Summary of Safety and Clinical Performance

Neuro-Patch®

Further information are in the work instruction 4-1-11-512-0 Instructions for Summary of Safety and Clinical Performance.

Prepared by:	Alexander Krump Tel: +49 7461 95 31 47 2 Fax: +49 7461 95 16 55 E-Mail: alexander.krump@aesculap.de	Medical Scientific Affairs B. Braun Aesculap Am Aesculap-Platz 78532 Tuttlingen/Germany
Document revision:	06	
Date:	28.09.2021	

Part 1: Intended for healthcare professionals

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.
The SSCP is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.
The following information is intended for users/healthcare professionals.

List of abbreviation / glossary

Basic UDI-DI	Basic Unique device identification device identifier
CAPA	Corrective and preventive action
CSF	Cerebrospinal fluid
FSCA	Field safety corrective action
FSN	Field safety notice
PUR947	Polyester urethane
SSCP	Summary of Safety and Clinical Performance

1 Device identification and general information

1.1 Device trade name

Neuro-Patch®

Table 1: Neuro-Patch - Article list

Reference Number	Description	Content
1064002	Neuro-Patch® 12 cm x 14 cm	1 piece
1064010	Neuro-Patch® 6 cm x 14 cm	1 piece
1064020	Neuro-Patch® 8 cm x 9 cm	1 piece
1064029	Neuro-Patch® 6 cm x 8 cm	1 piece
1064037	Neuro-Patch® 4 cm x 10 cm	1 piece
1064040	Neuro-Patch® 5 cm x 6 cm	1 piece
1064110	Neuro-Patch® 4 cm x 5 cm	1 piece
1064122	Neuro-Patch® 2 cm x 10 cm	1 piece
1064123	Neuro-Patch® 1.5 cm x 3 cm	1 piece
1064045	Neuro-Patch® 4 cm x 5 cm	2 pieces
1064053	Neuro-Patch® 2 cm x 10 cm	2 pieces
1064061	Neuro-Patch® 1.5 cm x 3 cm	2 pieces

1.2 Manufacturer's name and address

Aesculap AG
Am Aesculap-Platz
78532 Tuttlingen/Germany

1.3 Manufacturer's single registration number (SRN)

Manufacturer's single registration number: DE-MF-000005504

1.4 Basic UDI-DI

Basic UDI-DI for Neuro-Patch®: 4039239000001401ZR

1.5 Medical device nomenclature description

P900403 „NON-BIODEGRADABLE DEVICES, FILLER AND RECONSTRUCTIVE"

1.6 Class of device

According to the MDR 2017/745 Annex VIII, rule 8.2 Neuro-Patch® can be assigned as a class III medical device.

1.7 Year when the first certificate (CE) was issued covering the device

Neuro-Patch® is CE-certified since 1996.

1.8 Authorized representative if applicable; name and the SRN

Not applicable.

1.9 NB's name (the NB that will validate the SSCP) and the NB's single identification number

TÜV SÜD Product Service GmbH
Ridlerstraße 65
80339 München

Single identification number: 0123

2 Intended use of the device

According to the instructions for use (Mat. No. 12157732), the following information is provided to the user.

2.1 Intended purpose

Neuro-Patch® is used in neurosurgery as dura mater replacement.

2.2 Indication(s) and target population(s)

Note
The manufacturer is not responsible for any use of the product against the specified indications and/or the described applications.

Usage:
- For covering cerebral and cerebellar dura defects
- For cerebral decompression surgery when there is elevated intracranial pressure
- For covering spinal dura defects
- For spinal decompression surgery

2.3 Contraindications and/or limitations

Do not use:
- In infected regions
- In open cerebrocranial traumata
- In open spina bifida
- In case of known hypersensitivity against implant materials; for fixation materials please note the corresponding instructions for use
- In any application areas that are not mentioned in "Indications"

3 Device description

3.1 Description of the device

Neuro-Patch® is a synthetic, suturable dura substitution of fine fibred microporous fleece manufactured from a highly purified polyester urethane (Figure 1).

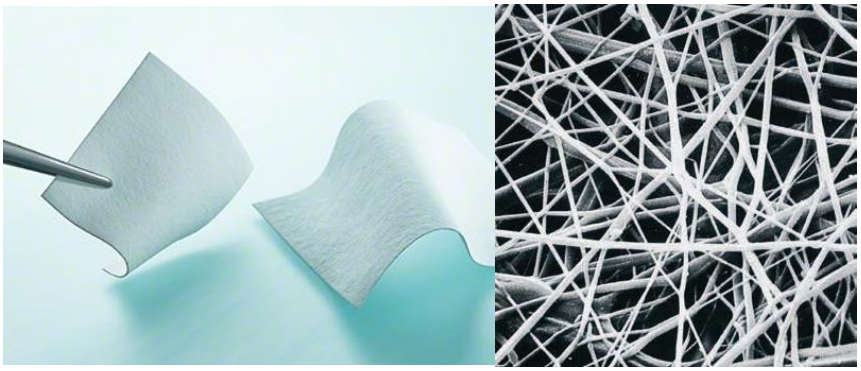

Figure 1: Product image of Neuro-Patch (left); microporous structure of Neuro-Patch (right).

Neuro-Patch® is composed of a polyester urethane (PUR947) which is non-absorbable.
The products belong to the group of neurosurgical implants.

- During the intended use, the following organs/tissue/body fluids come in contact with the devices: Bone tissue, dura mater, cerebrospinal fluid as well as blood.
- The application of the devices is invasive.
- The application period of the devices is long-term.
- The devices are intended for clinical users: Surgeon with required knowledge about the surgical technique and surgical training who is aware about the in vivo characteristics of the product, operating room personnel (set-up, handling, and functional check).
- Neuro-Patch® is a single use device and will be delivered sterile (sterilization method: ethylene oxide).
- The devices do not contain pharmaceutical components, animal or human tissue; they are no blood products and are not radioactive.
- No changes have been made to the product since the market launch of Neuro-Patch®.

3.2 A reference to previous generation(s) or variants if such exist, and a description of the differences

Since the market launch of Neuro-Patch® in 1996, neither the final product specifications of Neuro-Patch® has been further developed nor changed in terms of its product characteristics. No variants of Neuro-Patch® other than the different product and packaging sizes are available.

3.3 Description of any accessories which are intended to be used in combination with the device

Neuro-Patch® must be sutured with nonabsorbable suture material (polyester, polypropylene) and can be additionally fixed with fibrin glue.

3.4 Description of any other devices and products which are intended to be used in combination with the device

There are no other devices and products which are intended to be used in combination with the device.

4 Risks and warnings

4.1 Residual risks and undesirable effects

Potential complications that the manufacturer is currently aware of:

- CSF-Leakage
- Infection
- Adhesions
- Foreign body reaction

According to the product-related literature of Neuro-Patch® that were identified in the Clinical Evaluation Report, CSF leaks are a common complication with incidence rates from 0.0 % to 13.1%. Furthermore, incidence rates from 1.9% to 15.0% for infections have been reported. Foreign body reactions such as allergic reactions due to material incompatibilities or adhesions to the surrounding tissue were not reported for Neuro-Patch®. In comparison to the state of the art, CSF leaks are a common complication, regardless of the type of dural closure (incidence rates from 5.0 % to 29.6%). Furthermore, incidence rates from 5.64% to 12.5% for infections and 3.08% to 10.42% for the occurrence of foreign body reactions were reported.

Note:
The points mentioned above include potential clinical consequences.
No risks, side effects and interactions as a result of comorbidities of the patient have been identified.

4.2 Warnings and precautions

Clinical user

General safety information
To prevent damage caused by improper setup or operation, and to not compromise the manufacturer warranty and liability:

- Use the product only according to these instructions for use.
- Always follow the safety advice and information given in the instructions for use.
- Ensure that the product and its accessories are operated and used only by persons with the requisite training, knowledge and experience.
- Store any new or unused products in a dry, clean, and safe place.
- Keep instructions for use accessible to the user.

Note
The user is obligated to report all severe events in connection with the product to the manufacturer and the responsible authorities of the state in which the user is located.

Notes on surgical procedures

It is the user's responsibility to ensure that the surgical procedure is performed correctly. Appropriate clinical training as well as a theoretical and practical proficiency of all the required operating techniques, including the use of this product, are prerequisites for the successful use of this product.

Effective

Aesculap is not responsible for complications caused by:

- incorrect indication or implant selection
- incorrect surgical technique
- incorrect combination of implant components
- combination with components of other manufacturers not approved by Aesculap
- exceeding the limitations of the treatment method or non-observance of essential medical precautions

The user is required to obtain information from the manufacturer if there is an unclear preoperative situation regarding the use of the product.

Note

The use of atraumatic round body needles permits suturing without major damage to the implant.
In addition, fibrin glue can be used to achieve a sealing effect.

