BlueCross BlueShield of Arizona
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MEDICAL COVERAGE GUIDELINES
SECTION: SURGERY

ORIGINAL EFFECTIVE DATE: 04/15/14
LAST REVIEW DATE: 03/19/19
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

NANOKNIFE®

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Medical Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

Description:

The NanoKnife System or irreversible electroporation (IRE) is a minimally invasive technology that uses IRE, a non-thermal technology, to ablate soft tissue lesions through permeabilization of the cell membrane. Imaging techniques such as ultrasound or computed tomography (CT) are used to guide two or more NanoKnife IRE disposable electrodes in or around the targeted lesions. A series of short electric pulses are then sent from the electrodes directly into the lesions where cell death is caused. The FDA has approved the NanoKnife System with six outputs for the surgical ablation of soft tissue.

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Criteria:

- NanoKnife is considered ***experimental or investigational*** based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome, and
  3. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  4. Insufficient evidence to support improvement outside the investigational setting.

Resources:

Literature reviewed 07/31/18. We do not include marketing materials, poster boards and non-published literature in our review.

Resources published prior to 04/30/13 may be requested from the BCBSAZ Medical Policy and Technology Research Department.

1. CADTH Rapid Response Reports. *Irreversible Electroporation for Tumors of the Pancreas or Liver: A Review of Clinical and Cost-Effectiveness*. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health. Copyright (c) 2016 Canadian Agency for Drugs and Technologies in Health.; 2016.

2. Belfiore G, Belfiore MP, Reginelli A, et al. Concurrent chemotherapy alone versus irreversible electroporation followed by chemotherapy on survival in patients with locally advanced pancreatic cancer. *Med Oncol.* Mar 2017;34(3):38.

3. Belfiore MP, Ronza FM, Romano F, et al. Percutaneous CT-guided irreversible electroporation followed by chemotherapy as a novel neoadjuvant protocol in locally advanced pancreatic cancer: Our preliminary experience. *International journal of surgery (London, England).* Sep 2015;21 Suppl 1:S34-39.

4. Canvasser NE, Sorokin I, Lay AH, et al. Irreversible electroporation of small renal masses: suboptimal oncologic efficacy in an early series. *World journal of urology.* Mar 02 2017.

5. Cheng RG, Bhattacharya R, Yeh MM, Padia SA. Irreversible Electroporation Can Effectively Ablate Hepatocellular Carcinoma to Complete Pathologic Necrosis. *J Vasc Interv Radiol.* Aug 2015;26(8):1184-1188.

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Resources: (cont.)

6. Cheung W, Kavnoudias H, Roberts S, Szkandera B, Kemp W, Thomson KR. Irreversible Electroporation for Unresectable Hepatocellular Carcinoma: Initial Experience and Review of Safety and Outcomes. *Technol Cancer Res Treat.* Jan 25 2013.

7. Dollinger M, Beyer LP, Haimerl M, et al. Adverse effects of irreversible electroporation of malignant liver tumors under CT fluoroscopic guidance: a single-center experience. *Diagnostic and interventional radiology (Ankara, Turkey).* Nov-Dec 2015;21(6):471-475.

8. Fruhling P, Nilsson A, Duraj F, Haglund U, Noren A. Single-center nonrandomized clinical trial to assess the safety and efficacy of irreversible electroporation (IRE) ablation of liver tumors in humans: Short to mid-term results. *European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology.* Apr 2017;43(4):751-757.

9. Glybochko PV, Alyaev YG, Amosov AV, et al. [Irreversible electroporation to treat prostate cancer (Nanoknife)]. *Urologiia.* Dec 2016(6):153-157.

10. Kambakamba P, Bonvini JM, Glenck M, et al. Intraoperative adverse events during irreversible electroporation-a call for caution. *Am J Surg.* Oct 2016;212(4):715-721.

11. Kluger MD, Epelboym I, Schrope BA, et al. Single-Institution Experience with Irreversible Electroporation for T4 Pancreatic Cancer: First 50 Patients. *Ann Surg Oncol.* May 2016;23(5):1736-1743.

12. Kourounis G, Paul Tabet P, Moris D, et al. Irreversible electroporation (Nanoknife(R) treatment) in the field of hepatobiliary surgery: Current status and future perspectives. *J BUON.* Jan-Feb 2017;22(1):141-149.

