Effects of Silver[2,3]

Pathogenic bacteria contaminate the wound (i.e., no untoward evidence of infection); with subsequent colonization (i.e., multiplying bacteria) and infection (i.e., tissue invasion) (Figure 1). Controlling micro-organisms within a wound environment promotes wound healing. High levels of bacteria, MDROs, and bacterial biofilms impair wound healing by competing with host cells for nutrients and oxygen.[4] Bacterial wound infection causes raised blood cytokines, raised matrix metalloproteinase, and decreased growth factors which can have adverse effects on wound healing.

Figure 1. The Continuum of Wound Contamination to Wound Infection.[3]

Biofilms are complex communities of bacteria found on wound surfaces.[4] They are embedded in a polysaccharide matrix that functions as one organism within its own environment. Biofilms are prevalent in critically colonized wounds which can progress to wound infection. This bacterial load can be reduced by the removal of non-viable tissue with debridement or by using an antimicrobial dressing such as a sustained released silver dressing.

Pharmacology of Silver-Based Wound Dressings[2-7]

Silver is a topical antimicrobial agent with a renewed interest among the medical community because of the emergence of MDROs as well as the paucity in development of new antibiotics. Silver, an inert metal, is absorbed poorly by mammalian or bacterial cells.[4,5] However, wound fluids or other secretions ionize silver to a highly reactive ion that binds free sulfhydryl groups to inhibit bacterial respiratory transport chain and to induce bactericidal proton leak through the cell membrane.[4,5] Studies show that intracellular concentrations of 105–107 silver cations per cell are lethal and produce almost instantaneous cidal activity.[5] As an antiseptic wound dressing, silver reduces bio-burden in wounds and forms a protective barrier for wounds at high risk of infection or re-infection.[2-5] Silver-containing wound dressing may prevent the entry of microbes into vascular access sites, tracheostomy sites, externally placed orthopedic pins, post-surgical drains, chest drains, nephrostomy sites, and epidural catheters.[1]

Silver Delivery Systems in Wound Dressings.[3-7]

Historically, problems with silver wound dressings stemmed from low silver release levels, lack of penetration, rapid consumption of silver ions, and pro-inflammatory constituents that adversely affect wound healing[2-5]. Furthermore, all conventional ionic silver wound dressings on the market stop working once all the ions of silver are neutralized by captured electrons. Today, selection of a silver-containing wound dressing requires consideration of: 1) the characteristics of the ‘‘carrier’’ dressing; and 2) the delivery of silver by the dressing to the wound.[6] Silver-containing wound dressing employ silver either on the surface of the dressing or within the skeletal structure of the dressing (Table 3). Silver can coat the surface of the wound dressing to contact the wound and exert its antimicrobial action. Within the dressing structure, silver acts on bacteria that either absorbs into the dressing via wound exudates or diffuses from the dressing structure into the wound.[6] The amount of silver delivered to the wound is determined by the interactions between the delivery of silver to the wound and wound-derived chloride anions and proteins.[2,3,5-7] Lastly, SilvrSTAT represents a major breakthrough in silver-based wound dressing because its unique molecular structure allows it to kill continuously without the problem of neutralized silver ions.

Table 3. Comparative Properties of Silver Wound Dressings.[1]

Property	SilvrSTAT	Acticoat	Silvadene	Silvasorb
Total silver	32 ppm	86.7 – 116.2 mg/ 4x4 inch	10,000 ppm	1,320 ppm
Metallic nano silver	Yes	Yes	No	No
Continuous killing	Yes	Yes	No	No
FDA cleared to inhibit MRSA and VRE	Yes	No	No	No
Translucent	Yes	No	No	Yes
Ease of administration	Yes	No	No	Yes
Flammable	No	No	Yes	No
Adverse event profile	Excellent	Good	Fair	Fair
Cost	++	++	+	++

Sustained Silver-Releasing Systems—Nanocrystalline SilvrSTAT®[1-10]

