Supplementary

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Prontosan® solution and Prontosan® Debridement Pad in the treatment of different types of cutaneous wounds: expert-based statements, cases series and review of the literature

Supplementary Table 1. Evidence table of randomized controlled trials on Prontosan®.

Study title and/or first author	Journal (year)	Type of lesion	Outcomes	Outcome detection modality/time	Results	Notes
Randomized Controlled Trial of Polyhexanide/Betaine Gel Versus Silver Sulfadiazine for Partial-Thickness Burn Treatment - Wattanaploy	Int J Low Extrem Wounds. (2017)	Partial-thickness burn within 48 hours after injury and burns more than 10% of total body surface area (TBSA).	Clinical efficacy of polyhexanide/betaine gel vs Silver Sulfadiazine **Primary outcome**: healing time **Secondary outcome**: -Burn wound infection -Bacterial colonization -Pain during dressing change -Treatment cost -Satisfactory assessment	After each dressing change, the wound was photographed and the questionnaires were recorded. Burn wounds were evaluated daily by an experienced burn surgeon and nurse. Wound surface swab culture was routinely performed once a week as burn wound infection surveillance.	The wounds of all patients had complete epithelialization within 3 weeks. None of patients had burn wound infection or required surgical treatment. The healing time in the polyhexanide/betaine gel–treated group and the silver sulfadiazine–treated group was 17.8 ± 2.2 days and 18.8 ± 2.1 days, respectively (P = .13). The Kaplan-Meier analysis also showed no significant difference in healing time between the groups Six patients (26.1%) in the polyhexanide/betaine gel– treated group and 6 patients (26.1%) in the silver sulfadiazine–treated group had positive surface swab culture, but no signs or symptoms of infection; and routine swab cultures in the next week were negative. They did not receive any other treatment regarding positive swab culture. The treatment cost of both groups was not significantly different (P = .057). The pain score in the polyhexanide/betaine gel group was significantly less than that in the silver sulfadiazine group at 4 to 9 days and 12 days after treatment. (5.8 ± 0.9 vs 7 ± 1.1, 4.5 ± 1.1 vs 6.7 ± 1.1, 4.1 ± 1.3 vs 6 ± 1.2, 4.2 ± 1.2 vs 5.2 ± 1.2, 3.3 ± 1.1 vs 4.6 ± 1.1, 2.2 ± 1 vs 2.8 ± 1, and 1.5 ± 0.6 vs 1.9 ± 0.7, respectively), Staff consistently reported that polyhexanide/betaine gel was easier with regard to change dressing than silver sulfadiazine; and the wound dressing with polyhexanide/betaine gel was easier to evaluate than the wound dressing with silver sulfadiazine. The	Significant better results for polyhexanide/betaine gel on pain score

					patients were also satisfied with polyhexanide/betaine gel when compared with silver sulfadiazine. Satisfaction with polyhexanide/ betaine gel was only assessed as average to very good, while satisfaction with silver sulfadiazine was assessed as very poor to average.	
Effect of a wound cleansing solution on wound bed preparation and inflammation in chronic wounds: a single-blind RCT – Bellingeri A.	J Wound Care. (2016)	Pressure ulcers (PUs) or vascular leg ulcers (at least 1PU categ II or III according to NPUAP/EPUAP classific)	**Primary:** clinical efficacy (versus normal saline solution) in wound bed preparation (WBP) before debridement **Secondary**: pain at days 0, 7, 14, 21 and 28	-Wounds assessed using **Bates-Jensen wound assessment tool** (BWAT) at inclusion (T0), day 7 - 14 - 21 – 28 (T4). -**Wound inflammation**: analysis of a score from 5 BWAT items: exudate type, exudate amount, surrounding skin colour, peripheral tissue oedema, and peripheral tissue induration. **-Wound size measurement**: sterile rulers and gridded transparent acetate sheets; pictures of the wounds taken at each weekly assessment. **-Pain:** visual analog scale (VAS: values from 0=no pain to 10=worst possible pain). performed at days 0, 7, 14, 21 and 28.	Statistically significant differences between T0 and T4 in favor of SG for: - BWAT total score, (p=0.0248); -BWAT score for inflammatory items, (p=0.03); -BWAT scores for wound size reduction (p=0.049) and granulation tissue improvement (p=0.043), Pain assessment: no significant differences between CG-SG. Follow-up completed in 141 patients in SG and in 139 patients in CG	No adverse events recorded.
Evaluation of the Efficacy and Tolerability of a Solution Containing Propyl Betaine and Polihexanide for Wound Irrigation – Romanelli M	Skin Pharmacol Physiol. (2010)	Painful chronic leg ulcer >8 weeks old and clinical and instrumental signs of venous insufficiency	**Efficacy and tolerability** of a solution containing propyl betaine and polihexanide in order to control the bacterial burden of chronic wounds: Wound Size Measurements, Wound Surface pH Measurements, Pain Assessment were evaluated.	-Wound Size Measurement, -Wound Surface -pH Measurements, -Pain Assessment every day for 4 weeks	-Better pain control achieved during and at the end of treatment in SG than CG ($p < 0.05$). - End study pH measurement: significantly lower ($p < 0.05$) in SG than CG. -During 4wks evaluation, mean wound surface pH statistically significant higher values ($p < 0.03$) vs normal skin.	-No serious and/or unexpected adverse reactions
The effectiveness of a 0.1 % polihexanide gel - Valenzuela	ROL Enf (2008)	Chronic wounds of various aetiologies with granulation tissue	**Primary outcome**: Efficacy of cleansing and control of bacterial burden **Secondary outcome:** progression of bacterial burden in the wound bed and surface	Weakly assessment of wounds	Reversal in positive cultures (p=0.004), reduction in wound size (p=0.013), improvement in: -stagnation of cicatrisation process (p=0.000), -% of granulation tissue (p=0.001), -% of slough in the wound bed (p=0.002), -presence of purulent exudate (p=0.005), -skin condition nearby the wound (p=0.021), -pain control (p=0.049), -erythema in nearby skin (p=0.004), -edema in skin nearby the wound (p=0.000), -heat in the skin nearby the wound (p=0.004), -smell (p=0.029).	

RCT, randomized controlled trials; CG, control group; SG, sperimental group.

Supplementary Table 2. Evidence table of observational studies on Prontosan®.

