Evidence Table H-5d. Topical application observational studies

| **Author, Year Country Overall Quality Rating** | **Study Type** | **Eligibility Criteria** | **Exclusion Criteria** | **Number Screened/ Eligible/ Enrolled/ Analyzed** | **Age Sex Race** | **Ulcer Type/Severity at Baseline (Intervention Onset)** | **Treatment A** | **Treatment B** | **Treatment C** | **Duration of Followup** | **Study Setting:** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Harding, 1996115  US  Poor | Phase II, open, prospective uncontrolled study | Stage II PU with a minimum of 5 CM2 | Known sensitivity to study medication, a history of bleeding disorders, pregnant or lactating women, unwilling or unable to cooperate, and chronic or debilitating illness | NR/NR/NR/50 | Age ( Mean): 75 years  Female: 56%  Race: NR | All stage II | Collagenase ABC | NA | NA | 28 days | Hospital |
| Hindryckx, 1990116 Belgium  Poor | Unmatched prospective cohort | Inpatients with a decubitus ulcer with bacterial and/or fungal contamination | Leukopenia, general anti-biotherapy treatment during treatment with silver sulfadiazine cream, pregnancy, known allergy to sulfanilamides and/or components of the silver sulfadiazine cream | NR/NR/21/21 | Age (Mean) 75.7 years Female: 62% Race: NR | NR | Topical: Silver sulfadiazine cream plus pressure relief measures (e.g. position changes, gel cushions, water mattress) | NA | NA | Minimum of 3 weeks (results up to week 8 of followup shown) | Hospital |

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| Narayanan, 2005117  US Fair | Retrospective review | Documentation of at least 1 PU (stage I or II) during the study period. | NR | NR/NR/861/861 | Age:  < 60 years:10.0% 60-69 years: 10.1% 70-79 years:22.1% 80-89 years: 36.4% 90+ years: 20.6%  % Female: 67.1%  Caucasian: 83.3% | Stage I  24.6% vs. 8.8% vs. 66.7% Stage II: 10.6% vs. 21.8% vs. 67.7% | Balsam Peru, hydrogenated castor oil and trypsin (BCT) ointment- Xenaderm | BCT and Other | Other only | Until healed | Nursing home |
| Sherman, 1995118  US  Poor | Prospective controlled study | Patients whose PU had existed for at least one month | Patients with acute cellulites or underlying osteomyelitis | NR/NR/8/8 | Age (Mean): 58  Female: 0%  Race: NR | Stage:  II: N=22  III: N=33  IV: N=3  Location:  Sacrum: N=22  Lateral Foot: N=22  Ischium: N=1  Heel: N=1  Other: N=1 | Maggot therapy | Usual care | NR | 3 to 4 weeks | NR |
| Sherman, 2002119  US  Poor | Observational | Patients with nonhealing wounds, found to be appropriate for maggot therapy and informed consent. | Underlying osteomyelitis or rapidly advancing infection in need of surgery. | NR/NR/103/92 | Age: 64 years Female: NR Race: NR | All stage III PU  Location:  Foot and ankle: 21% (N=10) vs. 255 (N=11) Leg, knee, thigh: 6% (N=3) vs. 125 (N=5) Sacrum, ischium, trochanter: 695 (N=34) vs. 58% (N=25) Other: 4% (N=2) vs. 5% (N=2) | Maggot therapy- Maggots applied to wound at 5-8 per cm2 density for two 48 hour cycles each week. | Conventional treatment | NA | At least two weeks | Hospital |
| Wang, 2010120  China  Poor | Retrospective study | Infected diabetic foot ulcers or pressure ulcers after spinal cord injury | Systemic infection, positive blood bacterial cultures, gangrene of lesion | NR/NR/18/18 | Age (mean): 48  Female: 33%  Race: NR | NR | Maggot larvae were placed on a wound and covered with sterile gauze dressing soaked in saline. Both were changed every day. | Traditional dressing method | NR | Until healing | Hospital |