SilvrSTAT® represents a major breakthrough in silver-based wound dressings by incorporating metallic, nanocrystalline silver particles suspended in a highly purified gel (Figure 2a) within a flexible, three-dimensional fabric (Figure 2b).[1,2,6-8] This patented multivalent molecular structure gives SilvrSTAT® sustained biocidal activity because the charged particles of silver are not neutralized by captured electrons.[1] The multivalent silver oxide molecule is missing several electrons in its outer shell so it repeatedly "steals electrons" from bacteria and simultaneously "spins off" electrons gained from lyzed bacteria (Figure 2a).[2-10] This gives SilvrSTAT® the unique ability among silver dressings to give continuous killing of microbes; whereas all other cationic silver dressing stop killing once all silver cations are neutralized. These properties are not observed with either ionic or micronized silver.[7-9] Lastly, nanocrystalline silver binds aqueous molecules from wound exudates to yield a silver wound dressing that is both more stable and bioavailable than conventional silver wound dressings.[4-10]

Figure 2a. Chemical structure SilvrSTAT®.[1]

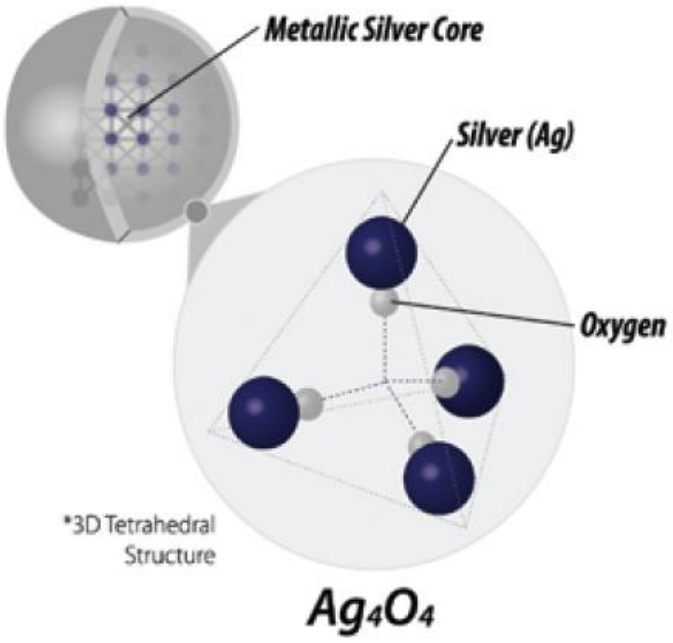
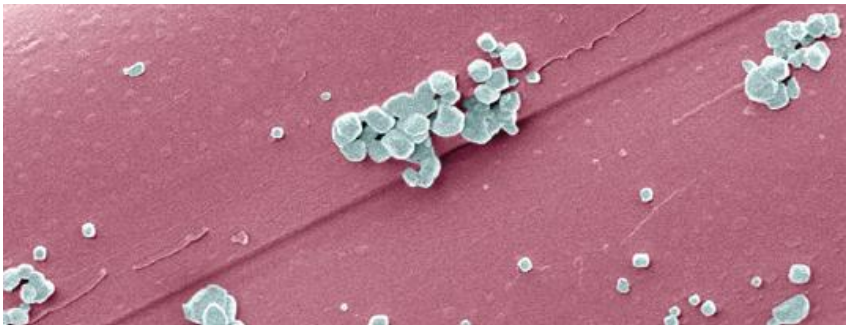


Figure 2b. Nanocrystalline Silver in Wound Dressing Fibers.[7]



Mechanism of Action of SilvrSTAT®[1,2,4-11]

SilvrSTAT® exerts three effects of silver (i.e., antimicrobial, pro-healing, and anti-inflammatory effects) that positively affect wound healing, which, though likely having separate mechanisms of action, are difficult to separate when assessing changes in wound healing.

