DE NOVO CLASSIFICATION REQUEST FOR AMFERIA WOUND DRESSING

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Solid wound dressing with permanently bound antimicrobial agent**. A solid wound dressing with permanently bound antimicrobial agent consists of a solid wound dressing containing antimicrobial permanently bound to the substrate surface. The solid wound dressing is used to cover and protect a wound, to absorb exudate, and to maintain appropriate moisture balance within the wound and is intended for use only on external cutaneous (skin) wounds. The solid wound dressing is provided sterile in a form able to hold structural integrity. Antimicrobials are used for protectant purposes only to reduce microbial growth within the solid wound dressing while in use, or to provide an antimicrobial barrier to microbial penetration through the solid wound dressing. This classification does not include solid wound dressings containing a medically important antimicrobial as defined in special control (1).

NEW REGULATION NUMBER: 21 CFR 878.4013

CLASSIFICATION: Class II

PRODUCT CODE: SHA

BACKGROUND

DEVICE NAME: Amferia Wound Dressing

SUBMISSION NUMBER: DEN250006

DATE DE NOVO RECEIVED: March 3, 2025

SPONSOR INFORMATION:

Amferia AB
% AZ BioVentureHub Astra Zeneca
Pepparedsleden 1
Mölndal, SE, 43183, Sweden

INDICATIONS FOR USE

The Amferia Wound Dressing is indicated as follows:

> Amferia Wound Dressing is intended to cover and protect dry-to-low exuding wounds (e.g. abrasions, skin tears, lacerations, incisions and surgical wounds, superficial and

partial-thickness burns, pressure ulcers, arterial ulcers), and to maintain an appropriate moisture balance within the wound.

LIMITATIONS

The sale, distribution, and use of the Amferia Wound Dressing are restricted to prescription use in accordance with 21 CFR 801.109.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

Amferia Wound Dressing is an occlusive, sterile, single use, solid sheet dressing. The solid sheet dressing is surface-modified with a permanently bound antibacterial peptide.

Amferia Wound Dressing is intended to act as a physical barrier to outside contaminants and is not intended to act on the surface or interior of the wound. The antibacterial surface modification only inhibits or minimizes bacterial growth on or within the dressing itself.

The solid wound dressing is made of permanently crosslinked Poloxamer 407, glycerol, and water and is surface modified with a permanently bound antibacterial peptide with the R(RP)4W4 sequence. The amount of the permanently bound antibacterial peptide present is 5.4 micrograms/cm^2.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The Amferia Wound Dressing is categorized as a device in prolonged (>24 h to 30 d) contact with breached or compromised surfaces. The sponsor has addressed the following biocompatibility endpoints according to the relevant FDA guidance and standards:

- Cytotoxicity – MTS Cytotoxicity Test (ISO 10993-5)
- Sensitization – Guinea Pig Maximization Test (ISO 10993-10)
- Irritation – Intracutaneous Reactivity (ISO 10993-23)
- Acute Systemic Toxicity (ISO 10993-11)
- Material-mediated pyrogenicity – Rabbit Pyrogen Test (USP <151>, ISO 10993-11)
- Subacute/subchronic systemic toxicity – Analytical chemical characterization and Toxicological risk assessment (ISO 10993-17, ISO 10993-18)
- Implantation – Porcine wound healing study (ISO 10993-6)

The results demonstrate that the Amferia Wound Dressing is biocompatible.

SHELF LIFE/STERILITY

The Amferia Wound Dressing is sterilized via e-beam irradiation in accordance with ISO 11137-2 to a sterility assurance level (SAL) of 10^{-6}. The shelf life was verified to be 18 months based on real time aging.

PERFORMANCE TESTING - BENCH

Moisture Vapour Transmission Rate and Free Swell Absorptive Capacity testing were performed to evaluate moisture permeability and absorptive performance of the Amferia wound dressing. The testing was based on EN 13726. Test results demonstrate that the subject device can maintain an appropriate moisture balance.

Non-leachability testing was performed to demonstrate that the antibacterial peptide is covalently attached to the solid wound dressing surface and does not leach from the dressing. Testing performed included:

- Zone of inhibition
- Microbiology testing after in vitro extraction
- Comparison of covalently bound vs physically absorbed peptide
- Exhaustive solvent extraction
- Targeted chemical analysis

There was no evidence of antibacterial peptide leaching from the Amferia wound dressing based on the results of the testing.

