

**Multi-Center Clinical Results
with PluroGel PSSD in Chronic Wounds**

Presented at a Satellite Symposium

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Summary

A new cell-friendly surfactant (surface active) material with silver sulphadiazine as an anti-microbial, PluroGel PSSD, has been successfully tested on non-healing wounds (including chronic wounds) in a number of hospital clinics and wound care centers in Europe. Six (6) of these centers (including one (1) university center and one (1) health insurance company's wound care center) from four (4) countries reported their results at a symposium during the EWMA 2012 Congress in Vienna, Austria.

Six (6) centers reported their results after using PluroGel PSSD on a total of 361 wound (289 patients). All centers reported that use of PluroGel PSSD resulted in reduction of infection, reduction of exudate, reduction of pain and reduction of peri-lesional skin inflammation in the majority of patients. All centers reported ease of use of PluroGel PSSD. Five (5) of the six (6) centers observed and reported increased cost-effectiveness using PluroGel PSSD, with one center not studying cost. Key reasons reported for cost reduction when using PluroGel PSSD were its usual use with inexpensive gauze or non-woven and inexpensive moisture barrier cover and easier faster dressing change. Significant progress in wound healing was reported in the majority of patients.

In these six (6) centers, PluroGel PSSD was applied in every stage of wound healing and on all types of wounds, from the simplest to the most difficult wounds. One (1) center used PluroGel PSSD only on wounds that had failed to heal with other therapies and protocols reported a 75% improvement or complete healing rate in the time range of three (3) months to over one (1) year. Three (3) centers which were able to report only their first 30 days of use of PluroGel PSSD demonstrated a 53% wound size reduction. One (1) center which was able to report the first 6 months of use of PluroGel PSSD demonstrated a 43% complete healing rate within 6 weeks of beginning use of PluroGel PSSD and the majority of remaining wounds not yet completely healed by the time of the symposium showed significant progress towards healing. One (1) center which was able to report the first one (1) year of use of PluroGel PSSD demonstrated a 55% complete healing rate within 12 weeks of beginning use of PluroGel PSSD and the majority of remaining wounds not yet completely healed by the time of the symposium showed progress towards healing.

Each of the centers noted that PluroGel PSSD was used in most patients for the complete treatment period (for a minimum of one month to more than one (1) year) without complication or negative effect of long-term use of the anti-microbial.

The clinical users from the six (6) centers concluded PluroGel PSSD is a new approach for non- healing

wounds, with very promising features and patient results: PluroGel PSSD provided an unexpected positive result for their patients (improved healing results with a reduction in inflammation and reduction in pain), an unexpected positive result for their clinical uses (faster easier dressing change) and in the five (5) of six (6) centers making observations, an unexpected positive result for their budgets (reduced cost due to reduced time to change the dressing and fewer and less expensive products used).

Introduction

Non-healing wounds (primarily diabetic ulcers, vascular insufficiency ulcers, pressures ulcers, non-healing surgical wounds and other non-healing wounds) have plagued humanity for thousands of years. Today, in many countries, including those in Europe, populations are growing older resulting in an increase in the number and rate of non-healing wounds. This in turn is placing an ever increasing burden on all public and private budgets, healthcare systems and healthcare personnel. Although there are hundreds of dressings and other products for the treatment of non-healing wounds and there is much research and many detailed protocols on how to treat them, the problem of non-healing wounds continues to be significant and not solved.

In an effort to improve patient results and overcome the problems of the many existing products and protocols, PluroGel, a new cell-friendly surfactant (surface active) material was developed by a leading university and research hospital in the USA. The idea for PluroGel was developed in the burn center at this university. To treat and protect these burn patients from infection, it is common to use, as a standard, a lipid soluble cream or ointment carrier containing a topical anti-microbial which is usually silver sulphadiazine. These products have certain disadvantages including pseudo-eschar formation and difficult and painful removal. Therefore, the university's researchers looked for another material to carry the anti-microbial. This led to the development of PluroGel. PluroGel is a surfactant (surface active) material in gel form that is a cell-friendly, bio-compatible cleaner and has functions and characteristics that are effective for both non-healing wounds and burns.

The university evaluated many different antimicrobials in PluroGel and decided for their preferences to use a version that includes a unique combination of three (3) different antimicrobials. In the process the university experimented with the worldwide standard-of-care anti-microbial silver sulphadiazine, or SSD, in PluroGel. This single antimicrobial version of PluroGel, with SSD, is now called PluroGel PSSD and is the subject of this report.