Note

During the application of Neuro-Patch in combination with bone cement, chemical damage of the patch material, depending on the application situation, cannot be excluded.

Sterility and storage

The product is EO sterilized and wrapped in sterile packaging.

- Store implant components in their original packaging. Remove them from their original protective packaging only just prior to implantation.
- Do not use products from open or damaged sterile packaging.
- Do not use the product after its use-by date.
- Store the product at 25 ± 5°C.
- Do not reuse the product.

The reprocessing of the product affects its functionality. Risk of injury, illness or death due to soiling and/or impaired functionality of the product.

- Do not reprocess the product.

4.3 Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable

Neither Corrective and Preventive Actions (CAPA) nor Field Safety Corrective Actions (FSCA) have been performed during the last 5 years.

5 Summary of clinical evaluation and post-market clinical follow-up (PMCF)

5.1 Summary of clinical data related to equivalent device, if applicable

Not applicable.

5.2 Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable

Clinical experience with Neuro-Patch® polyester urethane fleece as dura replacement material
The aim of the multi-center study, led by Professor LAUN and GRUNDMANN, was to evaluate the safety and performance of Neuro-Patch® in neurosurgical head surgery in terms of intraoperative handling, immediate postoperative complications and long-term compatibility of the product.
In total, 317 patients (160 females, 157 male) were enrolled in the multicenter study (n=5 clinics) and followed up for up to one year postoperatively. Neuro-Patch® was mainly used in the treatment of tumor diseases (n=271). Further indications were cerebrospinal fistulas, syringomyelia and subarachnoid hemorrhages).
With regard to the handling properties of the Neuro-Patch®, suturing, cutting, modelling, cerebrospinal fluid tightness and suture tearing were assessed. In general, the handling was judged satisfactory by the surgeons. Furthermore, complications such as CSF leaks and suture tearing were observed rarely.

Intraoperative complications were observed in 32 cases (10.1%). The most common were brain swelling and bleeding. A causal relationship with the application of Neuro-Patch® was not evident in any case. Regarding the complication rate during the immediate postoperative follow-up period, infection have been observed in ten patients. In the period between discharge and the first follow-up examination, wound dehiscence (n=2), infections (n=4) and brain swelling (n=2) were observed. None of the complications were related to Neuro-Patch®. Finally, the authors conclude that Neuro-Patch® is suitable for the use as a dura substitute due to its good handling characteristics and the low complication rate. Detailed information can be found in the final study report.

5.3 Summary of clinical data from other sources, if applicable

Next to the abovementioned clinical study prior CE-marking, several Expert-Reports and a customer survey regarding the safety and performance of Neuro-Patch® were initiated. Furthermore, in 2019 a PMCF-study (MiDura-study) has started. Regarding these activities, the following section provides detailed information.

Expert Reports
In addition to the clinical study by LAUN und GRUNDMANN, three clinical expert reports were prepared as part of the product monitoring in 2006 and 2020 respectively, to assess safety and performance.

Experiences based on applications of Neuro-Patch® in ca. 4000 neurosurgical interventions. Neuro-Patch® was also used in the context of extension plastic surgeries with increased intracranial pressure as well as for covering cerebral, cerebellar and spinal dura defects. Even in indications with an increased risk of infection (e.g. opening of the frontal sinus), no postoperative infections in connection with Neuro-Patch® could be observed. In general, Neuro-Patch® was sutured and only in rare cases additionally sealed with fibrin glue. Furthermore, there are no restrictions regarding the patient population so that Neuro-Patch® is also used in children.

The application of Neuro-Patch® positively because of its immediate availability, ease of manipulation for trimming the implant to the desired shape and for suturing due to a good compromise between strength and elasticity. Using Neuro-Patch® results in a rapid and easy achievement of immediate dural liquid tightness, whatever the dural defect or fragility of the residual dura mater in most cases. Regarding the surgical planning of operations in which long-term re-operations are expected, the clinical department indicate the use of Neuro-Patch® due "to the absence of any scar adhesions to the cerebral cortex in the event of re-operation (fewer adhesions than in the case of direct suture of the dura mater during the first operation), which is a very significant benefit as it makes re-operation shorter and potentially less damaging". However, no undesirable events relating to use (either infectious or inflammatory phenomena) have been observed until now.
Finally, dural liquid tightness is not achieved in 100% of all cases in which Neuro-Patch® is used in combination with fibrin glue in mid- and long-term periods which has also been observed in the study by GRUNDMANN and LAUN before (also see chapter 5.2 of the SSCP).

Neuro-Patch®: Customer survey

The purpose of this document is to report and summarize the findings of the Post-Market Clinical Follow-up (PMCF) measures determined in the PMS-/ PMCF-Plan for Neuro-Patch® as an action to assess the safety, quality and performance of the device during its whole product life cycle.
Between October 2019 and June 2020, 47 customers of Neuro-Patch® have been asked to fill a questionnaire on their use of Neuro-Patch® in clinical routine.

The results of the questionnaire show that the majority of users rate the handling and performance parameters as excellent or very good in all fields (ability to cut, adaption to anatomical structures, liquid tightness, tensile strength and suture retention strength). In total, more than 90% of the users are satisfied with the performance of the Neuro-Patch®.
No one rated the performance as poor and only a minority rated any of the parameters as "fair".

Literature on the product

DEL GAUDIO et al. compared the clinical outcome of dural peeling and duraplasty for the surgical treatment of Chiari Type I malformation. Therefore, the authors analysed the data of 28 patients who underwent cervical-cranial decompression (CCD) regarding the efficacy and complication rates of both procedures. In total, 18 patients underwent CCD with dura peeling and 10 with duraplasty. In the duraplasty group, dura grafting was completed using different materials according to the surgeon's preference, such as TissuDura covered with DuraSeal, Neuro-Patch® alone (n=1) and in combination with DuraSeal (n=5) or Tisseel (n=2); or fascia lata (n=1). The most common symptoms were headaches in both groups, frequently with effort-related acutization, then nausea and vomiting in the duraplasty group and hypoesthesia/paresthesia in the dura peeling group. As a main result, all patients in the duraplasty group clinically improved partially (50%) or had complete resolution of symptoms (50%), whereas only 12 patients in the dura peeling group observed improvement of the symptoms (28% with total resolution and 39% with partial improvement). Unfortunately, 6 patients didn't benefit from the surgical intervention and symptoms re-

mained stable. For the evaluation of the morphologic improvement, postoperative follow-up MRI examinations were conducted and available for 26 patients (100% of the dura peeling group and 80% of the duraplasty group). Morphologic improvement was assessed by the reappearance of CSF at posterior and/or inferior aspect of the amygdala; morphologic change of cerebellar tonsils, and subsidence of syringomyelia in patients in whom it was present preoperatively. The assessment did not find any statistical significance regarding the abovementioned parameters. Overall complications were more frequent in the duraplasty group than in the dura peeling group (70% vs. 0%). Four patients in the duraplasty group required multiple interventions because of complications (1 pseudomeningocele, 1 wound infection, and 2 hydrocephalus), whereas in the dura peeling group, two patients needed a late second surgery with DP because of the nonresolution of the preoperative symptoms. No patient had worsening of preoperative symptoms after surgery and no statistically significant difference in long-term outcome between both groups has been observed. Additionally, the authors did not report complications due to the use of dura substitutes. (1)

In a single-institution review of clinical data, CHEN et al. analysed the clinical outcome of different dural substitutes and identified risk factors for duraplasty-associated hemorrhagic complications. The analysis included patient data who underwent craniotomies or craniectomies for tumor, traumatic brain injuries and vascular lesions. Next to demographic data, the type and the number of dura grafts as well as the occurrence of postoperative complications such as sub- and extradural hematomas and subarachnoid hemorrhage were evaluated. In total, data of 212 patients were included for further analysis. Patients were divided into three groups, depending on the dura substitute they received. Neuro-Patch (n=121) was most frequently used, followed by Gore-Tex (ePTFE; n=78) and Biomesh (polyester silicone; n=13). Mean age of the patient was 52.7 years (range: 1 to 92 years) which did not differ significantly between the different groups. Primary diagnosis indicated tumor (n=155), traumatic brain injury (n=44) and vascular lesions (n=13), whereby in 10 patients complications have been documented. None of these complications were detected in patients who received Gore-Tex. In the Neuro-Patch® group as well as in the Biomesh group, five complications occurred (4.1% vs. 38.5%). Among the 10 patients who developed complications, 8 patients had subdural hematoma, one had epidural hematoma, and one developed subarachnoid hemorrhage and pneumocranium. Compared to Neuro-Patch®, patients who received duroplasty with Biomesh had a higher hemorrhagic complication rate. However, the development of complications associated with the use of an artificial dural substitute has rarely been reported before the study by CHEN et al. and has been considered infrequent. The authors assume different reasons for the development of hemorrhagic complications: Hemorrhage could result from the disruption of the local vessels by movement of the synthetic dural substitutes so that an insufficient fixation of the dura graft may result in movement of the implants which leads to disruption of the vessels. Another reason for the development of complications can be found in the fact that hemorrhage is the result of inflammation. The presence of synthetic dural substitutes in surgical wounds can induce a local tissue reaction from the edge of the dura and lead to the formation of a thick connective tissue so that rupture of these fragile vessels in response to minor trauma can result in bleeding. In patients who received Gore-Tex, no complications have been observed. Gore-Tex is a soft implant and allows the tissue to fixate the implant for a more stable feel. With regard to the material properties, Neuro-Patch® is similar to Gore‑Tex, whereas Biomesh is made

