Overview
Post Market Clinical Follow Up
of
MelMax, Principelle IF and Matrix wound dressings®

Date: 2018

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SUMMARY

This document provides an overall summary of results of PMCF data relevant for MelMax, Principelle IF and Matrix. It contains references to DerMax, our first product and related to MelMax.

In order to confirm the conclusion drawn from the pre-market clinical literature evaluation and in vitro studies and to assess if unforeseen hazards can be identified by field experience for which additional control measures are needed a Post Market Clinical Follow Up (PMCF) strategy was developed consisting of the following steps:

- review of literature and scientific clinical and safety data on wound care products containing honey
- evaluation of results of clinical (case) studies of MelMax, Principelle IF and Principelle Matrix
- evaluation of complaints related to MelMax, Principelle IF and Principelle Matrix

The objective of this PMCF study is to evaluate the clinical safety and performance of Principelle IF, MelMax and Principelle Matrix in order to

- confirm the conclusion drawn from the pre-market clinical evaluation literature evaluation and in vitro studies
- assess if unforeseen hazards can be identified by field experience for which additional control measures are needed.

Results from (recent) literature in general support the clinical benefit of honey containing wound dressings for the treatment of acute and chronic wounds. No safety related concerns were documented.

Based on the data obtained Post Market Clinical Follow up studies it can be concluded that MelMax, Principelle IF and Principelle Matrix dressings are clinically safe and perform like intended.

By these results the outcome of the pre-market clinical evaluation, literature evaluation and in vitro studies are confirmed. No unforeseen hazards were identified by field experience for which additional control measures are needed.

Taking the results of the literature and Post Market Clinical Follow up studies into consideration Principelle B.V. states that MelMax, Principelle IF and Principelle Matrix dressings are safe and perform when used as intended by the Instructions for Use.

1. INTRODUCTION

Dermagenics Europe initially obtained CE certification for MelMax in 2005.
Today MelMax, Principelle IF and Matrix are manufactured under the responsibility of Principelle B.V.

In order to confirm the conclusion drawn from the pre-market clinical literature evaluation and in vitro studies and to assess if unforeseen hazards can be identified by field experience for which additional control measures are needed a Post Market Clinical Follow Up (PMCF) strategy was developed consisting of the following steps:

- Review of literature and scientific clinical and safety data on wound care products containing honey
- Evaluation of results of clinical (case) studies of MelMax, Principelle IF and Matrix, collected by Principelle BV
- Evaluation of complaints related to MelMax, Principelle IF and Matrix, collected by Principelle BV

This document provides an overall summary of results of PMCF data relevant for MelMax, Principelle IF and Matrix.

Given the prolonged period of availability of the products on the international market and the number of patients having used the products in varied conditions, we can conclude these products have an excellent safety record.

In 2012-2013 we attempted to integrate Post Market Surveillance reports, trends and results with newly developed Clinical Review Portal.

As a functional part of the Principelle website, The Clinical Review Portal (CRP) was a digital tool to review clinical performance of Principelle products and provides evidence-based results.

Functions:
- Document individual patients and groups of patients (anonymous)
- Keep track of the effects of treatment
- Review the result of your clinical work and compare with others
- Offer advanced statistical processing of records
- Offer a template to build scientific posters
- Save pictures of any stage of treatment
- Future links to dedicated wound management software

The number of patient cases uploaded remained suboptimal. We investigated this problem and concluded that using the CRP results in extra administrative load for practitioners. Generally, all practitioners already use a wound documentation system in their organization. Principelle offered individual solutions to reduce the administrative load providing a light version of the Clinical Review Portal on a tablet.

Conclusions:
1)In general, from the current PMS results it can be concluded that the products perform very satisfactory. We have not had any adverse reactions since the establishment of the Company or in any other form or way in the preceding Company.
2)We may need to abandon the CRP and process more case work in-house

2. RELATION TO OVERALL RISK MANAGMENT

This PMCF evaluation is part of the overall risk evaluation of MelMax, Principelle IF and Matrix wound dressings[1].