Study title and/or first author	Journal (year)	Study design	Type of lesion	Outcomes	Outcome detection modality_time	Results	Notes
Cleansing versus tailored deep debridement, a fresh approach to wound cleansing: an Italian experience – Ricci E.	J Wound Care. (2018)	Prospective experimental cohort study	Venous and arterial leg ulcer, mixed ulcer, pressure ulcer, diabetic foot ulcer, other	If cleansing can aid effective wound bed preparation (WBP) WBP Score by Falanga; wound photographic relief; score of infection by Cutting and Harding Pain levels (VAS score). In Group B, periwound skin was also assessed as either normal, damaged, having erythema or macerated	Group A: removal of dressing and wound evaluation, cleansing with 10 ml of PP, photograph with digital camera. Application was with soaked cotton gauze, which was then removed at the specified time. To avoid drying out, PP was reapplied every five minutes. The wound was photographed at the final removal of the gauze. The type of dressing applied was evaluated Group B: Gauze soaked with PP solution was applied to the wound for 10 minutes, after which the gauze was removed and a non-adherent, secondary dressing was applied, in accordance with the site and the aetiological cause of the wound. On days 0, 7 and 14, photographs were taken with a digital camera, and clinical evaluation of the WBP score and the Cutting and Harding score was performed, along with evaluation	In Group A (n=40), after the two and five minute application, no change observed. At 10 minutes, an improvement was seen in 4/10 cases and at 15 minutes the improvement was in 5/10 patients. In Group B (n=30), over the 14 days, an improvement in the condition of the tissue, i.e. the wound bed was cleaned and debrided in 73% of cases, was observed. Patients experienced a reduction in pain. Periwound skin was improved in 29/30 cases, with only one case where the tissue deteriorated, as determined by the presence of maceration.	No adverse events or complications
Efficacy of a Gel Containing Polihexanide and Betaine in Deep Partial and Full Thickness Burns Requiring Split-thickness Skin Grafts: A Noncomparative Clinical Study – Kiefer	J Burn Care Res. (2018)	Prospective experimental cohort study	Deep tissue burn wounds requiring split-thickness skin grafting	Primary: healing of STSGs Secondary: tolerability and safety of PWX for moistening and cleansing	Clinical assessment every treatment day before applying PWX. Postoperative assessment: clinical evaluation and photo documentation of the grafted site. Time to complete reepithelialization estimated by clinical assessment from post operatory day 5 and every other day until complete graft take occurred. Re-epithelialization assessed on photographs using a photo-planimetric analyzing software (Optimas 6, Media Cybernetics, Silver Spring, MD). Percentage of epithelialization was determined in comparison to the size of the grafted area (cm2) immediately following skin grafting -Pruritus was assessed by asking the patient using a scale; -Erythema of the skin at the grafted site clinically assessed using a scale. -Pain at the grafted site was evaluated using an unmarked and unscaled 100 mm VAS	Except for one graft failure, all patients reached complete reepithelialization after one (n = 14), two (n = 31), or three (n = 5) administration of the gel. Median time to complete graft take: 7 days. No wound infections were reported. There was one case of graft failure classified as a serious adverse event. 12 patients (23.5 %) experienced one to 4 adverse events resulting in 28 individually different events. Mild to moderate pruritus at skin graft sites, with a possible relationship to PWX, occurred in 2 patients. A severe adverse event was reported in a patient due to itching in the donor area. The causal relationship to PWX was classified as unlikely as PWX was never applied to donor sites. The changes of pain over time showed a monotonic trend ($P < .01$; page test in ref. 22).Changes from baseline were not significant in trial centers 200 and 300, but significant in center 400 (Wilcoxon test, $P = .01$).	

A retrospective systematic data review on the use of a polihexanide- containing product on burns in children – Ciprandi G	Journal of Tissue Viability (2018)	Retrospective Cohort study	80.1% burns (scald, flame, contact, electric or explosion burns: any degree). Majority of burns (74.7%) were partial thickness burn (IIa and IIb)	Safety of Prontosan® products in children Physicians satisfaction	Burn wounds were characterised by their diagnosis (scald, contact, flame, electric), extent TBSA (Total Body Surface Area) and depth Dressings were changed on average every 2–4 days. Physicians satisfaction with the Prontosan® treatment assessed by a scale from 1 to 5 (Unsatisfied, Satisfied, Good, Very good, Excellent).	No safety concerns: 5 AEs (i.e. rash, itching, and hypergranulating tissue) were reported, none was serious or affected the healing process. Healing time was 11.5 days for a wound TBSA of less than 5% and was around 15 days for 5–19% TBSA. Healing time ranged from 8.5 days for superficial burns, 10.9 days for superficial partial thickness burns, 13.5 days for deep partial thickness burns to 17.2 days for full thickness burns. No negative feedback reported; all physicians were either 'Satisfied' with the treatment (73.2%), considered it 'Good' or 'Very good' (16.2% and 10.6%, respectively).	AEs in 5 children: itching (3), rash (1), hypergranulating tissue (1). 11 patients developed clinical signs of infection during treatment (mainly Staph. aureus). No severe events; all events resolved favourably with good healing results.
The Effectiveness of Topical Polyhexamethylene Biguanide (PHMB) Agents for the Treatment of Chronic Wounds: A Systematic Review - To	Surg Technol Int. (2016)	Systematic review of RCT	Chronic stalled wounds	Wound healing, reduction of bacterial burden, elimination of methicillin-resistant staphylococcus aureus (MRSA), and alleviation of wound-related pain. (Four studies reported wound healing. Two of these evaluated changes in wound surface area and the other two evaluated wound bed evolution.)		In five studies, participants randomly assigned to PHMB topical agents showed significant improvement in bacterial control compared to control groups. Five studies reported pain reduction. Topical PHMB may promote healing of chronic stalled wounds, reduce bacterial burden, eliminate methicillin-resistant staphylococcus aureus (MRSA), and alleviate wound-related pain	
0.1% Polyhexanide-Betaine Solution as an Adjuvant in a Case-Series of Chronic Wounds - Moore	Surg Technol Int. (2016)	Case series	Chronic non-healing wounds of various etiologies	-Number of days to wound closure, -change in absolute wound size, -number of patients requiring antibiotic therapy after initial consultation		Antimicrobial therapy was initiated in 5 of 49 patients. Days to wound closure revealed that venous wounds showed the shortest number of days to closure (29 days) with diabetic ulcers the longest (92 days). Significant comorbid conditions and concomitant medications were present in all groups and did not appear associated with closure rates.	
Evaluation of the effectiveness of a polyhexanide and propylbetaine-based gel in the treatment of chronic wound – Durante C.M.	Minerva Chir. (2014)	Prospective experimental cohort study	Wounds caused by chronic venous insufficiency or autoimmun	Effects (in combination treatment with a secondary dressing after appropriate cleansing) in: -reduction of the wound size; -evolution of the wound bed and edges; appearance of the surrounding skin;	At initial visit and after 7, 15, 30, 45, 60 days of treatment (but no later than the eventual complete healing of the wounds) wound size was measured by metric scale and/or two-dimensional photographic images. In multiple wounds in the same patient, the one	Decreased significantly (P<0.001) wound size (length: -17.5±21.4 cm, width: -15.5±21.1 cm; area: -8.3±16.7 cm2) and pain perceived (VAS: -4.67±2.7; FLACC<1±4); for patients less than 3 years old (FLACC scale). Wound bed: 90% reduction wound size, 80% relative	