of polyester and coated by silicone which are materials that may be responsible for a number of complications (2). Finally, the study by CHEN et al. identified possible risk factors for hemorrhagic complications for patients who had a higher prevalence rate of hepatitis, prior craniotomy for brain tumor, and received duraplasty with Biomesh. Nevertheless, the following limitations of the study must be taken critically into account for the interpretation of the results: Data extraction and analysis were performed retrospectively in this single hospital database. Therefore, a lack of data for parameters such as alcohol consumption or the physician's judgement and preference cannot be excluded. In addition, the postoperative imaging was not performed routinely so that interpretation of the results must be taken with caution (2).

In a case-control study, GABEREL et al. wanted to test the hypothesis that BioGlue® is a risk factor for the occurrence of surgical site infections (SSI). Therefore, relevant data such as the title of the intervention on the surgery board, microbiology laboratory data, and the review of all medical reports, including postoperative reports, discharge reports, and consultation reports were retrospectively reviewed. The retrospective analysis focused on patients who underwent craniotomy in the period between January 2006 and June 2007 and required a second operation to wash out the wound, who had an intraoperative culture grown, and who had an infection noted in the discharge report. The control group included patients who underwent craniotomy in the same period. According to the study design, two controls per case were randomly included. (3)
The use of BioGlue® and Neuro-Patch® were at the surgeon's discretion so that in cases of very small dura defects, BioGlue® was applied directly on a patch of Surgicel®. In larger defects, duraplasty was conducted, fixed with suture and optionally sealed with BioGlue® to enhance water tightness. Mostly, autografts were used for duraplasty, but if not available in sufficient quantity and shape, Neuro-Patch® was used. In total, 661 patients underwent craniotomy within the investigational period and 30 cases of SSI were identified. As mentioned above, 60 random patients who underwent the same surgical procedure were included as a control group. BioGlue® was used in 13 patients of the case group and in four patients of the control group (43.3% and 6.7%). Combined use of BioGlue® and Neuro-Patch® was found in 12 patients in the case group and in two patients in the control group. Regarding the length of surgery, a significant difference between the case group (mean: 311 min) and the control group (mean: 186 min) has been identified. In addition, in the case group proportionally more infratentorial surgeries than in the control group were performed (33.3% and 8.3%). In a univariate analysis four risk factors for SSI were identified (the use of BioGlue®, length of surgery, surgeon C and infratentorial surgery). In this analysis, the application of Neuro-Patch® didn't increase the risk for surgical site infections. Additionally, a multivariate analysis has shown that also younger age is a statistically significant risk factor for SSI, whereas infratentorial surgery and surgeon C were not shown to be independent risk factors (3). Comparing their results with literature data, the authors suggest that BioGlue® triggers a robust inflammatory response that may interfere with wound healing and therefore leads to reoperation. Regarding the combined use of BioGlue® and Neuro-Patch® significant differences between case and control group have been identified in both, univariate and multivariate analysis. The use of Neuro-Patch® alone was not found to be associated with surgical site infections. GABEREL et al. confirmed that Neuro-Patch® is safe when using alone, but is associated with a trigger factor for infection because it promotes bacterial growth as with other foreign materials implanted in the body (3).

A retrospective study by HUANG et al. could confirm the statement of GABEREL et al. that the use of Neuro-Patch® didn't increase the risk of surgical site infections. The authors reviewed the clinical database of their hospital for patients who underwent decompressive craniectomy for traumatic brain injury and subsequent cranial reconstruction in the period from January 2005 to December 2008. In total 132 patients underwent 135 decompressive craniectomies and cranioplasties (mean follow-up period: 33.2 months). The aim of the retrospective analysis was to evaluate the safety of dura substitutes focusing on Neuro-Patch®. Therefore, patients were subdivided in groups who receive Neuro-Patch® (n=50) and who did not (n=85). In patients who didn't receive Neuro-Patch®, hemostatic materials, including gelatin sponges or oxidized celluloses, were laid on the dura, without using any dural substitutes (4).
Analysis of morbidity after decompressive craniectomy have shown no significant difference regarding the occurrence of SSI between the groups. In total, 5 neurosurgical site infections have been observed of which two occurred in the Neuro-Patch®-group and three in the non-Neuro-Patch® group (1 scalp infection, 3 meningitis/ventriculitis, and brain abscess/empyema). In both groups, no CSF leakage has been observed. However, extra-axial hematoma occurred significantly more frequently in the Neuro-Patch® group than in the non-Neuro-Patch® group (18.0% vs. 3.53%). Morbidity rates after subsequent cranioplasty have shown no significant differences between the groups regarding the occurrence of SSI (Neuro-Patch® group: 8.0% vs. 7.06% in the non-Neuro-Patch® group), extra-axial hematoma (2.0% vs. 1.18%), subdural hygroma (2.0% vs. 1.18%) or CSF leakage (12.0% vs. 4.71%) (4).
Postoperatively, no significant differences were found between the two groups with regard to the occurrence of CSF leaks, infections and hygroma. However, extra-axial hematomas occurred significantly more frequently in the Neuro-Patch® treated patient group. The authors suspect the cause to be the interaction of the inert properties of the patch material in combination with a lack of sealing of the interface of dura replacement and natural tissue with fibrin glue by the user, which may create potential free spaces for fluid collection. On the other hand, multifocal bleeding caused by brain contusions, skull fractures or injuries to the temporalis, as well as the use of blood preservatives, makes hemostasis more difficult. The authors see possibilities to minimize hematomas by using optimized surgical techniques that minimize blood loss and reduce the occurrence of bleeding. Furthermore, the authors generally recommend the use of closed drainage systems to prevent the formation of hematomas in the open spaces. Based on the available data, the authors cannot detect any increase in the rate of infection and the occurrence of hydrodynamic complications (e.g. CSF leaks) in the context of the application of Neuro-Patch® during decompressive craniectomies so that Neuro-Patch® can be considered a reliable dura replacement material (4).

According to the treatment of trigeminal neuralgia, hemifacial spasm and other cranial nerve rhizopathies, microvascular decompression has become an accepted surgical treatment option. In an analysis by LI et al., experiences with the clinical application of Neuro-Patch® for the avoidance of CSF leaks in patients who underwent MVD surgery have been reported. Furthermore, analysis should compare the occurrence of CSF leaks and deep wound infections in patient groups who received Neuro-Patch® and who did not. In total, 217 patients were divided in a Neuro-Patch® group (n=103) and non-Neuro-Patch® group (n=114). All patients were followed up over a period of at least 6 months postoperatively. In the group who did not receive Neuro-Patch®, a watertight dural closure was achieved by interrupted sutures in which fascia or muscle grafts from the inferior portion of the incision were used. Then, the bone edges of the mastoid air

cells were thoroughly waxed for a second time (the first waxing was performed in the bone removal procedure). Fibrin glue was applied as an adjunctive sealant for dural and bone defects. After suturing the dura and waxing the mastoid air cells in the Neuro-Patch® group, a small piece of Neuro-Patch® was trimmed according to the durotomy shape and placed over the dura mater. Neuro-Patch® was pressed to the dura mater and fixed with fibrin glue. Finally, fibrin glue was applied to seal the bone defects and well-approximated layers were sutured (5).
Intraoperatively, the handling of Neuro-Patch® was evaluated as satisfactory. The patch could be easily trimmed and thorough adhesion of the dura mater and the Neuro-Patch® could be easily achieved with fibrin glue and gentle pressing. No postoperative CSF leakage occurred in the Neuro-Patch® group whereas in six cases of the non-Neuro-Patch® group CSF leakage was observed. Wound infection was observed in two cases of the Neuro-Patch® group and three cases of the group without Neuro-Patch® (1.9% vs. 2.6%). All the patient achieved good wound healing after proper management. However, regarding wound infection rate and CSF leakage rate between the groups, no statistical differences were found (5).