Antimicrobial Properties[1,2-10]

SilvrSTAT® rapidly kills microbes by blocking the cell respiration pathway. The efficacy of microbe killing is based not only on the amount of silver ion present, but likely also the presence of other silver radicals generated by a silver-releasing product. SilvrSTAT® releases less silver than other topical silver products, but the nanocrystalline structure in SilvrSTAT allows for a greater surface area for silver release over a longer period of time. The rate and degree of microbial killing is significantly faster with SilvrSTAT® than other silver products. A possible explanation is that silver and a number of potent silver radicals are released from the silver nanocrystals on the membrane. These radicals may have more potent antimicrobial properties than silver alone.

Prohealing Effects'[2-11]

SilvrSTAT® therapy has been associated with increased re-epithelialization of non-infected partial-thickness acute wounds. Therefore, in addition to antibacterial properties, there appears to be a prohealing property to silver. The mechanism of the prohealing properties has yet to be defined. In contrast, silver salts and complexes, especially silver nitrate and silver sulfadiazine, appear to impede re-epithelialization.

Anti-inflammatory Properties of Silver'[2-11]

Defining anti-inflammatory properties of silver, which can improve healing, is difficult because of silver's potent antimicrobial activity. However, silver does decrease surface zinc, a cofactor for metalloproteinase activity (MMP) activity. The decrease in MMP activity would be advantageous in a burn wound or a chronic wound; an excess of MMP activity may retard healing. Silver blocks MMP activity in an in-vitro model. Silver has also been reported to increase wound surface calcium. Calcium, in turn, has been reported to increase re-epithelialization rate. Since excess inflammation retards healing, an anti-inflammatory effect would be of benefit. However, further research is required to examine the prohealing effects of silver wound dressing.

In summary, the multiple actions of silver in the patented SilvrSTAT® formulation explains both its activity against multiple microbial pathogens and why SilvrSTAT® is the silver-based wound dressing with the most proven clinical uses (Table 4).

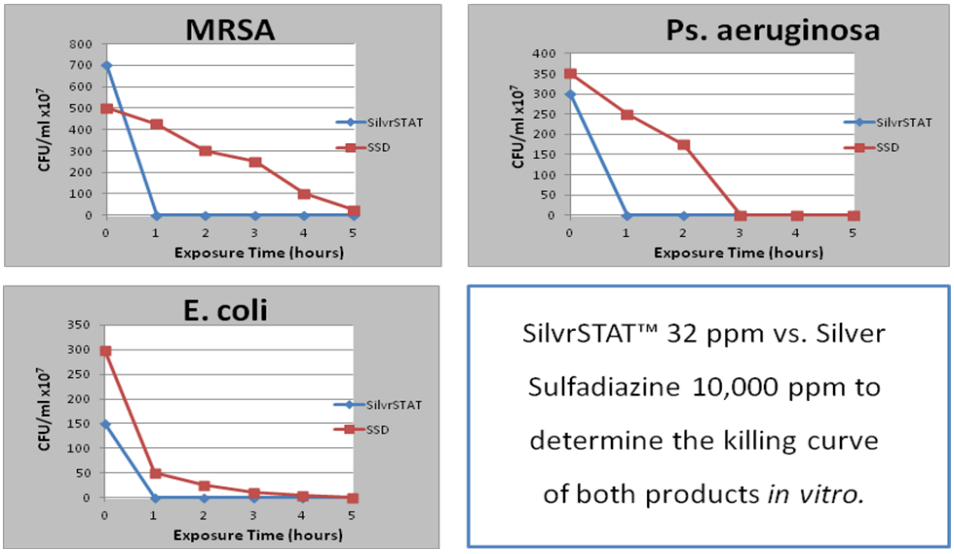
Table 4. Comparison of Proven Uses for Leading Silver Wound Dressings.[14]

