VALUE ANALYSIS BRIEF:
Clinical and Economic Evidence Supporting the Value of DERMABOND® PRINEO® Skin Closure System (22cm) in Hip and Knee Arthroplasty
EXECUTIVE SUMMARY

Burden of Wound Closure in Hip and Knee Arthroplasty

• Wound complications are one of the major sources of morbidity after hip and knee arthroplasty procedures and can prolong inpatient stay or lead to re-admissions.¹
  — Meta-analyses have reported that the rate of wound dehiscence and infections ranges from 1.3% to 4.8%, and from 3% to 20.9%, respectively.²³
• Surgical site infections (SSIs) occur in up to 19% and 28% of knee and hip arthroplasties respectively, with *Staphylococcus aureus* as one of the leading causes.⁴
  — SSIs are associated with a substantial burden, such as extended length of stay, excess mortality, reduced quality of life, increased readmissions, and a 3-fold increase in hospital costs.⁴⁵

Unmet Need

• There are several types of wound dressings used as part of wound closure care in hip and knee arthroplasty.⁶ However, an important limitation is the need for dressing changes which can be associated with important clinical and economic burden such as pain, healthcare resource professional time, pathogen exposure, and potentially restricted self-care.⁶⁷
• There is a need for a wound closure treatment that provides an ideal healing environment and helps reduce the clinical and economic burden of current care, such as frequent dressing changes, in hip and knee arthroplasty.

Clinical Value of the DERMABOND® PRINEO® System

• The DERMABOND® PRINEO® Skin Closure System:
  — The only skin closure device that combines the proven strength, flexibility, and antimicrobial protection of DERMABOND® Topical Skin Adhesive with the added support and security of a self-adhering mesh to further facilitate both wound-edge approximation and an optimal healing environment which may be particularly useful in surgeries such as hip and knee arthroplasty.⁸⁹
  — Proven 99% effective through 72 hours in vitro against bacteria most commonly associated with SSI, including *S. aureus, P. aeruginosa, E. coli, E. faecium,* and *S. epidermidis* (including MRSA and MRSE).⁹¹⁰
  — Demonstrated strength benefits compared to staples and sutures including: superior strength compared to 4-0 sutures or staples (p<0.01), equivalent strength to a 3-0 suture, and superior skin-holding strength vs. DERMABOND ADVANCED® Topical Skin Adhesive with subcuticular sutures.¹¹¹³
  — Demonstrated tension benefits with the ability to achieve better distribution of tension compared to staples or sutures.⁹¹⁴
• There are numerous patient benefits associated with the DERMABOND PRINEO System that can help enhance patient satisfaction and comfort including easier self-care, less pain at removal, no need for dressing changes, and the ability to shower immediately after a procedure if directed by their healthcare practitioner.⁸¹⁰¹⁵¹⁸

Economic Value of the DERMABOND PRINEO System

• There are several costly resources associated with wound closure and care in hip and knee arthroplasty such as SSIs, wound care dressings, and outpatient visits.¹¹¹⁹²¹
• Wound dressings are typically changed 3 to 5 times in hip and knee arthroplasty.²²²³
  — This results in an additional burden of increased staff time, potential risk for introducing SSI-causing pathogens to the wound, and material costs.²²²³
• Evidence demonstrates that in hip and knee arthroplasty, use of a wound dressing that lowers the frequency of dressing changes and wound complications may be cost-effective despite additional upfront costs.²²
• Given favorable outcomes observed, as well as the absence of need for wound dressing changes and staples removal, it is anticipated that the DERMABOND PRINEO System may provide important cost savings within hip and knee arthroplasty, particularly in the post-acute care setting.

*Clinical significance is unknown
Hip and Knee Arthroplasty and Wound Complications

• The estimated number of annual total hip and knee arthroplasties in the United States is 2.5 million and 4.7 million, respectively.24

• Wound complications are common in hip and knee arthroplasty and can include dehiscence, infection, inflammation, necrosis, abscess, and blistering.2,22
  – Meta-analyses have reported that the rate of wound dehiscence ranges from 1.3% to 4.8%, and the rate of infection ranges from 3% to 20.9%.2,3

• Factors that affect wound healing and associated complications include:
  – Operative factors (e.g., antibiotic prophylaxis)25,26
  – Wound factors (e.g., foreign body)26-28
  – Patient factors (e.g., age, comorbidities, smoking)29-32

• Infection at the wound site prolongs inflammation and immune response, potentially leading to the wound becoming chronic and non-healing.33,34