3. OBJECTIVE AND SCOPE

The objective of this PMCF study is to evaluate the clinical safety and performance of MelMax, Principelle IF and Matrix in order to

- confirm the conclusion drawn from the pre-market clinical evaluation, literature evaluation and in vitro studies.
- assess if unforeseen hazards can be identified by field experience for which additional control measures are needed.

4. APPLICABLE STANDARDS AND GUIDELINES

- EN ISO 14155-1:2011 Clinical investigation of medical devices for human subjects – General requirements
- EN ISO 14155-2:2011 Clinical investigation of medical devices for human subjects – Clinical investigations plans

MEDDEV 2.12-2 Guidance document on post market clinical follow up for medical devices.

5. PRODUCT DESCRIPTION

5.1 Product number and name

Product types: Wound Care Products

- MelMax®
- Principelle IF® dressings
- Principelle IF® ointment
- Principelle Matrix dressings

Product: MelMax®
Sizes: 5 x 6 cm / 8x10 cm / 8 x 20 cm

Product: Principelle IF® impregnated dressings
Sizes: 5x6 cm, 8 x 10 cm, 8 x 20 cm, 10x30 cm

Product: Principelle IF® ointment
Sizes: 10g and 20g tube

Product: Principelle Matrix®
Sizes: 10x10cm border and non-border

5.2 Product properties

MelMax/Principelle IF normalises the wound micro-environment by regulation of the MMP balance, inflammation and bacterial contamination. This results into better conditions for re-epithelialisation. The properties of MelMax like regulation of the bacterial contamination are also directed at the regulation of moisture content in the micro-environment of the wound.

Principelle Matrix
Hydrogel dressings help to provide an environment for optimal wound healing by managing wound exudate levels and protecting against wound dehydration and external bacterial contamination. The super-absorbent gel provides both cushioning and absorption. The partially hydrated nature of the dressing aids the process of autolytic debridement and helps soothe the wound on contact.
Two versions are available: Principelle Matrix and Principelle Matrix Border.

Both versions of Principelle Matrix have been formulated and designed specifically to encourage wound bed preparation, granulation and subsequent epithelialisation of chronic wounds, while minimizing pain levels and the risk of infection.

General device description MelMax, Principelle Impregnated dressings and Principelle Matrix

MelMax/Principelle IF is a sterile wound dressing, impregnated with an ionogen formulation and Buckwheat Honey. This honey is especially selected for medical use.
MelMax/Principelle IF is intended for use in all types of wounds, including burns.
The honey and the ionogen formulation is impregnated in an inert dressing material of acetate mesh fabric. Thanks to the structure of the acetate the honey and ionogen formulation is released to the wound equally.

Principelle Matrix
Principelle Matrix Border has an additional skin friendly, adhesive border (PU film barrier) causing the dressing to be more occlusive. Principelle Matrix is a copolymer gel dressing with an integral breathable PU film barrier and a wound-facing matrix layer. The border version has an additional skin friendly, adhesive overlay (PU film barrier) causing the dressing to be more occlusive.

MelMax is supplied in 3 sizes:
5 x 6 cm
8 x 10 cm
8 x 20 cm

Principelle IF is supplied in 6 sizes:
5 x 6 cm
8 x 10 cm
8 x 20 cm
10x30 cm
Tube 10g
Tube 20g

Principelle Matrix is supplied in 1 size:
10 x 10cm

Principelle Matrix Border is supplied in 1 size:
10 x 10cm (Island 6.8x6.8cm)

MelMax/Principelle IF is gamma sterilized. It shall be stored at room temperature, dry, and not in sunlight. It may also be stored in a refrigerator, but not in a freezer (5 - 25ºC). MelMax/Principelle IF has a shelf life of 3 years.

5.3 Indications
Medical purpose and performance
Product properties

MelMax/Principelle IF wound dressings regulate the bacterial contamination resulting in better cleansing of the wound.
MelMax/Principelle IF assists the acidity and moisture content of de wound.
MelMax/Principelle IF allows for proper drainage of wound exudates due to the open structure of the acetate mesh.
In case of moist or wet wounds, a secondary dressing may be applied on top of MelMax/Principelle IF providing absorption.