Proven Use	SilvrSTAT	Acticoat	Silvadene	Silvasorb
Management of 1st and 2nd degree burns	Yes	Yes	No	No
Adjunct for prevention and treatment of wound sepsis in patients with second and third-degree burns	No	No	Yes	No
Management of stasis ulcers	Yes	Yes	No	No
Management of pressure ulcers	Yes	Yes	No	No
Management of diabetic ulcers	Yes	Yes	No	No
Management of venous ulcers	No	Yes	No	No
MRSA & VRE	Yes	Yes	No	No
Lacerations, abrasions, skin tears	Yes	No	No	No
Surgical incision sites	Yes	No	No	No
Device insertion site wounds	Yes	No	No	No
Donor sites	Yes	No	No	No
Graft wounds	Yes	Yes	No	No

Clinical Efficacy

SilvrSTAT® 32 PPM silver hydrogel antibacterial wound dressing gel has demonstrated significantly superior bacteria kill times versus other currently available silver products approved for use in wound management. In-vitro comparison of Kill-time curves for SilvrSTAT® (32 ppm silver) and silver sulfadiazine cream (10,000 ppm) document a clinically relevant advantage for SilvrSTAT® for eradication of MDROs (Figure 3).[1]

Figure 3. Kill Time Curve for SilvrSTAT® versus Sulfadiazine Cream[1]



MRSA-Related Decubitus Ulcers in Long Term Care Facilities[10]

A study was conducted in long term care facility residents to assess the efficacy of SilvrSTAT® for healing pressure sores infected with nursing home acquired MRSA.[10] The study enrolled 308 long-term care residents from the upper Midwest. All residents suffered from nursing home acquired MRSA for more than one year.[10] All residents received topical

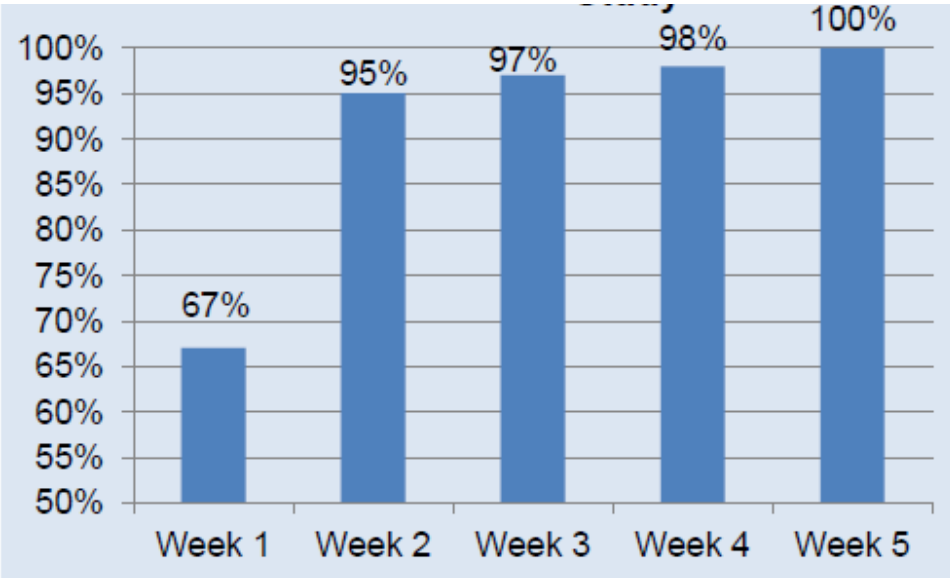
treatment with SilvrSTAT® twice daily in an open label trial. Each week during the course of treatment, the size and depth of the wound as well as the closure rate of the wound were photographed and digitized to determine time to closure and healing. These data were compared with corresponding average values for Wisconsin and for the United States during the same time frame. Treatment with SilvrSTAT® reduced the frequency of decubitus ulcers in the long term care setting (Table 5).