			e disease; diabetic wounds in lower limbs; pressure sores; perigastrostomy wounds; other types (scleroderma - connective tissue pathologies)	-assessment of pain by the patient during dressing changes, and microbiological examination of the wound.	with larger size has been selected: the length and the maximum width measured and the surface (length x width) was calculated. In each visit the patient's pain intensity at the local dressing changes was assessed (VAS or FLACC – Face, Legs, Activity, Cry, Consolability scale – in newborn babies and patients younger than 3 years of age). Also assessed type of pain and frequency. Data collected for: type of debridement; aspect of the wound bed; appearance of the periwound skin; aspect of the wound margins/edges, level of exudate. When possible, the presence of bacteria with its charge was evaluated. Finally, the type of secondary dressing and the frequency of treatment replacement were recorded.	reduction in pain vs baseline visit, with wound bed cleansed, granulating or re-epithelializing. -significant decrease in % of pts with wounds with fibrinous and partially necrotic bed, and/or with biofilm. -Edges of the wound and periwound skin: % of pts with improvement in wound edges and surrounding skin significantly increased: 75% reached complete skin integrity. In a smaller percentage, already at the initial visit, the wound edges (28%) or the peristomal skin (18%) was undamaged. -Reduction in exudate: 74% no exudate at final visit vs 15% of non exudative wounds at baseline.	
The Impact of Negative-Pressure Wound Therapy with Instillation Compared with Standard Negative-Pressure Wound Therapy: A Retrospective, Historical, Cohort, Controlled Study – Kim P.J.	Plast Reconstr Surg (2014)	Retrospective historical cohort-control study	Infected wounds (requiring admission with >2 operative débridements that received either NPWT or NPWT+instillation at the initial operation) Ischemic, Neuropathic, Decubitus, Surgical wound, Venous, Traumatic, Other (unclear) with at least two operative débridements	-Number of operating room visits, -length of hospital stay, -time to final surgical procedure during the admission period, -percentage of wounds surgically closed before discharge, -percentage of wounds that remained closed 30 days after discharge, -reduction in microorganisms.	- Number of operative visits: operating room admission for wound débridement or closure. - Length of hospital stay: days admission-discharge. -Time to final surgical procedure: days admission-final procedure during the admission period. -Clinical judgment, laboratory values, radiographic evidence, and qualitative culture results used by the surgeon to determine if wound was ready for closure. -Closure covering the wound by delayed primary closure, skin graft, or flap. -1 month fu after discharge assessment of Wound closed (absence of a break in the skin determined by surgeon). -Improvement in culture results (post debridement cultures from the first operative visit compared with pre débridement cultures from the second operative visit): no growth or decrease in cultured microorganism amount (e.g., heavy growth progressing to scant growth). The two groups were compared for the same 6-month period separated by 1 year.	Statistically significant difference in: -length of hospital stay between NPWT group and the 20-minute dwell time (20mdt) NPWT+instillation group (p = 0.034; 95 percent CI, 0.27 to 6.86), -number of operative visits between NPWT group and the 6-minute dwell time (6mdt) NPWT+instillation group (p = 0.043; 95 percent CI, 0.014 to 0.75) and between NPWT group and the 20-mdt NPWT+ instillation group (p = 0.003; 95 percent CI, 0.19 to 0.93), -time to final surgical procedure between the NPWT group and the 6-mdt NPWT group (p = 0.043; 95 percent CI, 0.065 to 4.04) and between NPWT group and the 20-mdt NPWT+instillation group (p = 0.0019; 95 percent CI, 0.39 to 4.36). -Percentage of wounds closed before discharge significantly higher in the 6-mdt NPWT+instillation group VS NPWT group (p = 0.0004). - Wound culture improvement not different between NPWT group and the 6- or 20-mdt NPWT+instillation grps; When Gram-neg bacter, Corynebacterium, and yeast were excluded from analysis, there was a significantly greater improvement in the 6-mdt NPWT+instillation group than in the NPWT group (p = 0.0001).	

Assessment of a wound cleansing solution in the treatment of problem wounds - Andriessen AE	Wounds (2008)	Retrospective analysis	Venous leg ulcers present for at least 3 months.	Clinical efficacy and cost-effectiveness: -time to healing, -wound bed condition, -pain, -patient comfort during dressing changes -wound cleansing	Time to ulcer closure (healing) and wound evolution: follow-up until ulcer closure (max observation 6 months)	Healed completely in 6 month: Saline/ringer (CG): 89% Polyhexanide containing solution (SG): 97% Healed in 3 months: CG: 28% SG: 60% (P<0.0001)	Infection during treatment: presence of clinical signs CG: 13% SG: 3%
Prontosan wound irrigation and gel: management of chronic wounds - Horrocks	uk (2006)	Case series	Encrustedc ontaminate d and chronic skin wounds whose duration exceeded 1 year and 'appeared' to contain biofilm	-Removal of biofilm: normal wound bed becoming visible within 3 weeks -Reduction in wound size -Compare use of antibiotic/silver prior to and during use of Prontosan -Patient comfort -Ease of application Note any adverse reactions	Clinical/visual evaluation, Photography and tracing	7 of the 10 patients had improvements within 3 weeks. As biofilm was eliminated, staff reported significant reductions in exudate levels. Photography and tracing confirmed visual assessment of reduction of wound size. Patients and staff reported that previously malodorous wounds no longer had an odour. All patients reported significant improvements of quality of lives and that the wound pain was either totally eliminated or considerably reduced. Morale and motivation improved in the community nursing teams. Visits by the community nurses reduced from daily to alternate days or twice weekly visits.	No adverse effects were noted with any patient.
Expert assessment on the benefits of systematic application of Prontosan® solution in wound treatment with particular focus on cost-efficiency when compared to current standard treatment (saline / Ringer) – Eberlein T	uk (2006)	Retrospective Cost-efficiency analysis	Ulcus cruris venosum	-Cost-effectiveness of Prontosan® solution in supporting wound healing (duration of treatment / healing success). -Percentage of healed wounds related to time (time to healing) at 6 months	Data collected and analysed from case records. All cases analysed had complete fu documentation (observed period= 6 months). Cases without fu documentation: not included. Wound duration: Total time wound condition existed. Healing: original defect stably and completely closed (epithelialised). Healing time: period from the beginning of the systematic observation until healing.	Healed wounds: CG: 47/53 (89%) in 6 months SG: 57/59 (97%) In 6 months Highly statistic. significant difference between SG and CG (p<0.0001) in time to healing. SG: the Kaplan-Meier mean time to healing:3.31 months (standard error 0.17) compared to 4.42 months(standard error 0.19) for subjects assigned Saline/Ringer solution.	No economic analysis data (despite declared) Infection during treatment: CG: 7/53 (13%) SG: 2/59 (3%)
Analysis of observational study on the tolerability and combinability of Prontosan® Gel- Mrowietz	Uk (2005)	Retrospective analysis of records	Arterial ulcer 4 mixed art-venous 2 diabetic 4,venous,19 pressure sores 1 others	- Tolerability and combinability of Prontosan®Gel. - Influence on wound odour - undesirable effects with concomitant use with wound dressings		Clear tendency to marked reduction in odour No therapeutic problems No influences on structure (loss of material structure, integrity of material and surface or mater consistency). Patients tolerability (local reactions such as burning sensation, pain, itching) was overall very good.	No provocation or intensification of negative wound margin and wound site reactions

Experiences in using polihexanide containing wound products in the management of chronic wounds – results of a methodical and retrospective analysis of 953 cases - Moeller A	uk	Retrospective analysis	Ulcer in diabetic foot syndrome, venous leg ulcer CVI III, decubitus from II degree, radiotherapy reaction, postoperative disturbance of wound healing	Cleansing effect of wound irrigation, moistening of the wound, skin compatibility, in terms of: -healing -improvement (wound size decreased >25%) -no improvement -Compatibility with different wound coverings, -wound odor (patient), -tolerability of combination therapy and praticability	Compatibility with other wound coverings evaluated macroscopically (changes in the structure or integrity of wound coverings or discolourations)	Wound closure with combination therapy 80%. Good moistening behavior predominantly. No evidence of incompatibility with any other coverings. No adherences. No skin irritations. 2/3 of pts found a great to complete reduction or improvement in odor. Good tolerability of products: 99% no pain or discomfort, 40% slight pleasant cooling effect	Wounds that didn't improve with combo therapy or with a deterioration were not evaluated for cleansing effect Very low methodological quality

P, Prontosan; uk, unknown; CG, control group; SG, sperimental group.

Supplementary Table 3. Evidence table of Randomized Controlled Trials on Prontosan® Debridement Pad.