Indications MelMax and Principelle IF wound dressings

Under the supervision of a health care professional MelMax/Principelle IF may be used for acute and chronic wounds. It is particularly suitable for decubitus, leg ulcers and diabetic ulcers. It may be used on moderately exuding, lightly exuding and dry wounds. With a suitable secondary dressing it can also be used on heavily exuding wounds. Depending on the wound type it may be covered by traditional dressings, or absorbing dressings such as Principelle Matrix.

Acute wounds
- Burns
- Surgical wounds
- Traumatic wounds

Other acute wounds where fast epithelialisation is required

Chronic wounds
- Leg ulcers
- Diabetic ulcers
- Decubitus ulcers

Indications Principelle Matrix wound dressings
Under the supervision of a health care professional Principelle Matrix may be used for the management of acute and chronic, non-infected or mildly infected wounds. It may be used on moderately exuding, lightly exuding and dry wounds. The dressing can also be used on more highly exuding wounds, though this will reduce the effective wear time of the dressing and the wound should be monitored accordingly.

For single use only
MelMax/Principelle IF and Principelle Matrix is for single use only. MelMax/Principelle IF is gamma ray sterilised. The sterility of MelMax/Principelle IF and Principelle Matrix is only guaranteed for undamaged and unopened packages. MelMax/Principelle IF and Principelle Matrix shall not be re-sterilised.

Storage
Store at room temperature (5-25^{0}C), dry and not in sunlight. MelMax/Principelle IF and Principelle Matrix may also be stored in a refrigerator, but not in a freezer.

5.4 Contra-indications
MelMax should not be used on patients with a known sensitivity to honey, Ionogen formulation or acetate.
Principelle Matrix is not indicated for full-thickness wounds, heavily bleeding wounds, third degree burns, or as a cover for deep narrow cavities or sinuses.

5.5 Instructions for Use
MelMax/Principelle IF Application:
1. Carefully inspect the wound.
2. Cleanse the wound according to standard instructions.
3. Open the blister packaging and remove the MelMax® dressing from the packaging. If the blister package has been opened or damaged, then consider the MelMax® dressing to be non-sterile.
4. Remove the front and back papers from the MelMax® dressing.
5. Apply the MelMax® and ensure that this leads to maximum contact with the wound.
6. Secure the MelMax® dressing with usual means, such as perforated adhesive tape.

Note: In cases of moist or wet wounds, MelMax® can be covered with a secondary dressing, which will result in the possible retention of absorption and wound exudates.

Dressing Changes:
1. Remove the secondary dressing.
2. Carefully remove MelMax®. If necessary, pre-moisten the dressing to facilitate removal.
3. Inspect and clean the wound according to standard instructions.
4. Apply a new MelMax® wound dressing.

Depending on the wound aspect dressing change is advised within 5 days.

Principelle Matrix Application
1. Allow Matrix to completely cover the wound and extend onto healthy tissue by approximately 15 to 20mm depending on the level of exudate.
2. Prepare the wound site by cleansing as needed; dry the surrounding skin.
3. Remove the sterile dressing from the package.
4. To apply the dressing, first remove part of the overlaid white plastic liner.
5. Position and smooth into place whilst removing the second half of the white plastic liner.
6. For Principelle Matrix Border: once the dressing is securely in place, peel away the supporting layer from the PU film.
7. For a borderless dressing: you may apply a secondary film dressing or bandage as required. To encourage autolytic debridement (by reducing vapour loss from the dressing), place an adhesive film over the entire dressing.
8. Check the wound regularly.

5.6 Package system
See STED file 1606-24

6. POST MARKET CLINICAL FOLLOW-UP

6.1 Literature review – see also doc. 1606-32 Principelle Honey Literature review

In 2007, as part of an observational study of the use of a honey impregnated dressing (MelMax®) in the treatment of wounds, Tissue Viability Consultancy Services (TVCS) performed a literature study particularly focusing on the role of pH in wound healing[6]. Both older and recent studies (2005-2006) showed a clear relation between a reduced pH, increased wound healing and decreased bacterial contamination or growth. The same correlation was described in various studies in which the acid characteristics of honey, supported by its high osmolarity, has a positive effect on wound healing and inhibition of bacterial growth.