Table 5. Long-Term Care Residents with Decubitus Ulcers[10]

Month	SilvrSTAT® Homes	Wisconsin Mean	National Mean
May 07	10.2%	12.2%	14.2%
June 07	9.6%	11.7%	14%
July 07	9.8%	11.7%	13.8%
Aug 07	12%	11.9%	13.7%
Sep 07	9.6%	11.2%	13.5%
Oct 07	9.6%	10.8%	13.4%
Nov 07	12.3%	10.8%	13.4%
Dec 07	10.2%	11.1%	13.4%
Jan 08	8.5%	11.3%	13.6%
Feb 08	7.4%	11.4%	13.6%

SilvrSTAT® produced successful closure of 95% and 100% of treated wounds at 1 and 5 weeks of treatment, respectively (Figure 4).[10]

Figure 4. Percent Wound Closure over Five Weeks.[10]



The use of SilvrSTAT® proved to be cost-effective for treatment of MRSA-related decubitus ulcers in nursing home residents (Table 6).[10]

Table 6. Cost of Treatment for Pressure Sores[10]

	Standard Cost of Decubitus Care	SilvrSTAT Cost of Decubitus Care	Cost Savings
Cost to Treat Wound	**$353,589**	**$148,001**	**$205,588**
Daily Cost of Wound Therapy Per Patient Day	**$31.25**	**$13.08**	**$18.07**

The authors concluded that SilvrSTAT® expedited wound healing by reducing inflammation and activating stem cells to reduce MRSA-related decubitus ulcers by 40%.[10] Furthermore, SilvrSTAT® reduced the cost of treatment.[10]

Adverse Drug Reactions[1-12]

Silver exhibits low toxicity in humans, and minimal risk is expected due to clinical exposure by inhalation, ingestion, dermal application or through the urological or hematogenous routes. Absorbed silver interacts with other metals and tissue proteins, but these interactions are neither clinically significant nor harmful. One important side effect of silver to note is argyria; the accumulation of silver granules in the skin leading to a permanent blue/gray discoloration. However, at least 10 grams of silver need to be absorbed before signs of argyria are present. Although unsightly, the pigmentation causes no harm or tissue toxicity. The most common causes of argyria are not from medicinal use of silver, but rather through constant environmental exposure. For example, silver miners or chemists who often work with silver may experience argyria.

SilvrSTAT® contains 32 ppm silver as nanocrystalline metallic particles and does not pose a risk for argyria because the molecules of SilvrSTAT® are not readily absorbed into the skin. Studies with SilvrSTAT® do not show evidence of argyria and the condition is not expected to occur since the concentration of nanocrystalline silver particles is small and disposed from the body within 48 hours without accumulation.

There are no known or reasonably suspected adverse reactions associated with the use of SilvrSTAT® Antibacterial Wound Dressing Gel.[1]

Drug Interactions[1,13]

SilvrSTAT® does not contain cationic silver. The silver particles in SilvrSTAT® have a neutral charge and will not interact with sodium chloride in normal saline to precipitate silver as insoluble silver chloride. Wounds may be cleansed with normal saline and then rinsed with a neutral solution.

The patented molecular structure of SilvrSTAT® will preclude it from being rendered inactive by substances in the wound bed that would otherwise chelate free silver ion or precipitate it as an insoluble salt and inhibit its cidal action. Thus sodium chloride, as found in wound exudates or normal saline will not inhibit the antibacterial action of SilvrSTAT®.

Papain containing wound dressings may be inactivated by silver-containing wound dressing and should not be used concomitantly.[13]

Precautions and Warnings[1]

SilvrSTAT® is intended for external use only. If condition persists or worsens, medical attention may be required. SilvrSTAT® contains 32 ppm silver as nanocrystalline metallic particles and does not pose a risk for argyria.