Study title and/or first author	Journal (year)	Type of lesion	Outcomes	Outcome detection modality_time	Results	Notes
Can dressings soaked with polyhexanide reduce bacterial loads in full-thickness skin grafting? A randomized controlled trial - Saleh	J Am Acad Dermatol (2016)	Full-thickness skin grafting wounds	**Primary outcome**: compare bacterial load reductions in both groups (lowering). **Secondary outcome**: development of SSIs **Tertiary outcome**: intranasal presence of S aureus and its relevance for the bacterial dynamics of surgical wounds (SSIs)	Single follow-up 7 days after surgery. Skin grafts assessed in terms of redness, edema, discharge, graft take, and pain resulting in an overall assessment by the blinded principal investigator classifying a wound as infected or noninfected. Digital photographs were taken of all wounds preoperatively and postoperatively. Bacterial samples were blindly collected from each patient. Swabs were taken in a controlled manner by swabbing in a circular motion for 10 seconds at 3 different phases. Before surgery before antisepsis, the skin area containing the suspected neoplasm planned for excision was swabbed to establish the starting bacterial load level. At end of surgery, the skin graft sutured to the wound was swabbed to establish a second starting load level. A final swab was taken from the wound 1 week after surgery after removal of the tie-over dress. Each swab was analyzed quantitatively by counting (CFU)/cm2 of area swabbed and type of bacteria present. Bacterial quantification done by serially diluting each swab to 3 different concentrations plating each concentrate onto a Todd-Hewitt agar plate using sterile glass beads and incubating all plates in 5% carbon dioxide at 378C for 24 hours. The CFU were then counted and were usually between 30 and 300 CFU. The CFU number was divided with the swab area to measure bacterial loads in CFU/cm2. Bacterial species were determined via matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. Intranasal swabs:Before surgery, an Eswab (Copan) was rotated in the patient's naris that was closest to the neoplasm planned for excision. Typing was performed using matrix-assisted laser desorption/ionization time-offlight mass spectrometry to detect presence of S aureus. No quantification was done on these swabs.	Only dressings soaked with PHMB inhibited growth of both S aureus and S epidermidis. No significant differences in patient characteristics in each group. Most wounds were on the nose, (most common site of skin malignancies) No significant differences among the groups in bacterial load levels measured before surgery, at end of surgery, and after 1 week. No significant differences were detected between the groups in terms of bacterial reduction via the 4 calculations described in ''Methods''. 10 wounds were assessed as infected to give an overall SSI rate of 25%. 8 of these wounds belonged to the intervention group, which had a statistically higher rate of infection (x2 4.8, P = .028). Statistical analyses showed that patient characteristics such as gender, age, and wound location did not correlate to SSI rates in this study. All patients with SSIs had a significantly higher bacterial load measured postoperatively after 1 week. When S aureus was isolated from wounds postoperat after 1 week, patients had a significantly higher bacterial load. Presence of S aureus intranasally before surgery was associated with a higher postoperative bacterial load. Whether coagulase-negative staphylococci (CoNS) were isolated from wounds postoperatively or not had no effect on postoperative bacterial loads, although a higher spread in the total CFUs was observed. The presence of S aureus at the end of surgery in patients resulted in significantly higher postoperative bacterial loads. Typing of all strains isolated from swabs revealed that CoNS and S aureus were the predominant species. The number of species isolated from all patients was highest in the swabs before surgery (27 different species) and lowest 1 week after surgery (8 species). Four of 10 infected wounds contained S aureus.	

Reducing the pathogen burden and promoting healing with polyhexanide in non-healing wounds: a prospective study-Ceviker	Journal of Wound care (2015)	Chronic non-healing wounds of patients who underwent cardiac surgery and had complications of a pressure ulcer (PU) or surgical site infection (SSI)	Efficacy on the bacterial burden, reduction in inflammation in the wound bed and wound size or closure of the wound after 21 days of wound dressing. **Primary outcome:** healthy and bloody granulation tissue on the wound site and negative bacterial cultures. **Secondary outcome**: closure of the surgical suture wounds or secondary intention. Differences in the C-reactive protein (CRP) levels and white blood cell (WBC) counts between the two groups	Data on the participants' surgery, measurement of wound size, length of the epithelialised wound tissue (mean of the three different wound points), culture results, temperature, CRP level, WBC count, and antibiotics usage. The researcher continued to collect a daily wound healing status, data about infection parameters (CRP level and WBC count) every third day, and weekly wound tissue cultures throughout the hospitalisation period of 21 days. The team surgeons decided upon the frequency and the type of the wound debridement. Debridement was conducted once every week or as required. The study was conducted for 21 days. After the study was terminated, moisturisation with RLS and wet gauze dressing was continued for all non-healed wound dressings.	40 pts randomized (20 pts per group). Nine patients excluded from the per-protocol analysis: four underwent negative pressure wound therapy, two dropped out of the study after 1 or 2 days due to an allergy to PHMB, and three died before completion of the 21-day follow-up. Therefore, 31 patients, 15 received PHMB (n=9 with PUs, n=6 for SSI) and 16 received RLS (n=9 with PUs, n=7 with SSI), Included in the PPA. Wound closure was successful in 17/31 (66.7% PHMB group, 43.8% RLS group, p=0.181) patients who were surgically sutured or healed by secondary intention. Wound tissue cultures in 19/31 patients (47.4% PHMB, 52.6% RLS, p=0.886) were negative, and wound size in all these patients were notably reduced in clinical observations. The average wound closure time for all the patients was around 15 ± 4 days (15 ± 5 days in the PHMB group and 16 ± 3 days in the RLS group, p=0.462). The length of the new epithelial tissue was measured at the end of 21 days in patients who had not achieved complete closure. The average length of the epithelialised scar tissue was 6.4 ± 4.4mm. The length of the new scar tissue was 10.4 ± 4.09mm in the PHMB group, and 4.22 ± 2.81mm in the RLS group and the difference was statistically significant (p=0.015). The patients groups were similar with respect to demographic characteristics, comorbidities, risk factors for infection, antimicrobial exposure, and the duration of and types of surgery. The mean duration of the non-healed wound before treatment was 27 days (range: 7–63 days). All patients received systemic antibiotics after the initial cultures and antibiogram results were obtained. No significant differences in type or number of antibiotics given to the two study groups. At the baseline, the mean CRP values and WBC counts were not significantly different between groups. Baseline CRP value was initially 95.3 ± 8.7 and was reduced to 7.8 ± 5.8 after 3 weeks of wound treatment with PHMB. Similarly, baseline CRP value was initially 88.2 ± 26.4 and was reduced to 18.3 ± 12.4 after 3 weeks of wound with RLS. The reduction of CRP was statistically significant within group comparison for both groups (p<0.001). CRP measurement was significantly lower after 12 days (p<0.05) in the PHMB group compared with the RLS group. The baseline WBC counts after the first week had a significant increase in	Adverse events 2 patients in PHMB group: pruritus, erythema, or both around the surgical wound judged as related to the study drugs Three patients died; one of them in the PHMB group who suffered from stroke