Minimum effective concentration (MEC) testing was performed to determine the minimum effective concentration of the antibacterial peptide required to support the intended use. The results demonstrated that the MEC is 5.4 $\mu g/cm^2$.

Antibacterial effectiveness testing was performed to characterize the performance of the Amferia wound dressing. The test method was based on AATCC 100, JIS Z 2801, and ISO 22196. Test results demonstrate a >4 log reduction against three gram-positive and three gram-negative bacterial species. The testing included modifications of the aforementioned standards – including conditioning the test article - to represent the clinical use of the product.

Bacterial barrier testing was performed to demonstrate prevention of the penetration of bacteria, including motile species, through the subject device. The test method was a modified version of the ASTM E3383 standard. Barrier effectiveness was evaluated, comparing the Amferia wound dressing to a control - unmodified material with no antibacterial peptide. Test results demonstrate that the Amferia Wound Dressing is an effective barrier against the penetration of three gram-positive and three gram-negative bacterial species, including motile species.

A wearability study was conducted by applying the Amferia Wound Dressing on intact skin of healthy volunteers with different secondary dressings for 72 hours. Photos were taken of the subject device at the beginning and end of the application period. Moisture retention and device stretch were evaluated at the end of the application period. Test results demonstrate that the Amferia wound dressing did not lose adherence or become excessively dehydrated over the 3-day study period though the moisture retention varied depending upon the secondary dressing

that was used. When using the recommended secondary dressing, dehydration percentage of the subject device was limited to 29.55-40.00% after 72 hours.

AMR risk was assessed for the Amferia wound dressing using a literature review approach. The antibacterial peptide is not a medically important antimicrobial and is not associated with a high level of AMR concern.

LABELING

The Amferia Wound Dressing labeling meets the requirements of 21 CFR 801.109 for prescription devices. It contains the indications for use, prescription only symbol, device description, contraindications, general warnings and precautions, instructions for use including disposal instructions, potential adverse events, storage conditions, and symbols and markings. Furthermore, the packaging includes a shelf life for the device.

The labeling also meets the requirements of the special controls set forth for this device type. It contains:

- Instructions regarding the proper placement, sizing, duration of use for the solid wound dressing, frequency of use, and removal of the solid wound dressing;
- A list of each ingredient or component within the solid wound dressing;
- Instructions to monitor for signs of infection;
- A statement regarding the potential retention of material in the wound or the surrounding area and instructions to remove this material, if observed;
- A contraindication for any known sensitivity to components within the product;
- A shelf life (i.e., maximum period the unopened solid wound dressing is stable while stored on the shelf under a specified range of environmental conditions);
- A maximum use life per application of solid wound dressing (i.e., period the solid wound dressing is recommended for use prior to removal);
- A statement regarding when to discontinue use of the solid wound dressing after multiple reapplications based on biocompatibility and performance testing;
- A statement of the role of the antibacterial in the product. All statements regarding the antibacterial are consistent with and placed in the context of the role as a protectant;
- A statement explaining that the antibacterial is not intended to affect wound bioburden.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a wound dressing with permanently bound antimicrobial agent and the measures necessary to mitigate these risks.

Risks to Health	Mitigation Measures
Adverse tissue reaction	Performance testing and technological characteristics Biocompatibility evaluation Antimicrobial leachability testing Labeling
Toxicity	Performance testing and technological characteristics Biocompatibility evaluation

	Antimicrobial leachability testing Labeling
Delayed wound healing	Performance testing and technological characteristics Biocompatibility evaluation Antimicrobial leachability testing Labeling
Incompatibilities with other therapies	Labeling
Contribution to the spread of antimicrobial resistance (AMR)	Exclusion of medically important antimicrobials Antimicrobial characterization and performance testing Antimicrobial leachability testing AMR risk assessment Labeling
Infection	Antimicrobial characterization and performance testing Shelf life validation Sterilization validation Labeling
Microbial growth within the product during use	Antimicrobial characterization and performance testing Antimicrobial leachability testing Sterilization validation
Product degradation during stated shelf storage	Shelf life validation Labeling
Retention of dressing material in wound	Performance testing and technological characteristics Labeling
Loss of barrier function	Antimicrobial characterization and performance testing

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the wound dressing with permanently bound antimicrobial agent is subject to the following special controls:

(1) The device must not contain antimicrobials considered by FDA to be medically important. Medically important antimicrobials are antimicrobials that are important for therapeutic use in humans and associated with a high level of antimicrobial resistance concern (AMR). Medically important antimicrobials include the following classes: Allylamines, Aminocyclitols, Aminoglycosides, Aminomethylcyclines, Amphenicols, Antifolates, Ansamycins, Azoles, Beta-lactams both with and without Beta-lactamase inhibitors, Carbapenems, Cephalosporins, Cephamycins, Cyclic Polypeptides, Dihydrofolate Reductase Inhibitors, Echinocandins, Fluorocyclines, Fluoroquinolones, Fosfomycins, Fusidanes, Glycopeptides, Glycylcyclines, Heterocyclic compounds, Hydroquinolones, Lincosamides, Lipoglycopeptides, Lipopeptides, Macrolides and Ketolides, Macrocyclic peptides, Monobactams, Nitrofurans, Nitroimidazoles, Oxazolidinones, Penems, Penicillins, Phosphonic Acid Derivatives, Pleuromutilins,

Polyenes, Polymyxins, Pseudomonic acids, Quinolones, Rifampin, Riminofenazines, Streptogramins, Sulfonamides, Sulfones, or Tetracyclines.

(2) Performance testing and technological characteristics must demonstrate the functionality of the device to achieve the intended use, including:
  (i) The physical and chemical characteristics of the solid wound dressing must be established. The following must be provided:
    (A) Identity, quantification, and purpose of each component in the finished product;
    (B) Description of the process by which the antimicrobial is bound to the substrate, including the resulting type of bonding (e.g. covalent, ionic, etc.);
    (C) Specifications and characterization of each component in the finished product; and
    (D) Final release specifications for the manufactured solid wound dressing.
  (ii) Performance data must demonstrate that components are present in appropriate amounts to perform as intended under anticipated conditions of use, including evaluation of expected worst-case conditions.
  (iii) The device must be demonstrated to be sterile.
  (iv) The device must be demonstrated to be biocompatible.
  (v) Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use, including evaluation of expected worst-case conditions.
  (vi) Performance data must support the shelf life of the device by demonstrating package integrity and product functionality over the identified shelf life.

(3) Antimicrobial characterization and performance testing must address the following:
  (i) The technological characteristics of the device must indicate the purpose of the antimicrobial and performance data must demonstrate it is present in appropriate amounts to perform as intended under anticipated conditions of use and storage conditions. If the antimicrobial is present as a microbial barrier to cover and protect a wound, microbial barrier testing must demonstrate elimination of passage of microorganisms through the solid wound dressing. If the antimicrobial is present to inhibit microbial growth within the solid wound dressing being used to cover and protect a wound, antimicrobial effectiveness testing must demonstrate inhibition of microbial growth within the solid wound dressing during use. This testing must include:
    (A) Establishment of the Minimum Effective Concentration (MEC) of the antimicrobial in the context of the final solid wound dressing;
    (B) Identification of the period of effectiveness (i.e., maximum product use life) based on concentration of antimicrobial, leachability data, and performance under expected worst-case simulated use conditions; and
    (C) For the tests conducted, evaluation with clinically relevant microbial species, including available strains of challenge organisms containing specific antimicrobial resistance mechanisms as part of expected worst-case scenario performance testing.

(ii) Performance test data must demonstrate that the antimicrobial is bound to the dressing substrate and does not leach from the dressing. This testing must include:
  (A) Extraction studies exposing the dressing to justified conditions to evaluate the leachability of the antimicrobial (e.g. prolonged extraction in solvents of different polarity at elevated temperatures); and
  (B) Assessment of the potential for substrate and/or coating degradation leading to leaching of the antimicrobial.

(iii) Evaluation and identification, based on literature review, of any probable risks for probable contributions to the development and spread of antimicrobial resistance (AMR) must be provided, and must include:
  (A) Identification of the antimicrobial, proposed mechanism(s) of action, and expected spectrum of activity; and
  (B) An AMR assessment for each antimicrobial, including the following characterization elements based on literature review:
    (1) Known resistance mechanisms;
    (2) Transmissibility of resistance mechanisms;
    (3) List of resistant microbial species; and
    (4) Potential for coselection (e.g., via coresistance or cross-resistance) for medically important antimicrobial resistance mechanisms.