SSD has been well known and well understood for over 30 years and used on millions of patients worldwide. It has many clinical advantages, including a broad spectrum of anti-microbial activity, low resistance and low allergy level as well as low toxicity to new skin cells. SSD has been “the gold standard in topical burn treatment, a useful anti-microbial agent ...”⁸. “There are several advantages to using silver sulphadiazine as compared to other topical antibiotic preparations. It is effective against a wide range of pathogenic bacteria, including methicillin-resistant *Staphylococcus aureus*, also known as MRSA. Serious side effects are rare. It can be applied to large areas of skin with a low risk of toxicity. It does not absorb deeply into the skin and so does not normally have a systemic effect on patients. Most side effects (such as skin discoloration, and burning or stinging sensations) associated with silver sulphadiazine are superficial.”⁹

At the time of introduction in Europe in late 2010, the PluroGel version with three antimicrobials had been successfully used at the university on more than 11,000 patients (over 2,000 burn patients and 9,000 non-healing wound patients). The success in the university burn center resulted in use in their non-healing wound center, including chronic wounds, with similar successful outcomes; more than 80% healing rate within average 12 weeks.

During the 2010 to 2012 period, a number of European hospitals, clinics and wound care centers tested PluroGel PSSD, a new PluroGel formula, which includes the widely accepted SSD because it is preferred by many doctors in European and other countries for the reasons reported above. Six (6) of these centers, three (3) hospitals and three (3) wound care centers including one (1) university center and one (1) health insurance company’s wound care center, presented their results in a satellite symposium during the EWMA 2012 Congress in Vienna, Austria, on 24th of May 2012.

Materials, Methods and Patients

Materials:

The product evaluated and reported in this multi-center study was PluroGel PSSD. To limit variability of treatment to one main variable (PluroGel PSSD), each of the six (6) centers used a variety of their other standard products with PluroGel PSSD, those other products being the usual products in use at their center (and most commonly were basic gauze or non-woven and a basic moisture barrier cover which are the simplest and least expensive of these other products used with PluroGel PSSD.) This facilitated the focus of the patient results and therefore the symposium to PluroGel PSSD which was the primary difference in products and protocols used.

PluroGel PSSD is composed of two components: PluroGel and Silver Sulphadiazine (SSD) in 1% concentration.

PluroGel has core and bio-physical functions. PluroGel core functions include: (1) 100% water solubility (which provides for a more continuous availability of the barrier anti-microbial and allows for PluroGel and the anti-microbial to reach the most difficult areas, where other products may not reach; (2) reverse thermal response where PluroGel becomes slightly thicker as it warms to body temperature and slightly less viscous as it cools to room temperature (which allows PluroGel to better stay on the wound to protect the wound); and (3) uniquely a biocompatible^{1, 2, 3}, cell-friendly cleaner^{1, 2, 3} (which allows PluroGel to be gentle to the wound and to begin the cleaning process while on the wound).

PluroGel bio-physical functions include: (1) help to maintain blood flow in the very small arteries and veins of the wound⁴; (2) improved tissue oxygenation in the wound and around the wound⁵; and (3) ability to manage Biofilm⁶ (PluroGel has been shown to prevent biofilm⁶, break-up biofilm⁶, and, allow the bacteria of the biofilm to enter PluroGel to be killed⁶).

PluroGel, as noted above, performs as a cleaner to begin the cleaning process at dressing change, as a barrier which helps to protect the wound and creates and maintains the ideal wound environment for the patient to do the healing. Due to these characteristics, PluroGel is an excellent material for non-healing wounds and burns, working without, or with reduction in, the typical problems of other products such as pseudo-eschar and painful and difficult removal.

In addition to the advantages of an ideal material which does not create, or significantly reduces, pseudo-eschar, use of PluroGel in chronic wound treatment resulted in reduced pain, reduced difficulty of dressing change and demonstrated its unique characteristic of staying thick at body temperature providing better protection for the wound, especially on wounds where normal creams, ointments and gels become more liquid-like and do not stay on the wound. While first developed and proven for burns, PluroGel demonstrated advantages for chronic wounds.

The second component, SSD, is described in detail above in the Introduction section.

Methods:

All clinical users performed the following procedure:

- General patient history and clinical evaluation
- History of the wound (including instrumental evaluation if necessary)
- Establishment of a wound care follow-up file (measuring size, exudation, infection, peri-lesional skin) and photographs of the patient’s progress; some of the clinical users classified pain and odor.
- Preparation of the wound by cleaning, debridement of the necrotic tissue (if necessary) and application to the wound border of a non-water soluble material (for example petrolatum) to protect the skin around

the wound by helping to keep the moisture in the wound and not on the skin (if necessary).