In a retrospective analysis, MALLITI et al. investigated deep wound infection rates of Neuro-Patch® and autologous material for dural closure in their clinical department. In total, 124 patients underwent duraplasty (Neuro-Patch®: n=61; Pericranium group: n=63) within the investigational period (January 2000 to December 2000) and were followed up for 12 months. The choice for synthetic dura substitute or autologous material depended on the surgeon's preference as well as the individual patient situation. As a result, the occurrence of deep wound infection differed significantly in both groups and were more frequent in patients who received Neuro-Patch® than in the autologous pericranium graft group (15% vs. 5%). Types of infection in the Neuro-Patch® group were meningitis (n=6), osteitis (n=1), and empyema (n=2), whereas in the pericranium group meningitis (n=1) and empyema (n=2) were observed. CSF leaks were more frequent in the Neuro-Patch® group compared to the Pericranium group (13.1% vs. 1.6%). Of the eight patients with CSF leakage in the Neuro-Patch® group, four patients with deep wound infection were observed. *Staphylococcus aureus* was the main organism responsible for deep wound infections, with a large proportion being methicillin resistant. Other organisms responsible for the infections were Gram-negative bacilli or *Propionibacterium acnes*. With regard to the results, MALLITI et al. conclude, that the use of Neuro-Patch® increases the risk of wound infection (6).
With respect to the results, HUANG et al. stated that there are several factors that may lead to surgical site infections. Especially, in traumatic brain injury (TBI) the operative field is often contaminated because of lacerating or penetrating injuries of the scalp, soft tissues, or bones. Fractures crossing paranasal sinuses or mastoid air cells also result in contamination. In addition, the typical mark incision with a long scalp pedicle predisposes to wound breakdown. Taken into account these parameters as well as their study results, HUANG et al. don't believe that nonabsorbable foreign material used in decompressive craniectomy affect the infection rate (4).
Additionally, LI et al. have concerns regarding the results by MALLITI et al. because the investigators did not demonstrate satisfactory similarity in all known determinants of outcome or adjust differences in the analysis (5). However, as a consequence of the results, MALLITI et al. tried to reduce the use of Neuro-Patch® in their clinical department to a minimum and to prefer the application of autologous dural grafts

whenever possible, knowing that their results have to be confirmed by an extensive prospective multicenter randomized trial (6).

Spinal cord herniation (SCH) is a rare condition that can occur spontaneously or after spinal surgery requiring a durotomy. In a case report, ELWAHAB and O'SULLIVAN report their results of treatment of SCH. The authors describe a case in which a patient complained of a painful cervical lymphadenopathy. A right-sided dumbbell neurofibroma at C2/C3 level could be identified by MRI examination. As a treatment of choice, a C2/C3 right hemilaminectomy and partial facetectomy was performed to expose the lesion. The tumor was found indenting the dura and pushing the thecal sac medially. The canalicular component was completely resected, but a small residuum was left laterally to avoid an injury of the vertebral artery. The dura mater was closed by suturing without using a dural graft. The recovery was uneventful and follow-up by MRI over four years revealed stable tumor remnant. Five years later, the patient presented again, complaining of neck pain and progressive weakness of the right upper limb, with loss of fine hand movements, numbness and tingling sensation in the right forearm, middle and ring fingers. MRI identified a pseudomeningocele with SCH through the operative defect at the level of C2 vertebra causing a compression of the cord by the bone edges. During surgical intervention, the defect was enlarged, and the arachnoid adhesions were divided. The cord was reduced back into the dural sac and the dural defect was closed with Neuro-Patch®. The patient had an uneventful recovery and reported an immediate improvement in the fine motor movements of his right hand and complete resolution of his neck pain.
In the following, several individual case reports are presented in which patients received Neuro-Patch®. Due to the small number of cases, the clinical evidence is low. However, for the purpose of completeness, these case studies are presented (7).

LEE et al. presented a case of a 41-year-old male patient who was admitted with severe acute headache, neck stiffness, and pronounced low-back pain radiating to both legs. The T2-weighted MR imaging showed irregular signal void and enlarged, varix like pouch formation with spinal cord compression at the T11-12 level. The angiogram revealed a dural arteriovenous fistula with subarachnoid hemorrhage. After laminectomy and vertical midline durotomy, the surgeon exposed variably sized dilated tortous and serpentine perimedullary veins with the hematoma compressing the spinal cord. An enlarged fistula was located at the ventral side of the T12 root. Temporary ligations were placed at the proximal end, interrupting the venous drainage of the fistula and causing the vein to turn blue. Then, the lesion was coagulated and ligated, the dura mater and surgical wounds were closed. Postoperatively, neurological examination revealed paraparesis (grade III-IV) after 4 hours following the ligation. Under the impression of epidural hematoma, an emergent decompressive surgery was performed. However, as there was no evidence of hematoma in the epidural space, the durotomy site was opened for exploration. Severe cord swelling was seen. Thus, an extended decompressive laminectomy with duroplasty using Neuro-Patch® was carried out, and a lumbar CSF drain was placed. The patient exhibited a complete paraplegia after the second operation. Spinal MR-imaging was obtained postoperatively, which confirmed spinal cord infarction from C5-6 to the conus medullaris. During the first 3 months postoperatively, neurological deficits improved gradually and reached a plateau in recovery. At the 1-year clinical follow-up examination, right leg weakness (grade IV) and disturbance of bowel and bladder function were still present. Repeated MR imaging 8 months later showed decreased size and intensities of spinal cord infarction, but hyperintensities were

still visible. However, the case-report did not show any incidence for complications related to the Neuro-Patch® (8).

Another case-report by MADURI et al. describes the treatment of a rare association of midbrain cavernoma and Benedikt's syndrome in a 49-year-old female patient who had a 3-year history of generalized seizures presented with recent onset of diplopia, difficulty swallowing and language problems associated with progressive right-sided weakness and a coarse right upper limb tremor. Neurological examination confirmed a complete left third cranial nerve deficit, oropharyngeal dysphagia, severe mixed aphasia, right-sided hemiparesis with no movement against resistance, right-sided hyperreflexia and dysmetria, and a right arm tremor present at rest, at posture and with intention. Additionally, MR imaging revealed a cavernous malformation located in the left midbrain tegmentum. T1 and T2 hyperintensity indicated subacute intralesional hemorrhage surrounded by hemosiderin deposition that extended to the ipsilateral cerebral peduncle. Furthermore, a left temporal convexity meningioma associated with enlargement of the sylvian fissure cistern due to local blockage of CSF circulation and a prerolandic left parasagittal meningioma were also present. The patient underwent a single-stage resection of the left temporal meningioma and mesencephalic cavernoma through a lefttemporal craniotomy and subtemporal approach. After evacuation of the associated hematoma, the cavernous malformation could be exposed and dissected from adjacent tissue with no additional retraction. Complete resection of the cavernoma was performed. Finally, the dura mater was reconstructed with a Neuro-Patch, fixed with sutures and sealed by Tissucol®. Postoperatively, upper limb tremor resolved immediately, and ptosis improved. At the 7-year-follow-up, the patient showed recovery from aphasia and dysphagia and regression of oculomotor palsy. No complications regarding the application of Neuro-Patch® were reported (9).

In a case series by WHITE and TSEGAYE, the treatment of idiopathic anterior spinal cord herniation in three cases was presented. Thereby, the focus of the investigations lies in the clinical outcome of the different surgical interventions so that the application of Neuro-Patch® is only mentioned. Nevertheless, the authors reported an improvement of the preoperative observed complaints such as leg stiffness, dyaesthetic discomfort, loss of temperature in the leg, worsening gait, hyperaesthesia as well as bilateral leg spasms sensation over the follow-up period (9 to 12 months). The use of Neuro-Patch® did not result in any complications. Therefore, it can be assumed that dural closure in spinal areas can be done with satisfying results (10).

A complication regarding the use of Neuro-Patch® was reported in a case-report by ASHA et al. A 55-year-old patient presented with a 5-month history of right sciatic pain and paraesthesia, caused by type-1-neurofibromatosis. He was also known to have three intradural thoraco-lumbar schwannomas, at T10, L3 and L5 Therefore, the patient underwent an L3 to L5 laminectomy, durotomy and excision of two schwannomas, whereas the durotomy incision was closed with Neuro-Patch® and DuraSeal®. In an early postoperative stage, the patient had an excellent recovery with no residual sciatic pain. Ten days post-operatively, he was re-admitted with clinical signs of an impending Cauda equina syndrome (11).
MRI scans revealed a large pseudomeningocele compressing the Cauda equina fibres. In a second surgery, a persistent small 2 mm gap in the suture line was seen at the apex of the durotomy. The gap has appar-

ently left the superior edge of the Neuro-Patch® unsecured. The defect was repaired and once again covered with DuraSeal. On follow up, 4 months postoperatively, he had full neurological recovery. The authors conclude that an insufficient fixation of the Neuro-Patch® led to a one-way flow of the CSF which results in the compression of the Cauda equina fibres. Obviously, this complication was caused by a handling mistake. Therefore, it is important to point out that the clinical performance of Neuro-Patch® can be regarded as reliable. Suitable proof of a watertight closure of the dural incision by the surgeon is required. Nevertheless, the authors stated that primary closure of the dural incision is probably the treatment of choice (11).