					both groups (p<0.001). However after 3 weeks, the WBC count was reduced to the normal range in both of the in PHMB and RLS wound treatment groups, respectively. For patients in the ITT population, initial rate of wound infection was not significantly different between groups. The infection rate of wounds decreased in both groups, but the decrease was not statistically different between PHMB and RLS groups	
Prospective cohort study on surgical wounds comparing a polyhexanide-containing biocellulose dressing with a dialkyl-carbamoyl-chloride-containing hydrophobic dressing - Nielsen	Advances in skin and wound care (2012)	Diabetic foot amputation wounds and surgical wounds (secondary -intention surg wounds)	-Pain levels -dressing adherence (absorb exudates without adhering to the wound bed) -the dressing in group A can be removed in 1 piece without leaving any residue in the wound bed, which enables assessment of the wound bed without additional cleansing; -dressing removal with the BWD + PHMB can be performed without anesthesia	Although most patients had postsurgical pain, before dressing removal, pain was recorded as 0 for all patients. The increase in pain level during dressing changes was assessed after the dressing using a 1- to 5-point scale. The mean pain score during dressing changes was compared with baseline, per patient, per group, and between groups and analyzed using an independent samples test. If patients indicated a pain increase during the dressing change, this was scored. When the score was greater than 3 (on a 5-point scale), the procedure was stopped. The patient would receive either local anaesthesia or general anaesthesia in those cases. Wound condition was documented using standardized digital photographs, which were assessed by 2 experienced wound specialists who examined the wound bed condition. Further clinical observation was used for wound bed inspection and assessment of periwound skin condition.	Types of surgical interventions were similar in both groups, (> forefoot or digit(s) amputations (82%) related to diabetic foot ulcers). No significant differences between groups. All dressings could be identified and removed in 1 piece in both groups. The mean pain score in group A (biocellulose dressing with polyhexanide) was 1.4 (SD T 0.67) and in group B 2.37 (SD T 1.13). Pain levels in group A as analyzed with an independent samples test were significantly lower upon dressing removal (t (59) = 4.026, P G .000), when compared with group B; in group A, 70% (n = 21/30) reported no pain versus 26% (n = 8/30) for group B (a hydrophobic dressing with dialkyl-carbamoyl-chloride). None of the patients in group A reported severe or excruciating pain versus group B, where 13% (n = 4/30) noted severe pain, and 3% of patients reported unbearable pain. These patients required general anesthesia to proceed with the dressing removal. The difference was significant in favor of group A (W2 (1, N = 60) = 4,29, P = .038). The dressing was reported to adhere significantly less (W2 (1, N = 60) = 27,15, P = .000) in group A, 23% (n = 7/30) versus 90% (n = 27) in group B. It was necessary to release the dressing from the wound bed, soaking it with saline in 17% (n = 5) of cases in group A and in 53% (n = 16) in group B (W2 (1, N = 60) = 8.86, P = .003). In both groups, the clinicians noted sufficient absorption of exudate	All enrolled patients (n = 60; n = 30/n = 30) included in the intention-to-treat analysis.
Comparison of PHMB-containing dressing and silver dressings in patients with critically colonised or locally infected wounds - Eberlein	Journal of wound care (2012)	Wounds of various aetiologies	**Primary outcome:** patient-reported pain (VAS) comparing day 0 and day 28 (end)+ pain reduction over time, on days 1, 3, 7, 14 and 21 **Secondary outcome:** antimicrobial effect (bacterial load), wound bed evolution and	Pain score VAS total pain (experienced during day and night) (retrospectively) +assessment of pain before dressing removal and 15min after completing the dressing change. Pain reduction was analysed per patient, per group and between groups. Patients were blinded to their treatment allocation. Frequency of assessments as for pain.	At the 28-day follow-up period, comparing day 0 vs day 28 scores, pain levels significantly reduced for both groups (paired t-test, both p < 0.0001). Comparing VAS scores between groups: significant improvement in VAS scores before dressing change in the BWD+PHMB group, compared with the Ag group, by day 1 (paired t-test, p=0.03). VAS scores continued to decrease by significantly greater amounts and	Target sample size not achieved (n=50), but study recruitment not extended as the deadline

			periwound skin condition, quality of life of patients, and clinicians' satisfaction	Bacterial count assessed using wound swabs according to Levine et al. Wound exudate assessed as mild/moderate/ high by trained, experienced clinicians, using a clinical scoring tool. Wound bed evolution assessed visually, objectively (using the digital Dutch Wound Care Society colour classification system) and as part of the Würzburger quality of life score. Condition of the periwound skin area (tolerability of the dressings): presence and rating of the adverse reactions of maceration and redness (4-point scale) + general score on tolerability (4-point scale) assessed on days 0, 1, 3, 7, 14, 21 and 28 by a clinical investigator blinded to the treatment allocation using a validated clinical scoring tool, based on the global assessment scale (IGA). Clinicians' opinion on treatment: score, on a 6-point scale. General assessment of dressings used in both groups, user satisfaction, dressings' handling and conformability, the simplicity of the treatment devices. Quality of life: Würzburger quality of life score	faster over the 28-day study period for BWD+PHMB compared with Ag-treated pts All pts included presented with critical colonisation or locally-infected ulcers, with very high bacterial load of +++. 25 different species of bacteria identified (Staphylococcus aureus mostly: in 37% of the wounds) Decrease of the critical bacterial burden to harmless contamination or eradication observed in both groups, but BWD+PHMB-treated patients had a significantly faster reduction. By day 3, 25% of wounds a reduction of the bacterial load to +/0 in BWD+PHMB group vs 0% in the Ag group (Fisher's exact test, p=0.03). By day 28, 50% of wounds in BWD+PHMB treated group vs 28% of the wounds in the Ag-treated group, but no longer statistically significant (Fisher's exact test, p=0.764). Total pain also reduced. At day 28 there were significantly more eradicated ulcers in the BWD+PHMB arm vs the Ag treatment arm (Cochran-Mantel-Haenszel Test, p=0.0009). But no significant difference between the two groups in wound evolution, used to measure healing time. Condition of the periwound skin: slight maceration in the BWD+PHMB group at day 7 (mean score=1.2), which decreased during the study period to a mean score of 0.8 by day 28. In the Ag group, less maceration and a significant reduction over the study period, with a mean score at 0.5 at day 1 and of 0.1 at day 28 (Cochran-Mantel-Haenszel test, $p < 0.0001$). Redness of the periwound skin reduced during the study period in both groups, with a significantly larger reduction in the BWD+PHMB treated group (Cochran-Mantel-Haenszel test, $p < 0.006$). Both the BWD+PHMB and the Ag dressings were very well tolerated; for the BWD+PHMB group, at day 1, the mean score was 1.3 and, at day 28, it was 0.8. For the Ag group, the mean score at day 1 was 1.6 and 0.1 at day 28. Investigators: good reports on both dressings, with all questions related to this topic showing a median score of 1–2 (6-point scale). No significant difference in general assessment and the satisfaction scored, but handling and conformability of the dressings significantly better for BWD+PHMB, whereas Ag had significantly better ratings for its ease of use (Cochrane-Mantel-Haenszel test, both $p < 0.005$). Dressings in both groups: improvement of patients' quality of life with the same four	had passed and the additional costs due to administration and an extended study period were not considered to be justified by the recruitment of additional patients No adverse or severe adverse events occurred. No development of a systemic infection noted in either of the treatment groups.

					subscores improving significantly over the study period (Q1, 2, 3 and 14;31 Cochrane-Mantel-Haenszel test, $p < 0.05$). BWD+PHMB also showed two more significantly improved sub-scores (Q5 and 15)	
Clinical evaluation of gauze-based negative pressure wound therapy in challenging wounds - Tuncel U	International Wound Journal (2012)	Wound drainage (> 5 days)+culture positive infection. Venous, diabetic and trauma ulcers and paraplegic and tetraplegic patients with pressure ulcer grades II and III	Effectiveness and safety. Wounds' sizes, number of debridement, bacteriology and recurrence	All patients were followed up for 12 months post-coverage, .	In group I (saline-soaked antibacterial gauze-based NPWT), average wound sizes of pre- and post-treatment periods were 50·60 ± 55·35 and 42·50 ± 47·92 cm2, ($P < 0·001$). Average duration of treatment was 25·52 ± 16·99 days, and average wound size reduction following the treatment was 19·99% in this group. In group II (polyhexanide solution dressings), the wounds displayed considerable shrinkage, accelerated granulation tissue formation, decreased and cleared away exudate. The average wound sizes in the pre- and post-treatment periods were 98·44 ± 100·88 and 72·08 ± 75·78 cm2, respectively ($P < 0·001$). Average duration of treatment was 11·96 ± 2·48 days, and average wound size reduction following the treatment was 32·34%. The patients treated with antibacterial gauze-based NPWT had a significantly reduced recurrence (2 wounds versus 14 wounds, $P = 0·001$), and increased number of culture-negative cases (22 wounds versus 16 wounds, $P < 0·047$) in a follow-up period of 12 months. Two cases of recurrence were found after discharge in group II, whereas there were 14 cases with recurrence in group I. The method resulted in almost two times faster wound healing than treatment with conventional antiseptic dressings. In addition, antibacterial gauze medium with NPWT was superior to conservative wound management in providing bacterial clearance in the treatment of infective wounds	At end treatment, 22 wounds had negative culture. In this group, 5 didn't require surgery. No complication as haematoma/excessive bleeding during the treatment period
Randomized controlled single center study comparing a polyhexanide containing bio-cellulose dressing with silver sulfadiazine cream in partial-thickness dermal burns - Piatkowski	Burns (2011)	up to 10% of total body surface area (TBSA) partial-thickness dermal second-degree burns	-Pain reduction (VAS), -healing time -wound bed condition, comparing day 0 (start) versus day 14 (end), -ease of dressing use -treatment costs	Pain status between dressing changes assessed using a 10 point VAS before dressing removal. Pain level during dressing changes was assessed after the dressing. Wound healing was documented using standardized digital photographs, assessed by two experienced wound specialists, that were blinded for the treatment. The patients were asked about the care of the wound dressing and possible impairment in their daily living. Treatment costs overall were counted up to the day of complete epithelization and are given in	Sixty patients included in the ITT analysis. The majority of burns were scalds (n = 33/72) mainly on the arms (n = 24) and on the thighs. The median healing time for both group A and B was ten days. There was a significant faster and better pain reduction observed for patients treated with BWD + PHMB ($p < 0.01$, Wilcoxon signed rank) both during and in between dressing changes. There was a lower frequency of dressing changes in group B compared to group A (1/day in group A versus 0.4/day in group B). Ease of use was	