- PluroGel PSSD use:
 - a) either PluroGel PSSD was directly placed in the wound by a spatula, then the wound was covered with appropriate gauze or non-woven and a moisture barrier cover
 - b) or PluroGel PSSD was spread with a spatula over a piece of gauze or non-woven, then the complete wound surface was covered with this gauze or non-woven and then usually with a moisture barrier cover
 - c) clinical users made sure that all the wound surface was covered with PluroGel PSSD
 - d) clinical users made sure that the normal skin was not covered with PluroGel PSSD
- Additional help (e.g. compression) was done if necessary
- Dressing change frequency was performed according to patient needs / type of wound (from twice daily to 1-3 times per week)

PluroGel PSSD was used in all stages of wound healing.

Patients:

In total, 361 wounds (289 patients) received PluroGel PSSD and were reported at the symposium by the six (6) centers.

All centers used PluroGel PSSD as the standard of care for this study.

The centers used PluroGel PSSD on all type of wounds in all stages of wound condition. The size of the wound ranged from small to large with extended wound surface area.

The following wounds were treated:

- Venous ulcers
- Arterial ulcers
- Mixed ulcers
- Hypertensive ulcers
- Vasculitis
- Diabetic wounds
- Infected wounds
- Pressure ulcers
- Post-traumatic/post-operative wounds

Three (3) centers reported only the first 30 days of use of PluroGel PSSD (due to the deadline for abstract submission to EWMA 2012). The remaining three (3) centers reported PluroGel PSSD use for each patient up to the point where the data for the presentation were collected.

One (1) center, a university hospital, focused on very difficult chronic wounds or complicated post-operative wounds that they had been treating without success (the

wounds did not heal) for an extended length of time, 3 months to over one (1) year, using multiple products and therapies. The remaining five (5) centers used PluroGel PSSD from the easiest to the most complicated wounds.

Table 1 reports patient information from the six (6) centers. Each hospital, clinic and wound care center followed its own data collection and reporting protocol. While these data collection and reporting protocols were similar, they did not facilitate a direct comparison of results. For example, the start date for each center was different in relation to the symposium deadline resulting in each center being able to follow patients for differing amounts of time. And, as previously noted, the end point for data reporting was different: three (3) centers reported results only during the first 30 days of use of PluroGel PSSD (due to deadline for EWMA abstract submission) whereas the remaining centers reported PluroGel PSSD results to the time of healing or to the time of the presentation at the symposium. These two variables did not allow many of the centers to follow patients to healing, resulting in an interim report on patient progress. Therefore the results reported do not have a common start point or common end point with many patients reported during mid-use of PluroGel PSSD.

Table 1: Patient Information for the PluroGel PSSD Patient Population at the Six (6) Centers

No. of centers (6)	Country	Time period reported	No. of wounds	No. Patients Reported	No. Patients with- drawn*	Type of wound	Size / difficulty / stage
1	Austria	1 year	247	190	60*	Arterial ulcers Venous ulcers Mixed ulcers Diabetic (Neuropathic) ulcers Postoperative wounds Traumatic ulcers Proctologic wounds	All sizes All difficulties All stages
3	Italy	30 days	58	43	0*	Arterial ulcers Venous ulcers Mixed ulcers Traumatic ulcers Hypertensive vasculitis Diabetic ulcers Pressure ulcers	All sizes All difficulties All stages
1	Netherlands	6 months	30	30	8*	Arterial ulcers Venous ulcers Mixed ulcers Hypertensive vasculitis Diabetic ulcers Pressure ulcers Postoperative wounds Traumatic ulcers	All sizes All difficulties All stages
1	Switzerland	1 year	26	26	0*	Postoperative wounds Traumatic ulcers Variety of ulcer types	Only wounds not healed using multiple products & protocols Treatment before PluroGel® PSSD from 3 months to over 1 year All sizes all stages
6			361	289	68		

*PluroGel PSSD was withdrawn in 68 patients for the reasons noted below in Table 2.

PluroGel PSSD was withdrawn in 68 patients for the following reasons:

Table 2: Summary of PluroGel PSSD withdrawal for the Six (6) Centers

Death	Patient drop-out*	Change of procedure**	Total
7	26	35	68
10%	38%	51%	100%

* Patient drop-out due to change of doctor, change of nurse, change of facility, patient non-compliance

** Change of procedure due to skin graft, difficult infection, allergy

Results

Table 3 reports wound progress at the six (6) centers.