XIONG et al. describe the treatment of wound infection after MVD for hemifacial spasm caused by the application of Neuro-Patch® for dural repair. Six days postoperatively, the incision wound was found to be infected, and abscesses were present deep in the incision. Fortunately, due to the tight closure of the Neuro-Patch®, the infection was not able to spread inside the skull. After 3 months of meticulous wound cleaning and drug treatment to promote the growth of granulation tissue, healing of the infection without removal of Neuro-Patch® was achieved (12).

A case report described by SUNG et al. describes the successful reconstruction in a patient who had intractable postsurgical wound infection with staged operation using vascularized rectus muscle and fascial flap in a patient with meningioma reconstructed with Neuro-Patch®. A 33-year-old woman had a meningioma in the right frontal convexity. After tumor resection, the dura mater was repaired with Neuro-Patch®. One month postoperatively, she experienced headache, fever, and dysarthria. Fluid collection and local heat were observed on the operation scar. At this time, a postoperative wound infection was diagnosed. Daily aspiration and antibiotic therapy for 10 days were not successful. Bacteriologic culture identified a heavy colonization of methicillin resistant *Staphylococcus aureus*. As a consequence of dehiscence of the dura and cerebrospinal fluid leakage, debridement and dura repair were performed as well as a drain inserted, but the infection could not be controlled during the following 1-week period. Finally, a two staged surgical procedure was planned because the infection was resistant to routine antibiotic medication. In the first step, vascularized rectus fascia and muscle were transferred to the contaminated and reconstructed dura after craniectomy. The removed calvarial bone was banked to the abdominal donor-site pocket after cleansing. In the second stage, cranioplasty was performed with the banked autologous calvarial bone. The banked calvarial bone was stored without contamination or mechanical destruction in her abdominal pocket, and it was fixated to the temporal bony defect site (13).

GALLO et al. retrospectively compared clinical and radiological outcomes of different operative techniques of cranio-cervical decompression (CCD) performed in adults with symptomatic Chiari malformation type I within a single neurosurgical center. The patients were divided in three cohorts according to the operative technique used: an extradural osteoligamentous decompression, decompression followed by dural opening either without duraplasty or with duroplasty. Together 67 patients underwent 69 CCDs of which ten surgeries were osteoligamentous decompressions only, 29 surgeries with an additional dural opening without duraplasty, and 30 with an additional dural opening with duraplasty. For duraplasty either one of the following three synthetic suturable durasubstitutes was used: DURA-GUARD Synovis Life Technologies Inc; Durepair™ Dura Regeneration Matrix, Medtronic; Neuro-Patch® B-Braun; or a pericranial autograft harvested from the superior portion of the incision was used. Patients who underwent osteoligamentous

decompression with dural opening and duraplasty had a significantly shorter median hospital stay, significantly fewer unplanned readmissions, significantly higher median values on the Chicago Chiari Outcome Scale and a lower a significantly lower post-operative complication rate compared to patients who underwent osteoligamentous decompression with dural opening but without duraplasty. Osteoligamentous decompression without dural opening revealed a 40 % failure rate and was ineffective in cases with syringomyelia. Patients without duraplasty after dural opening experienced the following postoperative complications: CSF leakage (34.5 %), intracranial infections (17.2 %), hydrocephalus (17.2 %), subdural fluid collections (13.8 %), and wound infections (10.3 %). Patients with duraplasty after dural opening experienced significantly fewer postoperative complications: CSF leakage (6.7 %), intracranial infections (3.3 %), hydrocephalus (3.3 %), subdural fluid collections (0 %), and wound infections (3.3 %). Yet, it is not described or discussed which kind of dural substitute was used in each specific case. The authors conclude that the benefits of performing a watertight, augmentative duraplasty include a better clinical outcome, lower complication rates, and a shorter hospital stay. An osteoligamentous decompression without dural opening alone appeared to be an insufficient and ineffective technique to be offered to
adults with Chiari 1 malformations. The publication shows the use of Neuro-Patch in clinical routine with a successful performance even though, it remains unclear how often Neuro-Patch was actually used within the group of surgeries with duraplasty (14).

BUJOREANU et al. presented a rare case of cerebrospinal fluid (CSF) rhinorrhoea secondary to a left transverse sinus thrombus which occurred during chemotherapy for breast cancer in a patient with persistent raised intracranial pressure. The 55-year-old woman underwent a three-layer repair using Neuro-Patch, septal cartilage and middle turbinate pedicle flap. There were no intraoperative or postoperative complications. An episode of transient rhinorrhoea occurred three months postoperatively for seven days following a long-haul flight, which settled following a temporary increased dose of acetazolamide. There has been no further recurrence of CSF leak at twelve months. The publication does not provide a data of high clinical power concerning the safety or performance of Neuro-Patch. Yet, this case report of the successful use of Neuro-Patch was included for clinical evaluation to provide circumferential information from clinical literature (15).

5.4 An overall summary of the clinical performance and safety

Safety and performance indicators which require support from relevant clinical data were defined and described. All indicators depend on factors that can be controlled by the manufacturer (e.g. material and manufacturing) as well as on situation-specific factors (e.g. surgical application, patient-specific factors), as well as on the surgical use and handling.

According to the current knowledge based on the state of the art as well as the product-specific datasets provided by tests, clinical data and scientific literature, the benefits overweigh the risks of the application of Neuro-Patch®. The analysis and assessment of potential risks has shown that there are no increased residual risks for patients, users or third parties in the context of the intended use of Neuro-Patch® which can be confirmed by the product-related clinical data. Risk reduction measures also were adequate.

The indications, contraindications and intended use defined for the Neuro-Patch® are clearly defined and cover an area that enables the user to achieve the expected goals, namely the safe and reliable covering of defects of the dura mater in cranial and spinal neurosurgical procedures.
The information materials provided by the manufacturer contain all relevant information to enable the user to a safe and reliable application of the Neuro-Patch® within its intended use. With regard to the suitability of the intended population for the application of the device, this can be confirmed by the presented clinical data. Furthermore, suitable evidence for the performance claims is available. The information presented in the IFU as well as in the various promotion materials are consistent and correct.
In addition, PMS-/PMCF-measures will be implemented (MiDura-Study), so that a continuously and close monitoring for the application of Neuro-Patch® can be guaranteed.
In conclusion, the presented and evaluated data in this report confirms the safety and clinical performance of Neuro-Patch®. Therefore, from a clinical point of view, the risk-to-benefit ratio is still regarded as positive.

5.5 Ongoing or planned post-market clinical follow-up

MiDURA-Study

In addition to the above-mentioned clinical data to prove the safety and performance of Neuro-Patch®, a post-market clinical follow-up study (PMCF study) has been planned and initiated in 2019 as part of the continuous monitoring over the entire product life cycle. The aim of this “Multicentric, international, prospective, observational, study using Neuro-Patch® in duraplasty in neurosurgery” (MiDura-Study) is to collect systematically and proactively data regarding the performance of Neuro-Patch®, like complications and handling, under daily clinical practice when used as intended by the manufacturer.
Currently, two study centers in Germany and one center in France signed the study contract, the Ethics Committee approvals were received and both sites in Germany were initiated. The first Patient was recruited in February 2020 (delayed to due change in the clinic personnel). Since then, in total 88 patients were included in the study. The interim clinical investigation report is currently in work.

5.5.1 Clinical Literature Review

Proactive continuous monitoring of scientific literature concerning the product and equivalent or similar products in order to identify scientific literature with regard to the specific product and the state-of-the-art of application of the device. Additionally, the monitoring of scientific literature allows the identification and evaluation of safety and performance issues (e.g. possible off-label-use).

5.5.2 Monitoring of Product databases

Proactive continuous monitoring of databases concerning the product and equivalent or similar products in Manufacturer and User Facility Device Experience (MAUDE). A search for MAUDE database will be performed annually with the product name of the competitor device mentioned in the PMS-/PMCF-Plan. This PMCF-measure will provide data on safety aspects which also may be relevant for the application of Neuro-Patch®.

6 Possible diagnostic or therapeutic alternatives

In order to ensure a safe closure of the dura mater, the user can choose from various methods and materials. Primary closure of the dura mater as preferred treatment method is still valid. If this is not possible, dura mater defects can be treated satisfactorily with the help of replacement materials. The use of autologous tissues (e. g. fascia lata, temporal fascia) is primarily used here as they cause only minor foreign body reactions. The disadvantages of these are the limited availability with regard to the treatment of larger dura defects and the additional incision for harvesting the graft, which represents an additional risk of infection. Materials of animal origin are characterized by a low foreign body reaction. Furthermore, they are absorbed by the body over time and support cell proliferation and tissue regeneration. However, there is a risk of transmission of zoonoses (e. g. bovine spongiform encephalopathy) when using these materials. The use of absorbable or nonabsorbable synthetic materials for dura replacement can reduce these risks, but complications due to adhesions, infections or CSF leakage due to needle penetration during fixation of the implant may also occur. Furthermore, synthetic materials offer an inert alternative that can be manufactured indefinitely with good handling qualities like strength, elasticity, malleability, and resistance to traction.