Clinical and Economic Burden of Surgical Site Infections

• Surgical site infections (SSIs) are common in hip and knee arthroplasty, with *Staphylococcus aureus* as one of the leading causes.4
  – Hip arthroplasty (median SSI rate: 2.1%; range: 0.05% to 28%).4
  – Knee arthroplasty (median SSI rate: 1.3%; range: 0.05% to 19%).4
  – *S. aureus* accounted for 35% of all orthopaedic surgery SSIs, of which 35.7% were specifically attributed to MRSA infections.4

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<th>Burden of SSIs in Hip and Knee Arthroplasty4,5</th>
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<td>Extended LOS</td>
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<td>Mortality</td>
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<td>Total Costs</td>
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• Some factors reported to be predictive for the risk of SSIs in hip and knee arthroplasty include osteoarthritis, diabetes, obesity, increasing age, wound dehiscence, duration of surgery, transfusions, wound drainage, length of stay, and bladder catheter.35-37

• A recent meta-analysis has shown several risk factors to significantly increase the risk of SSI, for example:35
  – Diabetes Mellitus: odds ratio = 1.26; (p < 0.001)
  – Prolonged Operative Time: odds ratio = 2.18; (p = 0.001)
  – Obesity (BMI > 40): odds ratio = 3.74; (p < 0.001)
  – Wound Dehiscence: odds ratio = 8.08; (p < 0.001)

Abbreviations: BMI = body mass index; LOS = length of stay; MRSA = Methicillin-resistant *Staphylococcus aureus*; MRSE = Methicillin-resistant *Staphylococcus epidermidis*

“Wound complications are one of the major sources of morbidity after orthopedic procedures and can prolong the inpatient stay or lead to re-admission.”1

Surgical site infections are reported to occur in up to 19% and 28% of knee and hip arthroplasties respectively.4

The odds of a surgical site infection are reported to be 8-fold greater with wound dehiscence.35
Limitations of Sutures, Staples and Wound Dressings

• Recent studies of sutures and staples in hip and knee arthroplasty suggest that a considerable risk of wound complications remains. Rates of wound complications were reported to range from 3.8% to 19.5%.38-40

• Findings from meta-analyses have reported that wound dehiscence and infection risk is comparable or higher with staples versus sutures.1,3

• Application of a wound dressing is necessary for proper wound management.6 Wound dressings provide mechanical protection, absorb exudate, stop bleeding and help create environment suitable for healing.6 However:
  — Wound dressings are not intended for wound closure and thus do not have the strength necessary to close wounds. As such, separate wound closure methods are required in addition to the dressing.
  — Many wound dressings do not have bacterial inhibition properties.6

• An important limitation of several wound dressings is the need for dressing changes, which is associated with important clinical and economic burdens.6,7
  — Patient dissatisfaction
  — Increased risk of pain
  — Time-consuming
  — Pathogen exposure
  — Restricted self-care
  — Post-operative care burden

UNMET NEED

• Current methods for wound closure, primarily sutures and staples, with a variety of wound dressings, may not provide an ideal healing environment due to:
  — Need for frequent dressing changes.6
  — Variability in patient, as well as caregiver, care.

• Minimizing postsurgical dressings and dressing changes may reduce risk for infection and allow easier self-care.4

• Several factors are cited as important goals of orthopedic wound closure and include: speed of wound healing, adequate closure, patient satisfaction, low complications, and cosmesis.1,39

• There is a need for a wound closure treatment that provides an ideal healing environment and helps to reduce the clinical and economic burden of current care such as the need for frequent dressing changes.
CLINICAL VALUE

Features of DERMABOND PRINEO System

• The DERMABOND PRINEO System (22 cm) uses 2 unique components allowing for uncompromising strength and wound healing:\textsuperscript{4,9}

  1. Liquid topical skin adhesive (2-octyl cyanoacrylate) formulation which sets in \( \sim \) 60 seconds when applied to mesh.\textsuperscript{8}

  2. Flexible self-adhesive polyester mesh that accelerates polymerization of liquid adhesive and conforms to body’s contours.\textsuperscript{8}

• The dual components make the DERMABOND PRINEO System particularly useful in surgeries such as hip and knee arthroplasty.