				Euro (s). Calculations were done according to Sellmer.	rated better for BWD + PHMB compared to SSD. The wound specialists that performed the dressing changes reported to prefer BWD + PHMB in terms of use and clinical performance compared to SSD. The BWD + PHMB was shown to be more cost-effective than SSD in the treatment of superficial burns. Total materials costs for 10 days treatment with SSD = s 69.51, when personnel costs are included the total = s 165.81. For the BWD + PHMB group total material costs for 10 days treatment = s 51.36, when including personnel costs the total = s 70.61. When using the BWD + PHMB for partial thickness burns up to s 95.20 can be saved for a 10 days treatment period.	
Reduction of bacterial burden and pain in chronic wounds using a new polyhexamethylene biguanide antimicrobial foam dressing-clinical trial results - Sibbald	Advances in skin and wound care (2011)	Chronic wound subjects, stratified to either foot or leg ulcers	**Primary outcome:** Reduction of superficial bacterial burden and promotion of healing (surface area change) **Secondary outcome**: surface colonization of the wound bed using swab culture (bacteriology), pain and other clinical signs of increased bacterial burden (pain, wound, and periwound assessments), and adverse effects	The percentage decrease in wound surface area calculated by measuring wound surface area during each study visit (week 2, week 4) and comparing to baseline. Wound surface areas were measured by multiplying the longest length by the widest width that were perpendicular to each other (length width = cm2). Pain: Subjects were asked to rate their current levels of pain at the study wound prior to dressing removal on a 5-point Likert verbal descriptor scale to assess the level of pain localized at the study wound. Subjects were requested to indicate pain levels 5 minutes after the randomized foam dressing was applied to the study wound. This pain assessment utilized VAS. Wound characteristics were documented using a standardized tool (NERDS and STONEES checklist) Periwound skin condition was evaluated and described. Wound swabs were obtained at baseline and at week 4 to determine the microbiological profile. The bacterial swab was obtained by rotating the swab tip 360 degrees in a 1-cm2 area of the cleanest part of the wound (Levine technique). The swab was then placed in the transport media to be sent to a Clinical Laboratory improvement Amendments–certified central laboratory for susceptibility testing, identification of microbes, and quantitative cultures. To provide quantitative culture data, the bacterial swabs were placed in a known aliquot of liquid (1 mL) and then serially diluted. Wound infection was equated to the equivalent of greater than 105 colony-forming units per milliliter. The number and types of bacterial species cultured were calibrated.	The wound surface areas between the 2 study groups were similar at baseline (P = .55). At week 2, the PHMB study group exhibited a 32% (32.0 cm2) median decrease in wound surface area as compared with the 21% (21.1 cm2) median reduction observed in the control group (P = .31). Upon completion of the study, subjects randomized to the PHMB foam dressing had a 35% median reduction (34.9 cm2) in wound surface area by week 4, compared with 28% (27.8 cm2) in the control group (P = .85). At baseline, no difference in the number of microorganisms recovered from wounds between the 2 study groups. At week 4, polymicrobial organisms were detected in 5.3% of wounds treated with PHMB foam dressing compared with 33% with the control foam dressing (P = .04). Logistic regression analysis examined factors that contributed to the reduction of bacterial burden on the wound surface. The PHMB-impregnated foam dressing was the only significant predictor of the reduction of wound superficial bacterial burden (P = .016) at week 4. Wound scores, NERDS and STONEES checklists, and periwound skin assessments were similar between the 2 subject groups at baseline. The percentage of maceration at the periwound demonstrated a similar trend during the study period in both study groups. From baseline to week 4, periwound maceration of the subjects allocated in the PHMB group increased from 36.8% to 57.9%, and subjects allocated to the control group increased from 47.6% to 61.9%. Baseline pain assessments were comparable between the 2 study groups (33.3% no pain PHMB foam vs 31.6% control, P = .79). At week	statistical analysis per protocol; (adverse event data analyzed by ITT principle). NO stat sign sample size Minimal adverse events reported, none related to the study dressings or procedures. 2 subjects in the control group developed infections localized at the study wound. 1 subject in the control group required a new prescription for systemic antibiotic related to the study wound. None of the subjects randomized to the PHMB foam dressing

					2, a higher proportion of subjects in the PHMB foam group (78.9%) reported no pain prior to dressing change than in the control group (33.3%), as measured by the 5-point Likert scale. The difference was significant (P = .0006). Pain ratings remained consistently lower through week 4, with 73.7% in the PHMB group reporting no pain (P = .02) versus 38.1% in the control group. At week 2, pain levels 5 minutes after dressing application were also measured via the VAS; the same trend in pain reduction was apparent, with subjects randomized to the antimicrobial foam dressing reporting greater comfort (P = .05).	developed wound

P, Prontosan; uk, unknown; CG, control group ; SG, sperimental group.

Supplementary Table 4. Evidence table of observational studies on Prontosan® Debridement Pad.