7 Suggested profile and training for users

The user should be a neurosurgeon. No additional training is required.

8 Reference to any harmonised standards and CS applied

Applicable harmonised technical standards as well as product specific standards related to Neuro-Patch® are listed below. Common specifications are currently not available. Additionally, all technical standards are listed in a separate document within the technical documentation (see CER, chapter 10.1 Reference 1 *Normen Liste Neuro-Patch*).

Norm / Standard	Datum / Date	Normentitel / Standard Title
DIN EN 1041	2013	Information supplied by the manufacturer of medical devices
DIN EN 556-1	2002	Sterilization of medical devices - Requirements for medical devices to be designated STERILE - Part 1: Requirements for terminally sterilized medical devices
DIN EN 556-1 COR 1	2006	Sterilization of medical devices - Requirements for medical devices to be designated STERILE - Part 1: Requirements for terminally sterilized medical devices -
DIN ISO 2859-1	2014	Sampling procedures for inspection by attributes - Part 1: Sampling schemes indexed by acceptance quality limit (AQL) for lot-by-lot inspection
DIN EN ISO 10993-1	2021	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management system
DIN EN ISO 10993-3	2015	Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
DIN EN ISO 10993-4	2017	Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood

DIN EN ISO 10993-5	2009	Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity
DIN EN ISO 10993-6	2017	Biological evaluation of medical devices - Part 6: Tests for local effects after implantation
DIN EN ISO 10993-7	2009	Biological evaluation of medical devices - Part 7: Ethylene oxide sterilization residuals
ISO 10993-7 AMD 1	2019	Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals - AMENDMENT 1: Applicability of allowable limits for neonates and infants
ISO 10993-9	2019	Biological evaluation of medical devices - Part 9: Framework for identification and quantification of potential degradation products
DIN EN ISO 10993-10	2014	Biological evaluation of medical devices - Part 10: Tests for irritation and delayed-type hypersensitivity
DIN EN ISO 10993-11	2018	Biological evaluation of medical devices - Part 11: Tests for systemic toxicity
DIN EN ISO 10993-12	2021	Biological evaluation of medical devices - Part 12: Sample preparation and reference materials
DIN EN ISO 10993-16	2018	Biological evaluation of medical devices - part 16: Toxicokinetic study design for degradation products and leachables
DIN EN ISO 10993-18	2021	Biological Evaluation Of Medical Devices - Part 18: Chemical Characterization Of Medical Device Materials Within A Risk Management Process
ISO/TS 10993-20:2006	2006	Biological evaluation of medical devices - Part 20: Principles and methods for immunotoxicology testing of medical devices
DIN EN ISO 11135	2020	Sterilization of health-care products - Ethylene oxide - Requirements for the development, validation and routine control of a sterilization process for medical devices
DIN EN ISO 11138-2	2019	Sterilization of health care products – Biological indicators – Part 2: Biological indicators for ethylene oxide sterilization processes
DIN EN ISO 11607-1	2020	Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems
DIN EN ISO 11607-2	2020	Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes
ISO 11737-1	2018	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products
ISO 11737-1 AMD	2021	Sterilization of health care products - Microbiological methods - Part 1: Determination of a population of microorganisms on products; Amendment 1
DIN EN ISO 11737-2	2010	Sterilization of medical devices - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process
DIN EN ISO 11737-2	2020	Sterilization of medical devices - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process (ISO/DIS 11737-2:2018); German and English version prEN ISO 11737-2:2018
DIN EN ISO 13485	2016	Medical devices - Quality management systems - Requirements for regulatory purposes (ISO 13485:2016); German version EN ISO 13485:2016
DIN EN ISO 13485 AMD 1 DRAFT	2019	Medical devices - Quality management systems - Requirements for regulatory purposes
DIN EN ISO 14630	2013	Non-active surgical implants - General requirements
DIN EN ISO 14971	2020	Medical devices - Application of risk management to medical devices
ISO 15223-1	2021	Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1: General requirements

DIN EN 62366-1, VDE 0750-241-1	2021	Medizinprodukte - Teil 1: Anwendung der Gebrauchstauglichkeit auf Medizinprodukte - Medical devices - Part 1: Application of usability engineering to medical devices
MIL-STD-810	2014	Environmental Engineering Considerations and Laboratory Tests
MEDDEV 2.71 rev. 4	2016	CLINICAL EVALUATION: A GUIDE FOR MANUFACTURERS AND NOTIFIED BODIES UNDER DIRECTIVES 93/42/EEC and 90/385/EEC
MDCG 2019-9	2019	Summary of safety and clinical performance
MDCG 2020-5	2020	Clinical Evaluation - Equivalence. A guide for manufacturers and notified bodies
MDCG 2020-6	2020	Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC.
MDCG 2020-7	2020	Post-market clinical follow-up (PMCF) Plan Template.
MDCG 2020-8	2020	Post-market clinical follow-up (PMCF) Evaluation Report Template.

Part 2: Intended for patients

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below is intended for patients or lay persons. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.
The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an Implant card or the Instructions for Use to provide information on the safe use of the device.

List of abbreviation / glossary

Basic UDI-DI	Unique device identification device identifier (An identification number that is not for a specific product but for a group of products with similar intended use)
CAPA	Corrective and preventive action (consists of improvements to the manufacturers processes taken to eliminate causes of non-conformities or other undesirable situations)
CSF	Cerebrospinal fluid (clear, colorless body fluid found in the brain and spinal cord)
FSCA	Field safety corrective action (FSCA is an action taken by a manufacturer to report any technical or medical reason leading to a systematic recall of devices of the same type by the manufacturer to the National Competent Authority.
FSN	Field safety notice (Communication to customers and/or users sent out by a manufacturer or its representative in relation to a Field Safety Corrective Action)
PUR947	Polyester urethane (synthetic material)

1 Device identification and general information

1.1 Device trade name

Neuro-Patch®

Table 2: Neuro-Patch - Article list

Reference Number	Description	Content
1064002	Neuro-Patch® 12 cm x 14 cm	1 piece
1064010	Neuro-Patch® 6 cm x 14 cm	1 piece
1064020	Neuro-Patch® 8 cm x 9 cm	1 piece
1064029	Neuro-Patch® 6 cm x 8 cm	1 piece
1064037	Neuro-Patch® 4 cm x 10 cm	1 piece
1064040	Neuro-Patch® 5 cm x 6 cm	1 piece
1064110	Neuro-Patch® 4 cm x 5 cm	1 piece
1064122	Neuro-Patch® 2 cm x 10 cm	1 piece
1064123	Neuro-Patch® 1.5 cm x 3 cm	1 piece
1064045	Neuro-Patch® 4 cm x 5 cm	2 pieces
1064053	Neuro-Patch® 2 cm x 10 cm	2 pieces
1064061	Neuro-Patch® 1.5 cm x 3 cm	2 pieces

1.2 Manufacturer; name and address

Aesculap AG
Am Aesculap-Platz
78532 Tuttlingen/Germany

1.3 Basic UDI-DI

Basic UDI-DI for Neuro-Patch®: 40392390000014O1ZR

1.4 Year when the device was first CE-marked

Neuro-Patch® is CE marked[1] since 1996.

[1] **CE marking** is a certification mark that indicates conformity with health, safety, and environmental protection standards for products sold within the European Economic Area (EEA). The CE marking is also found on products sold outside the EEA that are manufactured in, or designed to be sold in the EEA.

2 Intended use of the device

2.1 Intended purpose

Neuro-Patch® is used in neurosurgery as dura mater[2] replacement (further information can be found in chapter *5.1 Clinical background of the device*).

2.2 Indication(s) and target population(s)

- For covering cerebral[3] and cerebellar[4] dura defects
- For cerebral decompression surgery[5] when there is elevated intracranial pressure
- For covering spinal dura defects
- For spinal decompression surgery[6]

There is no restriction regarding the intended patient population additional to the indications/contraindications.

2.3 Contraindications and/or limitations

Do not use:

- In infected regions
- In open cerebrocranial traumata[7]
- In open spina bifida[8]
- In case of known hypersensitivity[9] against implant materials; for fixation materials please note the corresponding instructions for use
- In any application area that is not mentioned in "Indications"

3 Device description

3.1 Device description and material/substances in contact with patient tissues

Neuro-Patch® is a synthetic, suturable substitute for the replacement of the brain skin, also called dura or dura mater, of fine fibred microporous fleece manufactured from a highly purified polyester urethane (Figure 1).