| **Evidence Table**  **H-5d: Topical Application Observational Studies, continued** |  |  |  |  |  |  |  |  |
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| **Author, year Country Overall Quality Rating** | **Outcomes: Complete Wound Healing** | **Outcomes: Wound Surface Area** | **Outcomes: Healing Time** | **Outcomes: Infection Rate** | **Outcomes: Osteomyelitis Rate** | **Outcomes: Recurrence Rate** | **Outcomes: Pain** | **Other Outcomes: Specify** |
| Harding, 1996115  US  Poor | NR | Treatment A:  Baseline vs Day 28: 20.63 CM2 vs 17.78 CM2 (p=0.017) | NR | NR | NR | NR | NR | Odour, pus, inflammation, and necrosis scores all improved from baseline (p <0.001) |
| Hindryckx, 1990116 Belgium  Poor | NR | Treatment A:  85% (n=18)positive clinical evolution of pressure sores (disappearance of necrosis, development of granulation tissue, decrease in size)  14% (n=3) negative clinical evolution of pressure sores (increase in size) | NR | Treatment A:  57% (n=12) had secondary microorganisms in wounds | NR | NR | 0% (n=0)reported pain during dressing changes; 80% (n=17) had wound pain at start of treatment and 64% (n=11\_ 11/17 pain had subsided during treatment | 475 (n=10) achieved wound sterilization (no bacteria found for at least 2 consecutive weeks); sterilization achieved in 1-3 weeks for heel ulcers (n=6) and 1-5 weeks in sacrum ulcers (n=4); sterilization achieved in 4 cases of *S. Aureus* primary infection after 1 week and in an infection with gram-negative bacteria after 1-5 weeks |
| Narayanan, 2005117  US Fair | NR | Treatment groups A vs. B vs. C Mean duration of treatment for all ulcers in days (healed, not healed) Initial stage 1 wounds 72.1 vs. 94 vs. 87.6 Initial stage 2 wounds 81.4 vs. 151.5 vs. 157.2 | Time to heal, adjusted for covariates, all treated wounds with complete MDS data Treatment groups A vs. B vs. C Initial stage 1 Mean number of days (95% CI): 31.3 (-7.7 to 70.4) vs. 74.9 (42.6 to 107.2) vs. 62.3 (45.5 to 79.2) Initial Stage 2 Mean number of days (95% CI): 57.2 (44.0 to 70.4) vs. 70.5 (60.9 to 80.2) vs. 63.6 (58.9 to 68.3) | NR | NR | NR | NR | Percent of patients with wounds healed, adjusted for covariates, all patients with MDS data Treatment groups A vs. B vs. C Initial stage 1, % patients (95% CI):  74.3% (47.6 to 101.0) vs. 63.7% (44.4 to 83.0) vs. 37.4% (27.3 to 47.6) Initial Stage 2, % patients (95% CI) 53.1% (37.7 to 68.5) vs. 37.2% (28.5 to 45.9) vs. 37.1% (32.9 to 41.4) Initial stage 1 or 2, % patients (95% CI) (p<0.05 for Group A vs. B or C)  58.6% vs. 42.8% vs. 37.1% |
| Sherman, 1995118  US  Poor | NR | NR | Percent reduction per week:  Treatment A: 22%  Treatment B: 22% increase  (p<0.001) | NR | NR | NR | NR | NR |
| Sherman, 2002119  US  Poor | Treatment A:  39%  Treatment B:  21%  (p<0.001) | Treatment A:  -7.3 CM2  Treatment B:  +6.3 CM2  (p<0.05) | Average time to complete healing:  Treatment A: 13.4 weeks  Treatment B: 12 weeks | NR | NR | NR | NR | NR |
| Wang, 2010  China120  Poor | 100% in both treatment groups | NR | Time to wound healing:  Treatment A, 18.7 days  Treatment B, 30.6 days  (p=0.04) | All PU were infected at baseline, time to bacterial negativity was reported:  Treatment A:  10.4 days  Treatment B:  18.7 days  (p=0.022) | NR | NR | NR | NR |

| **Evidence Table H-5d: Topical Application Observational Studies, continued** |  |  |  |  |  |  |  |  |
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| **Author, year Country Overall Quality Rating** | **Harms: Pain** | **Harms: Dermatologic Complications** | **Harms: Bleeding** | **Harms: Infection** | **Other Harms: Specify** | **Severe Adverse Events** | **Withdrawal due to Adverse Events** | **Overall Adverse Events Rate** |
| Harding, 1996115  US  Poor | Treatment A:  N=1 | NR | NR | NR | NR | NR | NR | NR |
| Hindryckx, 1990116 Belgium  Poor | 0% (n=0)reported pain during dressing changes; 80% (n=17) had wound pain at start of treatment, 64% (n=11) pain had subsided during treatment | NR | NR | 50% (n=12)had secondary microorganisms in wounds | NR | NR | NR | NR |
| Narayanan, 2005117  US Fair | NR | NR | NR | NR | NR | NR | NR | NR |
| Sherman, 1995118  US  Poor | NR | NR | NR | NR | NR | NR | NR | NR |
| Sherman, 2002119  US  Poor | Treatment A: 0%  Treatment B: 4% reported discomfort | NR | NR | NR | NR | NR | NR | NR |
| Wang, 2010120  China  Poor | Treatment A:  Authors report that 1 patient in the combined group (diabetic foot and PU) reported bearable pain | NR | NR | NR | NR | NR | NR | NR |