Table 3: Summary of Wound Progress Using PluroGel PSSD for the Six (6) Centers

No. of centers (6)	Country	Reduced wound size within 30 days	Complete healing rate	Status of wounds not yet healed due to data cut off for reporting at symposium	Reduced infection	Reduced exudate	Reduced inflammation	Reduced Pain	Reduced pain during dressing change
3	Italy	53%	NR*	Continue PluroGel PSSD. Majority were observed to be progressing towards healing	Yes	Yes	Yes	Yes	Yes
1	Netherlands	NR*	43% (within 6 weeks)	Continue PluroGel PSSD. Majority were observed to be progressing towards healing	Yes	Yes	Yes	Yes	Yes
1	Austria	NR*	55% (within 12 weeks)	Continue PluroGel PSSD. Majority were observed to be progressing towards healing	Yes	Yes	Yes	Yes	Yes
1	Switzerland	NR*	75% within 52 weeks: wounds that could not be healed by other products or protocols)	25% change of therapy. Status NR*	Yes	Yes	Yes	Yes	Yes

* NR = Not reported

In the three (3) centers which only had time to report the first 30 days of use of PluroGel PSSD as the standard of care, a significant and fast wound size reduction rate was seen, average 53% reduction of wound size in first 30 days, based on 58 wounds of different sizes and types. These patients continued use of PluroGel PSSD and additional patients were included for use of PluroGel PSSD.

In the center which had enough time to report PluroGel PSSD use as the standard of care for six (6) months, a total of 28 wounds were treated (excluding the 8 patient drop outs). Patients entered the six (6) month PluroGel PSSD use period at different stages of wound healing and complexity. 12 wounds were reported healed within six (6) weeks of initiating PluroGel PSSD use (healing rate 43%) and the remaining wounds were reported to be improved and positively progressing to closure with continued use of PluroGel PSSD at the time the data were collected for the symposium. Additional patients were included for use of PluroGel PSSD.

In the center which had enough time to report PluroGel PSSD use as the standard of care for one (1) year, a total of 187 wounds were treated (excluding the 60 patient drop outs). Patients entered the 1 year PluroGel PSSD use period at different stages of wound healing and complexity. 102 wounds were reported healed within 12 weeks of initiating PluroGel PSSD use (healing rate 55%)

and the remaining wounds were reported to be improved and positively progressing to closure with continued use of PluroGel PSSD at the time the data were collected for the symposium. Additional patients were included for use of PluroGel PSSD.

In the university hospital reporting PluroGel PSSD results (this centers had enough time to report PluroGel PSSD use for over one year), 26 patients were selected because they all had failed treatments using both standard and non-standard wound care products and standard and non-standard protocols with treatment ranging from three (3) months to over one (1) year before using PluroGel PSSD. In this 26 patient non-healed population, PluroGel PSSD use was reported to have resulted in 75% of patients with healed wounds within average 3-6 months or the wounds finally improved enough to allow surgical wound closure. In the remaining patients, therapy with PluroGel PSSD was discontinued due to non-response and other treatments were initiated.

In addition to wound healing, clinical users reported the following for PluroGel PSSD:

- Reduction of infection
- Reduction of exudate
- Reduction of peri-lesional skin inflammation
- Reduction of pain within the wound
- Reduction of pain during dressing change
- PluroGel PSSD was used on all wounds
- PluroGel PSSD was used in all stages of the wound
- The product can be used at home due to ease of use

Each of the six (6) centers reported PluroGel PSSD product handling and application characteristics and

results. These results are provided below in *Table 4 Handling and Application for the Six (6) Centers*.

Table 4: Summary of Handling and Application of PluroGel PSSD for the Six (6) Centers

No. of centers (total 6)	Country	Ease of use	Ease of use in dressing change	Time between dressing changes	Reduction of products used	Reduction in dressing change time	Reduction in cost
1	Austria	Yes	Yes	2 times per day to 1 week	Yes	Yes	Yes
3	Italy	Yes	Yes	1 day to 1 week	Yes	Yes	Yes
1	Netherlands	Yes	Yes	1 day to 1 week	Yes	Yes	Yes
1	Switzerland	Yes	Yes	2 days to 1 week	NR*	NR*	NR*

* NR = Not reported

Clinical users reported the following product handling and application characteristics for PluroGel PSSD:

- Easy to use
- Fast dressing change
- Range of dressing change interval: 2 per day to 1 per week (2 per day sometimes at the beginning of PluroGel PSSD use then changing to longer intervals)
- Long term use of PluroGel PSSD without complication from the anti-microbial

Five (5) of the six (6) centers made observations on cost and reported the following with regard to cost-effectiveness (one center did not report on cost issues):

- Cost effectiveness because of the ease of use
- Cost effectiveness because of interval of dressing change
- Cost effectiveness because of reduced number and cost of products needed
- Cost effectiveness because of reduced administration of pain drugs

PluroGel PSSD reduced work for the wound care practitioner / nurse because it was easier and faster to do the dressing change. PluroGel PSSD easy and speed of use allowed dressing change by the patient or patient's family at home

Each hospital, clinic and wound care center presented case studies to demonstrate these results using PluroGel PSSD.

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Notes