---

[2] **Dura mater**: A membrane forming the outermost of the three coverings of the brain and spinal cord external to the arachnoid and pia mater.
[3] **Cerebral**: related to the brain
[4] **Cerebellar**: Relating to the part of the brain at the back of the skull, which coordinates and regulates muscular activity.
[5] **Cerebral decompression surgery** is a surgical procedure intended to relieve pressure on the skull
[6] **Spinal decompression surgery** is a surgical procedure intended to relieve pressure on the spinal cord or on one or more compressed nerve roots passing through or exiting the spinal column.
[7] **Cerebrocranial trauma**: Injury related to both, the head and the brain.
[8] **Spina bifida:** A congenital defect of the spine in which parts of the spinal cord and its meninges are exposed through a gap in the backbone.
[9] **Hypersensitivity**: Excessive response to the stimulus of a foreign agent, such as an allergen.

Effective

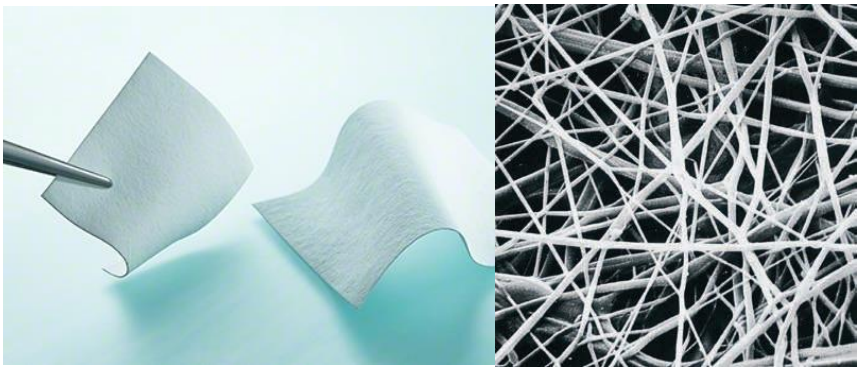

Figure 1: Product image of Neuro-Patch (left); microporous structure of Neuro-Patch (right).

Neuro-Patch® is composed of a polyester urethane (PUR947) which is non-absorbable[10]. Neuro-Patch® is not broken down by the body and remains permanently in the body.
The products belong to the group of neurosurgical implants.

- During the intended use, the following organs/tissue/body fluids come in contact with the devices: Bone tissue, dura mater, brain and spinal cord fluid (cerebrospinal fluid[11]; CSF) as well as blood.
- The application of the devices is invasive.
- The application period of the devices is long-term.
- The devices are intended for clinical users: Surgeons with required knowledge about the surgical technique and surgical training who is aware about the in vivo characteristics of the product, operating room personnel (set-up, handling, and functional check).
- Neuro-Patch® is a single use device and will be delivered sterile (sterilization method: ethylene oxide).
- Neuro-Patch® does not contain pharmaceutical components, animal or human tissue, is does not contain from blood-derived products and is not radioactive.
- No changes have been made to the product since the market launch of Neuro-Patch®.

3.2 Information about medicinal substances in the device, if any

Neuro-Patch® doesn't contain any medicinal substances.

3.3 Description of how the device is achieving its intended mode of action

- Surgeon chooses implant size suitable for the closure of the defect.
- Neuro-Patch® will be cut according to the application situation, in order to embed with as little stress as possible.
- Neuro-Patch® will be fixed by continuous stitching using a nonabsorbable suture material (polyester, polypropylene).

[10] **Non-absorbable**: Non-absorbable material remains stable and retains in the human body for unlimited time.
[11] **Cerebrospinal fluid**: A colorless liquid that is secreted from the blood into the lateral chambers (ventricles) of the brain and serves chiefly to maintain uniform pressure within the brain and spinal cord.

- The use of atraumatic round-bodied needles allows suturing without causing great damage to the implant.
- An additional seal with fibrin glue[12] can be used.

3.4 Description of accessories, if any

Not applicable.

4 Risks and warnings

Contact your healthcare professional if you believe that you are experiencing side effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.

4.1 How potential risks have been controlled or managed

Potential risks have been identified and controlled according to *DIN EN ISO 14971 Medical devices - Application of risk management to medical devices*.

4.2 Remaining risks and undesirable effects

The general risks associated with surgery are assumed known and are therefore not described.
Within the scope of the legal obligation to provide information, reference is made to the typical risks, interactions and side effects listed below.
Possible risks, side effects and interactions of the application currently known to the manufacturer are:

- CSF-Leakage[13]
- Infection[14]
- Adhesions[15]
- Foreign body reaction

Compared to the application of alternative dura substitutes, the occurrence rates of the abovementioned risks during the use of Neuro-Patch® can be regarded as acceptable.

Note:
The points mentioned above include potential clinical consequences.
No risks, side effects and interactions as a result of comorbidities of the patient have been identified.

4.3 Warnings and precautions

Clinical user
General safety information

[12] **Fibrin glue** is an adhesive for wound closure.
[13] **CSF-Leakage** is an involuntary discharge of cerebrospinal fluid.
[14] **Infection**: A disease caused by germs or bacteria.
[15] **Adhesion** is a union of two surfaces that are normally separate.

To prevent damage caused by improper setup or operation, and to not compromise the manufacturer warranty and liability:

- Use the product only according to these instructions for use.
- Always follow the safety advice and information given in the instructions for use.
- Ensure that the product and its accessories are operated and used only by persons with the requisite training, knowledge and experience.
- Store any new or unused products in a dry, clean, and safe place.
- Keep instructions for use accessible to the user.

Note
The user is obligated to report all severe events in connection with the product to the manufacturer and the responsible authorities of the state in which the user is located.

Notes on surgical procedures
It is the user's responsibility to ensure that the surgical procedure is performed correctly. Appropriate clinical training as well as a theoretical and practical proficiency of all the required operating techniques, including the use of this product, are prerequisites for the successful use of this product.
Aesculap is not responsible for complications caused by:

- incorrect indication or implant selection
- incorrect surgical technique
- incorrect combination of implant components
- combination with components of other manufacturers not approved by Aesculap
- exceeding the limitations of the treatment method or non-observance of essential medical precautions

The user is required to obtain information from the manufacturer if there is an unclear preoperative situation regarding the use of the product.
Note
The use of atraumatic round body needles permits suturing without major damage to the implant.
In addition, fibrin glue can be used to achieve a sealing effect.

Note
During the application of Neuro-Patch in combination with bone cement, chemical damage of the patch material, depending on the application situation, cannot be excluded.

Sterility and storage
The product is EO sterilized and wrapped in sterile packaging.

- Store implant components in their original packaging. Remove them from their original protective packaging only just prior to implantation.
- Do not use products from open or damaged sterile packaging.
- Do not use the product after its use-by date.
- Store the product at 25 ± 5°C.
- Do not reuse the product.

The reprocessing of the product affects its functionality. Risk of injury, illness or death due to soiling and/or impaired functionality of the product.

- Do not reprocess the product.

4.4 Summary of any field safety corrective action, (FSCA including FSN) if applicable

When necessary, field safety corrective actions or field safety notifications were issued regarding the products. For Neuro-Patch® neither Field Safety Notices (FNS), Field Safety Corrective Actions (FSCA) nor Corrective and Preventive Actions (CAPA) were required.

5 Summary of clinical evaluation and post-market clinical follow-up

5.1 Clinical background of the device

Neuro-Patch® is used in neurosurgery as dura mater replacement. The dura mater is the outermost of the three types of brain skin, also called meninges. Together with the arachnoidea and the pia mater it builds the enclosing of the brain and the spinal cord. The meninges encapsulate the central nervous system and prevent a loss of cerebrospinal fluid. CSF protects the nervous system from mechanical influences and plays a role in maintaining cerebral metabolic balance and is also necessary for temperature control. After cranial or spinal neurosurgery in which an opening of the brain skin was required, the dura mater opening is preferably closed by suturing. In some cases, like the removal of tumors (such as meningioma or glioma), craniectomy e. g. therapy of Chiari malformation, the dura mater may be surgically removed, may shrink or be harmed during the procedure. The dura loss requires a sufficient dura replacement by a graft to avoid CSF leakage associated complications, which can manifest as peridural collection of CSF, fistulae, meningitis, cerebritis or brain abscess.

5.2 The clinical evidence for the CE-marking

Clinical evidence for CE-marking is based on laboratory testing, scientific literature, market feedback and clinical data with the devices from clinical studies.

5.3 Safety

According to the analysis of the market feedback, the data generated in a clinical study with implants, the scientific literature and the analysis from the implant registries, no systematic failures or complications related to Neuro-Patch® were observed. Thus, the safety of the Neuro-Patch® is confirmed.