• The DERMABOND PRINEO System has proven 99\% effective through 72 hours \textit{in vitro} against bacteria most commonly associated with for SSIs, including \textit{S. aureus, P. aeruginosa, E. coli, E. faecium, and S. epidermidis} (including MRSA and MRSE).\textsuperscript{9,10}

Clinical Studies of DERMABOND PRINEO System

• The DERMABOND PRINEO System has been studied in 4 randomized trials with a total of 430 patients evaluated across a variety of surgery types (abdominoplasty, breast, and trauma lacerations).\textsuperscript{15,41-43}

  − Comparable wound closure efficacy versus sutures\textsuperscript{41,43}

  − Decreased skin closure time by 5.19 to 13.66 min (breast and abdominoplasty; \( p<0.0001 \))\textsuperscript{41,43} and procedure time by 13 min (abdominoplasty; \( p<0.05 \))\textsuperscript{15} relative to sutures.

  − Favorable cosmetic results up to 30 days\textsuperscript{42} and up to 1 year\textsuperscript{15,41,43}

  − Less pain at removal compared to adhesive strips\textsuperscript{15}

  − Low rates of adverse events (e.g., blistering or infection)\textsuperscript{15,41-43}

• The topical skin adhesive component of DERMABOND PRINEO System has been extensively studied in over 40 RCTs*, with several finding positive outcomes in hip and/or knee arthroplasty.\textsuperscript{44-47}

Patient Benefits of DERMABOND PRINEO System

• The DERMABOND PRINEO System (22 cm) design, supported with proven clinical data, contributes to numerous benefits that can help enhance patient comfort and satisfaction including:

  − Easier self-care as post-surgical dressings are not needed (i.e., no dressing changes required).\textsuperscript{10,17}

  − Designed to provide microbial barrier protection against organisms commonly responsible for surgical site infections.\textsuperscript{5,10}

  − The ability for patients to shower immediately after procedure if directed by their healthcare practitioner.\textsuperscript{8}

  − Easy mesh tape removal when wound is sufficiently healed.\textsuperscript{18}

  − Less pain at removal vs other wound closure methods\textsuperscript{15,41,43}

  − Good cosmetic results.\textsuperscript{15,41,43}

Abbreviations: MRSE = Methicillin-resistant \textit{Staphylococcus epidermidis}

*See appendix for full list of references.

*Clinical significance is unknown
Strength of DERMABOND PRINEO System

• The DERMABOND PRINEO System (22 cm) has demonstrated the following benefits pertaining to strength:
  − Superior strength compared with 4-0 sutures or staples (p<0.01).\textsuperscript{11}
  − Equivalent strength to a 3-0 suture.\textsuperscript{12}
  − Superior skin-holding strength vs. DERMABOND ADVANCED Adhesive alone and DERMABOND ADVANCED Adhesive with subcuticular sutures (p<0.05).\textsuperscript{13}

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<th>Comparative Skin-Holding Strengths\textsuperscript{11}</th>
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<td>Max. Load (N) prior to 3-mm gap (±1-mm)</td>
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<td>166.5</td>
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Tension load needed to achieve a 3-mm gap in porcine samples close with DERMABOND PRINEO Skin Closure System (22 cm), surgical staples or sutures. Incisions closed with DERMABOND PRINEO Skin Closure System (22 cm) required significantly greater loads to close the 3-mm gap.\textsuperscript{11}

Tension Distribution of DERMABOND PRINEO System

• The DERMABOND PRINEO System (22 cm) has demonstrated the following benefits pertaining to tension distribution:
  − Disperses tension gently and evenly across the entire incision area.\textsuperscript{9}
  − Better distribution of tension compared with staples or sutures.\textsuperscript{14}
  − Visual maps of tension across incisions revealed sutures and staples had high concentration points of tension while DERMABOND PRINEO System had more uniform tension distribution.\textsuperscript{15}

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<th>Mapping of tissue movement under 1 lb of tensile load</th>
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In a head-to-head study vs. staples and subcuticular sutures, incised tissue samples were approximated using 3-0 suture, skin staples or DERMABOND PRINEO System (22 cm), respectively. Samples were then placed in a device and tensioned mechanically. Digital Image Correlation (DIC) technology was used to map strain (as revealed by tissue movement). Black spacing in mapping image is due to the sensors not being able to capture any readings. Study performed ex vivo.
Opportunity for Cost Savings in Hip and Knee Arthroplasty

• Several resources and costs are associated with wound closure in hip and knee arthroplasties. Some examples include the following:

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<th>Resource</th>
<th>Unit Costs</th>
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| Wound Closure Devices         | Traditional sutures: $2 to $83 (avg. material costs)²  
Barbed sutures: $24 to $106 (avg. material costs)²  
Staples: $6 to $8 ³⁴⁶ |
| Wound Dressing                | $1 to $39 ²²¹¹ |
| Operative Time                | $28 to $103 per minute³ |
| Hospital Stay*                | $2,212 per inpatient day⁴⁹ |
| Surgical Site Infection       | $36,651 per case⁴  
(range: $11,224 to $88,134) |
| Nursing Time*                 | $34.14 per hour⁵⁰ |
| Physician Office Visit        | $118 per visit¹⁹ |

*National average cost per inpatient day and average cost for registered nurse, costs not specific to hip and knee.