Study title and/or first author	Journal (year)	Study design	Type of lesion	Outcomes	Outcome detection modality/time	Results	Notes
Prontosan Debridement Pad: Made Easy – Irving S.	uk (2018)	Case series	Long term, chronic leg ulcer	Clinical effectiveness in removing biofilm as part of the debridement process		Patients satisfied with treatment. All patients tolerated the product. Clinical judgement to determine effective results; regardless of whether the wound was pre-soaked or not. Clinician noted: effects improved when wound pre-soaked, but using the product independently is an effective option where necessary.	
Advances in wound cleansing: an integrated approach – Ovens L.	uk (2018)	Case series	Pyoderma gangrenosum, arterial ulcer, venous ulcer, diabetic ulcer	**Clinical evaluations** using the Protosan Debridement Pad in practice		See previous results (casistic duplication)	
A cohort study on the efficacy of a polyhexanide-containing biocellulose dressing in the treatment of biofilms in wounds - Lenselink	Uk (2011)	Prospective cohort study	Non-healing locally infected and/or critically colonised wounds of various aetiologies that showed clinical signs of biofilm	Eradication of biofilms Safety and efficacy endpoints **Primary outcome**: % of wounds healed and reduction of biofilm, comparing day 0 with week 24 results. **Secondary outcome**: reduction of wound area, wound bed condition, the shift from yellow tissue to epithelialisation (indicating the 'starter function' of the dressing used — that is, that the wound is no longer stagnating, with signs of a progression toward heal-ing) and pain reduction, comparing day 0 with week 24 results. Safety of dressing use and handling of the dressing were evaluated.	Maximum follow-up: 24 weeks or until full healing. Wounds assessed through clinical observation, using a clinical scoring tool based on the validated tool developed by Dissemond et al. Assessments twice a week at dressing change and at week 24, by the clinical nurse specialist (EL). After 24 weeks, reduction of the biofilm was scored on a three-point scale, and results compared with baseline. The occurrence of systemic and/or invasive local infection was evaluated using clinical observation, following expert opinion, and the EWMA position document. Cleansing efficacy and stimulation of autolytic debridement was evaluated comparing the percentage of granulation and percentage epithelial tissue (time to 75% granulation and 50% epithelialisation) present at day 0 and after 24 weeks, using the Dutch Wound Care Society colour classification system. First the reduction of biofilm was scored and then the percentage of black, yellow and red tissue, as well as epithelial tissue, was assessed.	Of the 28 patients included in the study, 16 (nine females, seven males), completed the study period. 8 patients (29%) discontinued due to reasons not study related and 4 patients (14%) discontinued due to copious production of exudate, which could not be handled effectively by the dressing. At 24 weeks, 12 (75%) wounds had healed. For those wounds that had not closed, the wound size had reduced by a mean of 9.6 ± 14.5cm2 (61%) of the wound surface, from a mean of 15.3 ± 14.5cm2 at day 0 to mean 6.0 ± 13.0cm2 at week 24. Ten patients (63%) had a good reduction of biofilm, five (32%) scored 'moderate' and one (6%) had no reduction noted. The 63% that scored a good reduction of the biofilm went on to wound closure. For all patients, the mean percentage of granulation tissue present in the wound bed had increased significantly ($p < 0.04$) when comparing day 0 (38.2 ± 34.6%) with week 24 (77.4 ± 36.0%). The percentage of yellow tissue present in the wound bed had decreased significantly ($p <$	analysis was not done on an intention-to-treat basis No patients experienced a systemic infection (n=0).

					Pain at dressing change assessed by the patient using a 10- VAS comparing day 0 with 24 weeks. Pain was assessed 10 minutes before, during and 10 minutes after the dressing change, and a mean was taken of the three measurements.	0.01) when comparing day 0 (61.8 ± 34.6%) and week 24 (22.6 ± 36.0%). All participants reported a reduction in pain after study dressing application. The mean VAS score at day 0 was 7.4, which reduced to a mean of 3.2 by week 24.	
Feasibility and clinical applicability of polihexanide for treatment of second-degree burn wounds - Daeschlein	Skin Pharmacol Physiol (2007)	Case series	II-degree burn wounds (healing decubitus ulcers) +average burns of 28% of TBSA which could not be primarily treated with skin grafts due to inadequate wound bed conditions	Clinically and histologically re-epithelialization		In all patients, treated areas epithelialized without any further débridement after 10+/-1 days with complete absence of pain. No fibrin discharge on the wound compared with the topical treatment with silver nitrate. The cooling effect of the evaporation of the solution on the skin was reported to be pleasant and allows the rewetting of the wound dressings to be left to the patients themselves.	No cases of wound infection occurred.

P, Prontosan; uk, unknown; CG, control group; SG, sperimental group.

Supplementary Table 5. Experts-based recommendations on Prontosan® Debridment Pad use in acute and chronic wounds.

N.		Median	IQR	Grade of strength
1	Lesions that will benefit most from Prontosan Debridment Pad (PDP) are: • Post-traumatic wounds (post-acute phase) • Mixed wounds • Inferior limbs wounds • Venous wounds • Intermediate-deep thickness burn wounds • Grafting wounds • Diabetic foot • II and III stage pressure ulcers (not undermined)	9	8-9	**Strong**
2	Prontosan Debridement Pad should not be routinely used in: • IV stage pressure ulcers (undermined) • Cancer-related or necrotic wounds	8	7-9	**Strong**
3	Lesions that will benefit most from Prontosan Debridment Pad are those characterized by: • Clean wound bed • Wound bed preparation score (WBPS) B or C	8	7-8	**Strong**
4	Prontosan Debridment Pad use is not advisable only in: • Severe cardiopathies • Bullous diseases • Severe pain (>7)	8	7-9	**Strong**
5	In patients taking oral anticoagulation treatment, Prontosan Debridment Pad can be used adopting appropriate surveillance measures.	8	8-9	**Strong**
6	Prontosan Debridment Pad use is limited to medical and nurse health care professionals with expertise in wound care. Caregivers can use it if enabled and trained in wound debridement.	8	6-9	**Strong**
7	To ensure the most effective application of Prontosan Debridment Pad (PDP), refer to user instructions available on the packaging. Further suggestions are: • Impregnate Prontosan Debridement Pad with 15-20 mL of Prontosan solution at each application • Use Prontosan Debridement Pad after a compress of 10-15 minutes. • Use Prontosan Debridement Pad once as a disposable device • Follow local proceedings to create a steril field • Use more than a Prontosan Debridement Pad for wide lesions (10 x 10 cm) • Use Prontosan Debridement Pad with centrifugal movements	9	8-9	**Strong**
8	The application of Prontosan Debridement Pad is advisable at each dressing change. The minimum follow-up is of four weeks	9	8-9	**Strong**
9	Prontosan Debridement Pad is compatible with any other premedication. A prior compress of the wound with Prontosan solution at variable times (5'-10'-15') according to the wound stage (see table B) is advisable.	9	8-9	**Strong**
10	The main outcome to pursue is a deep wound cleansing assessed by the Wound bed preparation score (WBPS). In burn wounds the main outcome is the percentage of regression of the wound	9	8-9	**Strong**
11	Wound debridement using Prontosan Debridement Pad should be carried out until the achievement of a Falanga score A, meaning a cleansed and granulating bed wound (see table A and B)	9	8-9	**Strong**

Supplementary Table 6. Characteristics, clinical data and outcome of 13 patients treated with Prontosan® Debridement Pad.

ID	Age gender Comorbidity	Type of lesion	Modality/ timing PDP application	Concomitant treatments	Outcomes	Outcome detection modality/timing	Follow-up	Results
1	64 M Paraplegia, insulin-dependent diabetes, vasculopathy, malnutrition	Surgical wound dehiscence of a IV stage perianal pressure injury submitted to toilette + preparation of a covering local fasciocutaneous flap	Application every 24 h: 15 minutes wrap with Prontosan solution, repeated and careful debridement with PDP, disinfection with Prontosan solution on a sterile gauze for 10 days.	Medication with Aquacel Ag+ external polyurethane foam Invanz 1g+ Targosid 400mg. Nutritional support (Abound 2 packs) Fluidized anti-bedsores bed Bladder catheter Temporary Stoma	Reduction of bacterial contamination Cutaneous swab negativization	Serial cutaneous swab Periodic control before and after PDP with Moleculight WBPS	10 days	Pain relief wound size reduction Biofilm absence No signs of Infection, infiammation or bacterial contamination
2	76 M Vasculopathy, malnutrition	Chronic smelly left pretibial ulcer (post-chronic osteomyelitis) with exudate	Application every 48 h: 5 minutes wrap with Prontosan solution, repeated and careful debridement with PDP, disinfection with Prontosan solution on a sterile gauze for 4 weeks.	Medication with Aquacel Ag+ external polyurethane foam after every application of PDP. Augmentin 1 gx3 for 6 days, then 1x 2 for 15 days. Then: Bactrim 160 mg+180 mg 1x 3 for 3 days, then 1x2 for a month.	Reduction of bacterial contamination	Serial cutaneous swab Periodic control before and after PDP with Moleculight WBPS	4 weeks	Pain relief wound size reduction Biofilm absence No signs of Infection, infiammation or bacterial contamination
3	78 M Vasculopathy, malnutrition	Dehiscence of a xifopubic surgical wound (27 cmq) (previously submitted to positioning of porcine scalp then reabsorbed) after a Hartmann.	Application every 24 h: 15 minutes wrap with Prontosan solution, repeated and careful debridement with PDP, disinfection with Prontosan	Medication with Aquacel Ag+ external polyurethane foam after every application of PDP.	Prevention of bacterial contamination	Serial cutaneous swab Periodic control before and after PDP with Moleculight WBPS	4 weeks	Pain relief wound size reduction Biofilm absence No signs of Infection, infiammation or bacterial contamination