6 Possible diagnostic or therapeutic alternatives

When considering alternative treatments, it is recommended to contact your healthcare professional who can consider your individual situation.

6.1 General description of therapeutic alternatives

There are different types of dura substitutes available on the market. Main difference can be found in the various number of materials that are used. Next to patients own body grafts (also called autografts or

autologous materials[16]), different materials of animal (xenografts[17]) or synthetic origin[18] are available. Every material type exhibits advantages and disadvantages which limit its application.
Autografts e.g. pericranium or fascia lata are obtained from the same patient and used to close the dura defect during the surgery. The preparation of an autograft results in a prolonged surgery, often a second incision thus aggravating the surgical trauma and may increase the morbidity risk[19] for the patient. Additionally, the autograft is available on a limited base and some major dura defects cannot be closed with autogenic material. However, autografts show the advantage of a low immune response.
To avoid a longer surgery time and a second incision, allografts[20], xenografts and synthetic grafts have been introduced. Allografts and xenografts are absorbable, biocompatible[21] and less burdensome for the patient. However, the use of human dural tissue (allografts) is associated with the risk of Creutzfeldt-Jakob disease. Creutzfeldt-Jakob disease is a fatal brain disorder and the diagnosis is difficult. Measurements of the brain activity (electroencephalogram[22]) as well as imaging methods may indicate the disease but a distinct prove is only possible postmortem. Brain specimen contain spongy cavities, exhibit loss of neural cells and show plaques, which point towards Creutzfeldt-Jakob disease. In most cases, depending on the species, Creutzfeldt-Jakob disease breaks out in late age and is not immediately diagnosed after implantation. As an alternative, there are also non-nervous tissue allografts available e.g. acellular dermis.
A possible alternative to allografts are xenografts produced from animal origin, such as equine, porcine or bovine tissues. Xenografts are processed tissues such as freeze-dried pericardium, small intestinal submucosa or split-thickness skin. The original tissue of xenografts is processed to a purified and low allergenic collagen texture. The collagen is known for its chemotactic properties and attracts fibroblasts to adhere. The porous structure serves as scaffold for fibroblasts which will form the neodura. Collagen based products are available as bilayer, as well as monolayer, in suturable and in onlay versions. Synthetic grafts have been developed for dura substitution since they are considered reliable due to a reproducible manufacturing process. Moreover, they are ubiquitously available, but not absorbable and sometimes difficult to handle. However, these grafts are used as a dura substitute with a positive clinical outcome.

7 Suggested training for users

The user should be a neurosurgeon. No additional training is required.

[16] **Autograft or autologous material**: A tissue or organ that is transplanted from one part to another of the same body
[17] **Xenograft**: A graft of tissue taken from a donor of one species (e. g. cattle, horse) and grafted into a recipient of another species
[18] **Synthetic origin**: Material produced by chemical or biochemical processes.
[19] **Morbidity risk**: Likelihood of a complication or undesirable side effect following surgery or medical treatment.
[20] **Allograft**: A tissue graft from a donor of the same species as the recipient but not genetically identical.
[21] **Biocompatible**: Foreign material that is compatible with living tissue, as a prosthetic material or device that is not rejected or does not cause infection.
[22] **Electroencephalogram**: A test or record of brain activity.

Effective

8 Signatures

This document is signed electronically (see last page).

Revision history

No.	Type of Revision	Date	Revision validated by the Notified Body
01	Initial preparation of the SSCP	24.06.2020	Validation language: English
02	Update of the SSCP according to the Feedback of the Notified Body (MDR_IVDR Request for Additional Information and Deficiency Report Clinical No. 1; Order no: 713197662; Dated: 2020-12-28)	11.03.2021	Validation language: English
03	Update of the SSCP according to the Feedback of the Notified Body (MDR_IVDR Request for Additional Information and Deficiency Report Clinical No. 2; Order no: 713197662; Dated: 2021-03-19)	12.04.2021	Validation language: English
04	Missing document history of Rev. 3 included	21.05.2021	Validation language: English
05	Update according to the minor update 2021 of the CER: Part 1 – Chapter 5.3 Literature on the product: Addition of two newly identified product specific publications. Part 1 – Chapter 5.5 MiDURA-Study: Information updated to the current state of the study.	15.07.2021	Validation language: English
06	Update of the SSCP according to the Final Technical Report of the Notified Body (see Report number: 713197662). - Update of the SRN - Update of chapter *8 Reference to any harmonised standards and CS applied*	See "Effective Date" on approved document	Not yet validated by the NB

9 Literature Cited

1. Del Gaudio N, Vaz G, Duprez T, Raftopoulos C. Comparison of Dural Peeling versus Duraplasty for Surgical Treatment of Chiari Type I Malformation: Results and Complications in a Monocentric Patients' Cohort. World Neurosurg 2018; 117:e595-e602.

2. Chen PY, Chen SY, Chen TY, Chen HJ, Lu K, Liang CL, Liliang PC, Wang KW, Yang SN, Huang CY, Wang HK. Symptomatic hemorrhagic complications associated with dural substitutes. Formosan Journal of Surgery 2018; (51):15–20.

3. Gaberel T, Borgey F, Thibon P, Lesteven C, Lecoutour X, Emery E. Surgical site infection associated with the use of bovine serum albumine-glutaraldehyde surgical adhesive (BioGlue) in cranial surgery: a case-control study. Acta Neurochir (Wien) 2011; 153(1):156-62; discussion 162-3.

Effective

4. Huang YH, Lee TC, Chen WF, Wang YM. Safety of the Nonabsorbable Dural Substitute in Decompressive Craniectomy for Severe Traumatic Brain Injury. The Journal of Trauma Injury, Infection, and critical Care 2011; 71(3).

5. Li N, Zhao WG, Pu CH, Shen JK. Clinical application of artificial dura mater to avoid cerebrospinal fluid leaks after microvascular decompression surgery. Minim Invasive Neurosurg 2005; 48(6):369–72.

6. Malliti M, Prage P, Cury C, Chomette E, Nataf F, Roux FX. Comparison of Deep Wound Infection Rates Using A Synthetic Dural Substitute (Neuro-Patch) Or Pericranium Graft For Dural Closure: A Clinical Review Of 1 Year. Neurosurgery 2004; 54(3).

7. Abd Elwahab SM, O'Sullivan MJ. Spinal cord herniation after resection of cervical spinal neurofibroma with a unique presentation. Spine J 2015; 15(4):e1-3.

8. Lee S-H, Kim K-T, Kim S-M, Jo D-J. Extensive spinal cord infarction after surgical interruption of thoracolumbar dural arteriovenous fistula presenting with subarachnoid hemorrhage. J Korean Neurosurg Soc 2009; 46(1):60–4.

9. Maduri R, Barbagallo G, Iofrida G, Signorelli M, Signorelli F. Regression of Benedikt's syndrome after single-stage removal of mesencephalic cavernoma and temporal meningioma: a case report. Clin Neurol Neurosurg 2013; 115(6):748–50.

10. White BD, Tsegaye M. Idiopathic anterior spinal cord hernia: under-recognized cause of thoracic myelopathy. British Journal of Neurosurgery 2004; 18(3):246–9.

11. Asha MJ, George KJ, Choksey M. Pseudomeningocele presenting with cauda equina syndrome: is a 'ball-valve' theory the answer? British Journal of Neurosurgery 2011; 25(6):766–8.

12. Xiong N, Tan DA, Fu P, Huang Y, Tong S, Yu H. Healing of Deep Wound Infection without Removal of Non-Absorbable Dura Mater (Neuro-Patch): A Case Report. Journal of Long-Term Effects of Medical Implants 2011; 71(3):533–7.

13. Soon Sung K, Hak C. Staged reconstruction of infected dura mater using vascularized rectus abdominis muscle. J Craniofac Surg 2012; 23(6):1741–3.

14. Gallo P, Copley PC, McAllister S, Kaliaperumal C. The impact of neurosurgical technique on the short- and long-term outcomes of adult patients with Chiari I malformation. Clin Neurol Neurosurg 2021; 200:106380.

15. Bujoreanu I, Ferguson M, Saleh H. Chemotherapy associated dural sinus thrombosis presenting as a cerebrospinal fluid leak. BMJ Case Rep 2020; 13(6).

Title: Neuro-Patch_SSCP.docx Initiator: Alexander ? Krump

This document is signed electronically in compliance with the B. Braun electronic signature policies and procedures by following persons:

UserName: Krump, Alexander (krumalde)
Title: Senior Project Manager
Date: Tuesday, 28 September 2021, 09:29 W. Europe Daylight Time
Meaning: Document signed as Author
==========

UserName: Lange, Katharina (langktde)
Title: Head of Clinical Evaluation / Clinical Studies & Medical Affairs
Date: Tuesday, 28 September 2021, 15:43 W. Europe Daylight Time
Meaning: Approve Document
==========