(4) Any statements in the labeling must be clear such that they may be understood by the end user, supported by appropriate evidence, and consistent with the intended use of covering and protecting a wound, absorbing exudate, and maintaining appropriate moisture balance within the wound. The labeling must include:
  (i) Instructions regarding the proper placement, sizing, duration of use for the solid wound dressing, frequency of use, and removal of the solid wound dressing, if applicable;
  (ii) A list of each ingredient or component within the solid wound dressing;
  (iii) A warning statement regarding any known incompatibilities with other potential therapies;
  (iv) Instructions to monitor for signs of infection;
  (v) A statement regarding the potential retention of material in the wound or the surrounding area and any applicable instructions for removal of this material;
  (vi) A contraindication for any known sensitivity to components within the product;
  (vii) A shelf life (i.e., maximum period the unopened solid wound dressing is stable while stored on the shelf under a specified range of environmental conditions);
  (viii) A maximum use life per application of solid wound dressing (i.e., period the solid wound dressing is recommended for use prior to removal);
  (ix) A statement regarding when to discontinue use of the solid wound dressing after multiple reapplications based on biocompatibility and performance testing;
  (x) A statement of the role of the antimicrobial in the device. All statements regarding the antimicrobial must be consistent with and placed in the context of the role as a protectant;
  (xi) A warning statement regarding the potential for selection of antibiotic resistant organisms if the wound dressing contains an antimicrobial that may indirectly

select for organisms with medically important antimicrobial resistance mechanisms; and

(xii) A statement that the antimicrobial is not intended to affect wound bioburden.

BENEFIT-RISK DETERMINATION

Amferia Wound Dressing is intended to cover and protect dry-to-low exuding wounds (e.g. abrasions, skin tears, lacerations, incisions and surgical wounds, superficial and partial-thickness burns, pressure ulcers, arterial ulcers), and to maintain an appropriate moisture balance within the wound.

The risks of the device are based on nonclinical laboratory and animal studies as well as information about the many solid wound dressing devices available on the market in the United States.

Probable risks associated with use of this device include adverse tissue reaction, toxicity, delayed wound healing, incompatibility with other therapies, contribution to the spread of antimicrobial resistance, infection, microbial growth within the product during use, product degradation during stated shelf life storage, retention of dressing material in wound, and loss of barrier function.

Clinical safety and performance data are not available for the subject device. These risks are informed in part by probable risks established for other solid wound dressing devices. The probable risks for other solid wound dressing devices were established through premarket submission reviews, FDA Advisory Committee meetings, review of adverse event reports, review of past recalls, and review of scientific literature. The proposed special controls are intended to mitigate these probable risks to health, and these special controls have been met for the subject device, Amferia Wound Dressing.

The probable benefits of the device are also based on nonclinical laboratory and animal studies as well as information about the many solid wound dressing devices available on the market in the United States.

Probable benefits associated with use of this device include covering and protecting a wound, absorbing exudate, and maintaining appropriate moisture balance within the wound. To protect means to provide a physical barrier to the external environment. The probable benefits of the antibacterial peptide include reducing bacterial growth within the solid wound dressing while in use or providing a barrier to bacterial penetration through the solid wound dressing.

As noted above, clinical safety and performance data are not available for the subject device. These benefits are informed in part by probable benefits established for other solid wound dressing devices. The probable benefits for other solid wound dressing devices were established through premarket submission reviews, FDA Advisory Committee meetings, review of clinical guidelines, and review of scientific literature. It has also been noted that the availability of a variety of wound dressings to support different approaches to care for the many types of wounds with heterogeneous wound bed characteristics can provide clinical benefit.

PATIENT PERSPECTIVES

This submission did not include specific information on patient perspectives for this device.

BENEFIT/RISK CONCLUSION

In conclusion, given the available information above, for the following indication statement:

Amferia Wound Dressing is intended to cover and protect dry-to-low exuding wounds (e.g. abrasions, skin tears, lacerations, incisions and surgical wounds, superficial and partial-thickness burns, pressure ulcers, arterial ulcers), and to maintain an appropriate moisture balance within the wound.

The probable benefits outweigh the probable risks for the Amferia Wound Dressing. The device provides benefits and the risks can be mitigated by the use of general and the identified special controls.

CONCLUSION

The De Novo request for the Amferia Wound Dressing is granted and the device is classified as follows:

Product Code: SHA

Device Type: Solid wound dressing with permanently bound antimicrobial agent

Regulation Number: 21 CFR 878.4013

Class: Class II