In 2006 Molan[7] reported positive findings using honey in wound care, reviewing 17 randomised controlled trials involving a total of 1965 participants and 5 clinical trials of other forms involving 97 participants being treated with honey containing products. In addition, he reported the effectiveness of honey in assisting wound healing has also been demonstrated in 16 trials on a total of 533 wounds on experimental animals.

Robson[8] reported in 2009 a study to compare a medical grade honey with conventional treatments on the healing rates of wounds healing by secondary intention. A sample of 105 patients were involved in a single center, open label randomized controlled trial in which patients received either a conventional wound dressing or honey. Data were collected between September 2004 and May 2007. The median time to healing in the honey group was 100 days compared with 140 days in the control group. The healing rate at 12 weeks was equal to 46.2% in the honey group compared with 34.0% in the conventional group, and the difference in the healing rates (95% confidence interval, CI) at 12 weeks between the two groups was 12.2% (-13.6%, 37.9%). The unadjusted hazard ratio (95% CI) from a Cox regression was equal to 1.30 (0.77, 2.19), P = 0.321. When the treatment effect was adjusted for confounding factors (sex, wound type, age and wound area at start of treatment), the hazard ratio increased to 1.51 but was again not statistically significant. It was concluded that wound area at start of treatment and sex are both highly statistically significant predictors of time to healing. It was concluded that these results support the proposition that there are clinical benefits from using honey in wound care, but further research is needed.
Robson[9] reported in 2009 another paper a case study were the use of Leptospermum honey resulted in a successful treatment of 4 patients with radiation-induced skin injury.

Based on literature data Subrahmanyam[10] discussed the use of honey in the treatment of burn wounds and assessed honey's current status as a burn wound dressing. It was concluded that with the increased number of reports on the use of honey in burns and wounds, honey as an alternative treatment for such injuries is gaining increased acceptance from clinicians. However, discussion about the type of honey to be used is still ongoing, as also about the need to sterilize the honey before use. Further prospective randomized studies using various types of honey with varied properties may help

to standardize the particular type of honey to be used. Present evidence supports the finding that honey, thanks to its various modes of action, is useful in superficial and partial-thickness burns.
Gethin[11] reported a series of case studies where Manuka honey was used in the treatment of leg ulceration. The aims of the study were to gain insight into the practical use of Manuka honey in wound management. The objective was to test the feasibility of further rigorous research into the use of honey in the management of chronic wounds. Instrumental case series were used to examine the use of Manuka honey in eight cases of leg ulceration. To collect the necessary data, photographs, acetate tracings, data monitoring and patient comments and observations were used to add greater reliability and validity to the findings. The wounds were dressed weekly with Manuka honey. The results obtained showed three males and five females with ulceration of different aetiologies were studied. A mean initial wound size for all wounds of 5.62 cm(2) was obtained. At the end of four-week treatment period, the mean size was 2.25 cm(2). Odour was eliminated and pain reduced. The conclusions drawn were that the use of Manuka honey was associated with a positive wound-healing outcome in these eight cases. Arterial wounds showed minimal improvement only.

Rose Cooper[12] describes in the booklet HONEY: A modern wound management product published by UK Wounds the clearance of infection by honey and the safety in use of honey.
Clearance of infection
Applying honey dressings to wounds has been reported to:

- Clear infection rapidly
- Heal deeply infected surgical wounds

Wounds not responding to conventional therapy with antibiotics and antiseptics have been healed by application of honey dressings, including wounds infected with methicillin-resistant Staphylococcus aureus (MRSA) [13, 14], Pseudomonas aeruginosa[15] and other bacteria resistant to antibiotics

Safety in use
No adverse effects have been reported in 500-plus cases in publications on using honey on wounds, and 140-plus cases reported on using honey in ophthalmology. There are no reported cytotoxic effects that would slow the healing process, whereas all antiseptics in common use can be harmful to body tissues[16], including silver as released from nanocrystalline silver dressings[17]