		It had a partially fibrinous and exuding fund.	solution on a sterile gauze for 4 weeks.					
4	48 M	Intermediate degree domestic burn (intermediate-deep proximally) of the left thigh (25x13 cm) caused by a chemical drain cleaner	10 minutes wrap with Prontosan solution, followed by a mechanical debridement with the microfiber Pad soaked with 20 ml di Prontosan every 48 hours for the first week and subsequently every 4 days. After the first 12 days of treatment, given the spontaneous reepithelization, treatment pursued only with Prontosan solution wrap and collagenase until complete recovery.	Application of a collagenase-ointment and non stick gauze. Occlusive dressing with cotton gauze. Oral antibiotic therapy (Amoxicillin) for the first 5 days post-burn.	Complete debridement capability of wound fund); Induced pain (assessed by VRS scale); Clinical signs of local infection (presence of reddened perilesional tissues, purulent and/or smelly exudate) Wound size reduction(cmq) Lesion improvement (cleansing and complessive surface reduction)	Weekly superficial swab The first 4 evaluations: every 48 hours; the following 4: every 4 days. Final evaluation: 4 weeks after the beginning of the treatment. Pain assessment with VRS scale	12 days	Faster and more effective wound debridement easing of the slough breakdown Soft cleansing. No clinical signs of local inflammation and bacterial contamination exudation regressed rapidly Pain reduction (-50% VRS) wound size reduction (-97%)
5	48 M	Intermediate-deep degree domestic burn (deep proximally) caused by sulphuric acid of the deltoid region and superior lateral part of left arm (15x8 cm). The proximal part showed a dry eschar, whitish, adherent to	Wrap with gauze soaked with Prontosan solution for 15 minutes followed by a mechanical debridement with microfiber PDP, soaked with 20 ml of Prontosan. Treatment started 72 hours after burn and has been repeated every 48	Application of a collagenase-ointment and non stick gauze. Occlusive dressing with cotton gauze. Oral antibiotic therapy (Amoxicillin) for the first 5 days post-burn.	Wound size reduction (cmq) Complete debridement capability of wound fund; Induced pain (assessed by VRS scale); Clinical signs of local infection	Routinely exams Weekly superficial swab until the fifth week of observation. Clinical evaluation and outcome measurement every medication	5 weeks	Biofilm absence pain worsening wound size reduction (-85-90%) No signs of Infection, infiammation or bacterial contamination

		underlying tissues. Few exudate.	hours for 2 weeks. Subsequently, frequency of medications has been reduced (every 4 days for 3 weeks).		(presence of reddened perilesional tissues, purulent and/or smelly exudate)			
6	70 F Diabetes and peripheral vasculopathy	Chronic vasculitic ulcer of right foot showing a fibrinous fundus	Application of Prontosan solution for 5 minutes and debridement with PDP for 4 weeks.	Treatment with silver Sulfadizine and hydrofiber	Pain Wound size reduction Clinical signs of local infection (presence of reddened perilesional tissues, purulent and/or smelly exudate)		3 weeks	Pain reduction (-50% VRS), wound size reduction (-75%) Biofilm absence. No signs of Infection, infiammation or bacterial contamination
7	71 M	Chronic phlebostatic ulcer (from 5.5 y) of the right leg	Prontosan solution wrap for 5 minutes for 4 weeks. Every 7 days bandage removal and debridement with PDP	Application of silver Sulfadizine Elasto-compressive bandage with zinc oxide	Local and general symptoms improvement (pain) Clinical signs of local infection (presence of reddened perilesional tissues, purulent and/or smelly exudate)	- Pain scale (VRS)	4 weeks	Biofilm absence pain reduction (-80% VRS) wound size reduction (-75%) No signs of Infection, inflammation or bacterial contamination
8	40 F Drug abuse	Chronic vasculitic ulcer (from 3 ys) of the right and left lower limbs with serous-fibrinous fund	Prontosan solution wrap for 5 minutes on the right and 10 minutes on the left, followed by PDP debridement for 4 weeks with medication 2 times/week	Application of silver Sulfadizine ointment and Acquacell	Pain reduction Wound size reduction Clinical signs of local infection (presence of reddened perilesional tissues, purulent	- Pain scale (VRS)	4 weeks	Biofilm absence pain reduction (-80% VRS) wound size reduction (-75%) No signs of Infection, inflammation or bacterial contamination

					and/or smelly exudate)			
9	62 M Lower limbs varicose veins + post thrombotic syndrome (previous left iliac-femoral DVT)	Skin wound of the medium third of the left leg	Prontosan solution wrap for 5 minutes followed by debridement with PDP for 4 weeks	Application of Promogran Ag Elasto-compressive bandage with zinc oxide with weekly replacement	Wound size reduction Clinical signs of local infection (presence of reddened perilesional tissues, purulent and/or smelly exudate)	- Pain scale (VRS)	4 weeks	Biofilm absence pain reduction (-80% VRS) wound size reduction (-75%) No signs of Infection, inflammation or bacterial contamination
10	61 F Rheumatoid arthritis	Chronic internal and external perimalleolar vasculitic ulcers (from 7 ys) of the left leg covered with biofilm	Prontosan solution wrap for 5 minutes on the internal malleolar lesion and 10 minutes on the external lesion, followed by debridement with PDP for 4 weeks	Bionect Hydrofiber Bandage with zinc oxide (after a week of treatment) for 9 days Steroids and antioedema drugs	Pain improvement Biofilm disappearance	Pain scale At 15 days and at 4 weeks	4 weeks	Biofilm absence pain reduction (-80% VRS) wound size reduction (-75%) No signs of Infection, inflammation or bacterial contamination
11	72 F Hypertension, Horton arteritis.	Necrotic post-traumatic infected ulcer (2.5x2 cm) for 10 weeks with subcutaneous extension	Dressing 2 times/week with hydrofiber and debridement with PDP	Hydrofiber Contenitive bandage with tubular. Deltacortene 25 mg die	Pain reduction Wound size reduction Clinical signs of local infection (presence of reddened perilesional tissues, purulent and/or smelly exudate)	NRS scale WBP scale Weekly control for 5 weeks	5 weeks	Pain relief wound size reduction Biofilm absence No signs of Infection, infiammation or bacterial contamination

12	76 M Hypertension, AF in NOAC. Vasculopathy (submitted to angioplasty in 2016), diabetes, varicose veins	Left Internal malleolar arterial-venous ulcer (for 3 ys). Fundus covered by fibrin and biofilm (WBP score C2)	Alternate days: cleansing with Prontosan, debridement with PDP for 4 weeks	Dressing with alginate Short stretch elastocompression	Pain reduction Wound size reduction Clinical signs of local infection (presence of reddened perilesional tissues, purulent and/or smelly exudate)		4 weeks	Pain relief wound size reduction Biofilm absence No signs of Infection, infiammation or bacterial contamination
13	Gangrenosum pyoderma, Hypertension.	Lateral ulcer of the left lower limb with slough, extended to muscular fascia. Classifiable as C3 WBP score for 3 ys.	Cleansing with Prontosan and weekly debridement wit PDP for 5 weeks.	Dressing with polyurethane foam and elastic tubular	Pain reduction Wound size reduction Clinical signs of local infection (presence of reddened perilesional tissues, purulent and/or smelly exudate)	Weekly assessment	5 weeks	Pain relief wound size reduction Biofilm absence No signs of Infection, infiammation or bacterial contamination