Dosage and Administration[1]

Apply approximately 15 gm of SilvrSTAT® Antibacterial Wound Dressing Gel directly to the affected area and cover with an appropriate dressing. For burns, SilvrSTAT® should be applied to the affected area and allowed to dry. SilvrSTAT® Wound Dressing Gel should be changed every 24 hours, but frequency will depend on type and condition of wound.[1]

How Supplied[1]

SilvrSTAT® Wound Dressing Gel is available in 1 ounce (30 gm) and 3 ounce (90 gm) tubes (Table 7). Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

Table 7. SilvrSTAT® Wound Dressing Gel Packaging

SilvrSTAT® Item #	1 oz	3 oz
AmerisourceBergen (SAP / legacy)	10125528 / 242-406	10125529 / 242-412
Anda	391117	391118
Cardinal	4755112	4755120
McKesson	2008431	2008449
MedAssets (item / catalogue)	445792 / 831060006714	471152 / 831060006738
Owens & Minor	003060006714	003060006738

Storage[1]

Store at room temperature.

Formulary Consideration - Unique Advantages of SilvrSTAT®[1,2,7,8]

SilvrSTAT® should be recommended for formulary inclusion because it offers numerous unique and distinct, patented characteristics when compared to currently available silver wound dressings:

1. Pure, crystalline, metallic silver approximately 5 to 7 nanometers in size.
2. Each nanoparticle of silver is covered by an Ag_40_4 - Ag^2 oxide charged coating.
3. The silver oxide coating separates the nanocrystalline silver particles by 2 to 3 nanometers and allows them to attract electrons individually.
4. The nanoparticles resonate at the frequency of ultraviolet light that kills microbes and explains the catalytic action that sustains the biocidal action of SilvrSTAT® after the silver oxide coating strips away.
5. Produces rapid and continuous bactericidal activity.
6. Only silver wound dressing FDA-cleared to inhibit MRSA and VRE
7. Low 32 ppm silver concentration and will not stain the skin or pose a risk for argyria
8. No known or expected adverse events
9. Hydrogel formulation may facilitate autolytic debridement of necrotic tissue
10. Contains no sulfa or alcohol
11. Non-flammable
12. May be used with hyperbaric oxygen therapy

References:

1. SilvrSTAT Antibacterial Wound Dressing Gel. ABL Medical Data on File. 2013
2. Nowack B, Krug HF, Height M. 120 years of nanosilver history: Implications for policy makers. Environmental Science & Technology. 2011;45:1177-183.
3. Expert Working Group Consensus. Appropriate use of silver dressing in wounds. Wounds International 2012.
4. Percival SL, Bowler PG, Russell D. Bacterial resistance to silver in wound care. J Hosp Infect. 2005;60:1-7.
5. Atiyeh BS, Costagliola M , Hayek SN, et al. Effect of silver on burn wound infection control and healing: Review of the literature. Burns. 2007;33:139-48.
6. Lansdown ABG. A pharmacological and toxicological profile of silver as an antimicrobial agent in medical devices. Adv Pharmacolol Sci. (doi:10.1155/2010/910686).
7. Seltenrich N. Nanosilver: Weighing the risk and benefits. Environmental Health Policy. 2013;121:A220-A225.
8. Rustum R. Ultra-dilute Ag-aquasols with extraordinary bactericidal properties: role of the system Ag-O-H20. Materials Research Innovations. 2007;11:3-18.
9. Demling RH, DeSanti L. Effects of silver on wound management. Wounds. 2001;13(Suppl A):1–15.
10. Silver Sol improves wound healing: Case Studies in the use of Silver Sol in closing wounds (including MRSA), preventing infection, inflammation and activating stem cells. J Scientific Healing and Outcomes. 2009;1.
11. Fong J, Wood Fiona. Nanocrystalline silver dressing in wound management: a review. International Journal of Nanomedicine. 2006;1:441-49.
12. Korani M, Rezayat SM, Gilani K, et al. Acute and subchronic dermal toxicity of nanosilver in guinea pig. International Journal of Nanomedicine. 2011;6:855-62.
13. Drugs.com. Drug interactions between chlorophyllin coppercomplex/Papain/urea topical and Silverstat (http://www.drugs.com/drug-interactions/chlorophyllin-copper-com).
14. SilvrSTAT Antibacterial Wound Dressing Gel Package Insert. Acticoat Package Insert. Silvadene Package Insert.