See doc. 1606-32 Principelle Honey Literature Review

6.2 PMCF data and Case studies: MelMax and Principelle IF wound dressings

6.2.1 Evaluating MelMax in intractable wounds: A Series of Case Studies

Hampton study[2, 6]
Tissue Viability Consultancy Services (TVCS) were invited to undertake a series of case studies on MelMax with the aim of evaluating the efficacy and potential of MelMax honey impregnated dressing in achieving wound healing in common types of wounds found in patients in the community.
The study aims and objectives were to gain real world learning of the dressing to provide guidance to clinicians and to evaluate the effectiveness of MelMax in non-healing chronic wounds of longer duration than 3 months.
This was a descriptive non-blinded study using individual case studies with a sample size of 31 patients with recalcitrant wounds (non-healing wounds present for more than 3 months). The study duration was officially 6 weeks for each patient, but decisions to continue beyond the study time was based on clinician assessment of patient need. The actual cut off point was finally between 6 and 10 weeks and this was possible due to the unstructured methodology using individual case studies.
The selected patients were those with chronic, non-healing wounds and the status of ‘non-healing’ was established by the investigator. The assessment was undertaken by research nurses, trained to undertake wound assessment, and the subjects were carefully selected to provide a cross section of the wound population. Those with established arterial disease considered detrimental to healing were excluded from the study.
Measurements were undertaken on week 1 and the final week. The parameters measured were pain levels during wear time, reduction in exudate, rate of healing and ease of use. Evidence of healing was demonstrated with photography and planimetry measurements

Based on the results it was reported that it is difficult to say precisely whether the reduction in exudate, pain and odour can be attributed to the honey in MelMax or to the healing that occurred. Nevertheless, prior to MelMax, the wounds were either static or and therefore, complete healing 16% of the wounds and 51% of the wounds were in a healing status in a six week period is very significant and suggests that MelMax not only provides an optimum healing environment but also addresses the bacterial loading within these wounds.
There is often a perception that honey will increase pain in painful wounds. This could be attributed to the production of hydrogen peroxide in honey, and MelMax is low in this production. The patients in this evaluation reported very little pain prior to application of MelMax and this pain had reduced post MelMax. No patients experienced pain on removal and none experienced pain immediately following application. Therefore, no one experienced pain that could be related to MelMax. MelMax was found to be simple to apply and easy to remove.
The surrounding skin improved in each case of maceration or skin damage found at the start of the evaluation. This could be due to the healing that occurred during the evaluation, or it could be due to MelMax providing the optimum environment in the wound. Why it occurred is almost irrelevant as it only occurred after MelMax had been applied, suggesting that in some way, MelMax was responsible, whether due to the support MelMax gave to the healing process, or due to the change in bacterial load.
It was concluded that MelMax is a simple method of delivering an ancient remedy to the wound. The benefits of using honey are without doubt, but the side effects of some honey (pain and method of delivery to the wound) can limit their use. MelMax is easy to apply, does not need complex explanations of why it benefits the wound, which allows easy education of nurses and provides them with a cost-effective method of reducing bacteria in a wound. This would make MelMax a rival to the high cost silver market, which is popular with nurses at present.

Hoeksema/Pirayesh study[18]
Hoeksema and Pirayesh were invited to undertake a series of case studies on MelMax with the aim of evaluating the potential efficacy of the MelMax dressing in the treatment of infected burns and residual burn defects which were either treated conservatively or with surgical excision and split thickness skin grafting.
A total of 21 patients were recruited in this study and sufficient data was available in 19 patients with a total of 35 target wound sites.
The objective of this clinical prospective phase I pilot study was to determine the efficacy with regard to the normalization of the wound. The parameters measured were reduction of excessive inflammation, regulation of critical contamination or infection, regulation of the level of exudates, and facilitation of re-epithelialisation.
Burn wounds were allocated to a surgical or conservative therapy pathway according to the assessment of burn depth Laser Doppler Imaging.
The treatment resulted in an overall full closure of 94% with a mean healing time after start of therapy was 25.6 days. A reduction of exudates and recruitment of controlled amount of granulation tissue with progressive epithelialisation leading to stable wound closure have been observed. In addition, often reduced microbiological species has been reported.