• Wound dressings are typically changed 3 to 5 times in hip and knee arthroplasty²²,²³
  — Results in the additional burden of increased staff time, potential risk for introducing SSI-causing pathogens to the wound, and material costs²²,²²,²³

• Evidence demonstrates that in hip and knee arthroplasty, use of a wound dressing that lowers the frequency of dressing changes and wound complications may be cost-effective despite additional upfront costs.²²

• A recent study of 250 Medicare beneficiaries with total joint arthroplasty, including hip and knee replacements, reported that post-discharge payments accounted for 36% of the total episode-of-care payments.⁵¹
  — Resource use in post-acute care, after hip and knee arthroplasty, such as dressing changes or staple removal, remains a top area of focus for optimizing costs for payers.⁵²

“Post-discharge care costs were found to account for over 1/3 of total episode costs in total joint (e.g., hip and knee) arthroplasties."⁵¹

* Breakdown of procedures by MSRG in the total weighted costs include: MS-DRG 462 (2%), 466 (4%), 467 (19%), 468 (8%), 469 (9%), and 470 (58%).
ECONOMIC VALUE

Current Healthcare Performance Metrics and Wound Closure

• U.S. healthcare reform goals are to improve quality of care, patient outcomes and satisfaction, and total performance scores (TPS) while reducing hospital acquired conditions (HAC) and episode of care costs.54-57

• Reimbursement implications associated with wound closure care in hip and knee replacement surgery:
  
  − CMS stopped payment of HACs such as SSIs.56
  − CMS will reduce payment to hospitals in top 25% of HAC rates.56
  − Readmissions program: penalties for readmissions.55
  − Value Based Purchasing and potential impact to patient experience.54
  − Bundled payment incentivize coordination across care continuum.51,57

• On April 1, 2016, CMS’ first mandatory bundle for hip and knee replacement was implemented in 67 U.S. regions (~800 hospitals).53 This program established one price to compensate total joint providers for an entire episode of care, rather than the individual components of care.53
  
  − Providers accountable for quality and cost of care to 90 days
  − Fixed reimbursement amount to be shared among all providers
  − Hospitals to keep costs below $25,565 per episode or face penalty
  − Medicare target episode prices to inform penalties or rewards
  − Bundled payments increasingly used with private insurers

Current Healthcare Performance Metrics and Wound Closure

• The DERMABOND PRINEO System has the following advantages that may translate into less healthcare resources and avoided costs.10
  
  − No need for wound dressing changes (i.e., avoided material costs and healthcare professional visits).8
  − Antimicrobial protection to potentially help minimize the risk of SSIs.10
  − No need for staple or suture removal, potentially avoiding follow-up visits.8

• The advantages with the DERMABOND PRINEO System are particularly important for managing post-acute care costs, which is an important consideration with recent health reform and bundled payments.

The clinical and economic burden of wound closure in hip and knee arthroplasty in the U.S. is substantial. With recent healthcare reform, decision-makers will need to consider products that provide the best clinical outcomes while balancing costs.

The DERMABOND PRINEO System is a wound closure product that provides uncompromised strength and protection which may help reduce costly healthcare resources, particularly in the post-acute care setting (e.g., dressing changes).
REFERENCES

8. Ethicon Inc. DERMABOND® PRINEO® Skin Closure System (22 cm) Instructions For Use. LAB100114233v2. 5/15.
11. Data on File, Ethicon Inc. Study to compare the tissue holding strength of DERMABOND® PRINEO® 22 cm Skin Closure System (DP22) to conventional wound closure techniques. AST-2014-0246.
13. Data on File, Ethicon Inc. Advanced study comparing tissue holding strength of DERMABOND® PRINEO® Skin Closure System 22 cm (DP22) to DERMABOND ADVANCED® with and without Subcuticular Sutures. ADAPTIV#100253930.


For complete indications, contraindications, warnings, precautions, and adverse reactions, please reference full package insert.

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