Rucigaj study[19]
Rucigaj recruited 60 patients with venous leg ulcers. Patients were randomly positioned into one of two groups by closed numbered envelopes and subsequently observed for 8 weeks or less if ulcers were healed. Ulcers in group 1 were treated with MelMax and the ulcers in group 2 were treated with silver-based dressings. The aim of the randomized study was to compare the cleaning and “antiseptic” activity of the two different dressings on the healing rate of venous leg ulcers, characterised by delayed or stopped healing, risk of infection, foul odour or discoloration of granulation tissue.
It was concluded that the ulcers treated with MelMax showed similar or faster cleaning and healing than ulcers treated with silver-based dressings (ActiSorb Ag – J&J/Systagenix).
Honey based dressings reduce the need for systemic antibiotics. One patient in the MelMax group needed antibiotics versus 6 patients in the control group.

6.2.2 PMS data – MED 2005

Post market data were obtained from 31 patients treated with MelMax in the Netherlands and the EU in a 12 months period. The patient had an age between 4 months and 82 years.

Common treatment goals were:

- to close the wound
- to prepare the wound bed for further treatment, e.g. skin transplantant
- to prevent infection from occurring or spreading

The following wound types were recorded:

Wound type	**N**
Leg ulcer	4
Diabetic ulcer	1
Pressure ulcer	1
Burns II degree/donor sites	20
Surgical wound	4
Wound after amputation	1

The following results were documented at the time:

Treatment result	**N**
Full closure	16
Improvement	12
No improvement	2
Allergic reactions	0
Other adverse events	0
Pain likened to stinging/burn sensation	1

The clinical performance of MelMax has been recognized as very effective.
In addition, it was concluded that MelMax® is easy and safe to use for both chronic and acute wounds.

6.2.3 PMS data – MED 2006

Post market data were obtained from 67 patients treated with MelMax in the Netherlands and the EU in a 12 months period.

Common treatment goals were:

- to close the wound
- to prevent infection from occurring or spreading

The following wound types were recorded:

Wound type	**N**
Chronic ulcers	67

The following chronic indications have been described:

- Leg ulcers, venous and arterial
- Decubitus
- Diabetic ulcers
- Post surgical*

The following results were documented at the time:

Treatment result	**N**
Improvement/healed	65
No improvement	2

*One patient with a post-surgical abdominal wound has been treated $1^{1/2}$ years with MelMax without any side effect and with a good clinical performance. The wound bed has been prepared for a successful closure after Meek Wall graft procedure.

6.2.4 PMS data – MED 2007

Post market data were obtained from 37 patients treated with MelMax in the Netherlands and the EU in a 12 months period.

Common treatment goals were:

- to close the wound
- to prevent infection from occurring or spreading

The following wound types were recorded:

Wound type	**N**
Chronic ulcers	37

The following chronic indications have been described:

- Leg ulcers
- Decubitus
- Diabetic ulcers
- Post burn defects

The following results were documented at the time:

Treatment result	**N**
Improvement	31
No improvement	3
No compliance of the patient	1
Allergic reactions	1
Pain	1

* One patient reported skin rash and itch upon application. Review of the information and comments by the medical director has been accepted. No allergic test was indicated

The clinical performance of MelMax has been recognized as very effective.
MelMax treatment has been analyzed as a cost-effective treatment.

6.2.5 Clinical PMS data 2012-2016

No (incidence/complaint) reports have been forwarded. From our active soliciting in the market we have received no complaints or incidences.

We are currently reviewing the strategy to become more actively involved in actual case work together with the clinical staff available at our distributors or their end customers.

6.3 Complaints [5]

In the period June 2007-April 2010 no complaints were received on the following subjects:

- packaging
- shipment
- invoicing
- labeling
- leaflet
- instructions
- use of product in general
- marketing and sales
- pain

Based on these results it was concluded that MelMax/Principelle IF dressings are accepted as very reliable products.
No medical device related adverse event has been reported for MelMax/Principelle IF since its first market introduction.

7. OVERALL CONCLUSION

Results from (recent) literature in general support the clinical benefit of honey containing wound dressings for the treatment of acute and chronic wounds. No safety related concerns were documented.

Based on the data obtained Post Market Clinical Follow up studies it can be concluded that Principelle IF/MelMax dressings are clinically safe and perform like intended.

By these results the outcome of the pre-market clinical evaluation, literature evaluation and in vitro studies are confirmed. No unforeseen hazards were identified by field experience for which additional control measures are needed.

Taking the results of the literature and Post Market Clinical Follow up studies into consideration Principelle Inc. states that Principelle IF/MelMax dressings are safe and perform when used as intended by the Instructions for Use.

8. REFERENCES

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More literature available in File "Literature Review" doc. 1606-32

9. NOTE ON DERMAX

The initial protease modulating dressing DerMax started our development. In 2007 the product was sold to 3M Medical and we continued with MelMax. The difference between the two products is the substitution of the carrier. DerMax uses polyethylene glycol. MelMax uses Buckwheat honey as a carrier. The extra function of this component gives the product its antibacterial activity.

The post-market surveillance of DerMax bears on MelMax also. For this reason, we have included DerMax related data here.

Over a period of four years (2003-2006) a total of 181 wounds have been reported.
Following the PMS standard procedure 55 wounds and through observational clinical studies 121 wounds have been reported.
The following types of wounds, mainly chronic, have been described:

- Leg ulcers
- Decubitus
- Diabetic ulcers
- Post-surgical

Out of the 60 PMS reported wounds 78% did show complete healing and/or improvement.

The poor healing tendency of the remaining 22% of the reported wounds was mostly related to the following indications:

- **Decubitus**

Decubitus grade IV stage, which is in line with the outcomes of the observational pilot study of the van Leen study. The underlying pathology is often mostly complex.

- **Leg ulcers**

Leg ulcers treated over a prolonged period with antiseptic agents show a disturbed bacterial flora balance. An acute termination of this anti-septical treatment might cause a re-activated inflammatory response. This response is based on the prolonged application of anti-microbial agents. The wound environment can be out of balance based on toxic activity of these agents.
One report described an enlargement of two wounds with an increased pain sensation.

- **Post-surgical**

Three large abdominal (wounds?) following total wound dehiscence, Platzbauch, did not show any improvement.
These wounds are classified as extremely hard to heal wounds.

No correlation could be found between the DerMax treatment and the poor healing tendency of these indications.

Pain sensation
Seven reports, which mean 4% of the total 176 wounds, have described a stinging and/or burning pain sensation upon application.

The citric acid content might cause this painful reaction, though other components could be suspect as well. One may argue that any dressing will cause this sensation on this patient/wound.
It is unsurprising that it is painful in leg ulcers and not pressure ulcers due to the fact that leg ulcers are often superficial and have the nerve endings exposed.
In pressure ulcers, the nerve endings are damaged, or the tissue is dead (neuropathy) and no longer contains nerve endings.
DerMax is also less likely to cause pain in diabetic foot ulcers, as very many of these ulcers are caused because there is a lack of sensation due to neuropathy.

Dissemond reported however in the observational clinical test with leg ulcers a pain reduction after the DerMax treatment.

The following recommendations have been communicated:
- Good analysis of the type of ulcer and underlying pathology is required.
  Arterial ulcers are described in the literature as painful caused by ischaemia.
- Pain will be reduced once the treatment is combined with a more occlusive/moist treatment.
  In that case a Hydrogel or a Hydrocolloid dressing is recommended as
  a secondary dressing to cover DerMax.

No further side efects have been reported.

Final conclusion:
The clinical performance of the DerMax treatment has overall been recognized as very effective.

10. TYPICAL CASE LOAD

Please observe separate folder ‘PMS Typical case load Principelle’