13. Lambert L, Horejs J, Krska Z, et al. Treatment of locally advanced pancreatic cancer by percutaneous and intraoperative irreversible electroporation: general hospital cancer center experience. *Neoplasma.* 2016;63(2):269-273.

14. Mansson C, Brahmstaedt R, Nilsson A, Nygren P, Karlson BM. Percutaneous irreversible electroporation for treatment of locally advanced pancreatic cancer following chemotherapy or radiochemotherapy. *European journal of surgical oncology : the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology.* Feb 10 2016.

15. Martin RC, 2nd, Kwon D, Chalikonda S, et al. Treatment of 200 locally advanced (stage III) pancreatic adenocarcinoma patients with irreversible electroporation: safety and efficacy. *Annals of surgery.* Sep 2015;262(3):486-494; discussion 492-484.

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Resources: (cont.)

16. Narayanan G, Bhatia S, Echenique A, Suthar R, Barbery K, Yrizarry J. Vessel patency post irreversible electroporation. *Cardiovasc Intervent Radiol.* Dec 2014;37(6):1523-1529.

17. Niessen C, Beyer LP, Pregler B, et al. Percutaneous Ablation of Hepatic Tumors Using Irreversible Electroporation: A Prospective Safety and Midterm Efficacy Study in 34 Patients. *J Vasc Interv Radiol.* Apr 2016;27(4):480-486.

18. Niessen C, Thumann S, Beyer L, et al. Percutaneous Irreversible Electroporation: Long-term survival analysis of 71 patients with inoperable malignant hepatic tumors. *Sci Rep.* Mar 07 2017;7:43687.

19. Paiella S, Butturini G, Frigerio I, et al. Safety and Feasibility of Irreversible Electroporation (IRE) in Patients with Locally Advanced Pancreatic Cancer: Results of a Prospective Study. *Dig Surg.* Feb 28 2015;32(2):90-97.

20. Petrou A, Moris D, Paul Tabet P, David Wensley Richards B, Kourounis G. Ablation of the locally advanced pancreatic cancer: An introduction and brief summary of techniques. *J BUON.* May-Jun 2016;21(3):650-658.

21. Qin Q, Xiong ZA, Liu Y, et al. Effects of irreversible electroporation on cervical cancer cell lines in vitro. *Mol Med Rep.* Sep 2016;14(3):2187-2193.

22. Ricke J, Jurgens JH, Deschamps F, et al. Irreversible Electroporation (IRE) Fails to Demonstrate Efficacy in a Prospective Multicenter Phase II Trial on Lung Malignancies: The ALICE Trial. *Cardiovasc Intervent Radiol.* Jan 22 2015.

23. Savic LJ, Chapiro J, Hamm B, Gebauer B, Collettini F. Irreversible Electroporation in Interventional Oncology: Where We Stand and Where We Go. *RoFo : Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin.* Apr 13 2016.

24. Savic LJ, Chapiro J, Hamm B, Gebauer B, Collettini F. Irreversible Electroporation in Interventional Oncology: Where We Stand and Where We Go. *RoFo : Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin.* Aug 2016;188(8):735-745.

25. Scheltema MJ, van den Bos W, de Bruin DM, et al. Focal vs extended ablation in localized prostate cancer with irreversible electroporation; a multi-center randomized controlled trial. *BMC Cancer.* May 05 2016;16:299.

26. Scheltema MJ, van den Bos W, Wagstaff PG, et al. Irreversible electroporation, a new modality in Focal Therapy for prostate cancer. *Arch Esp Urol.* Jul 2016;69(6):337-344.

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Resources: (cont.)

27. Ting F, Tran M, Bohm M, et al. Focal irreversible electroporation for prostate cancer: functional outcomes and short-term oncological control. *Prostate cancer and prostatic diseases.* Mar 2016;19(1):46-52.

28. Trimmer CK, Khosla A, Morgan M, Stephenson SL, Ozayar A, Cadeddu JA. Minimally Invasive Percutaneous Treatment of Small Renal Tumors with Irreversible Electroporation: A Single-Center Experience. *J Vasc Interv Radiol.* Oct 2015;26(10):1465-1471.

29. UpToDate. Image-guided ablation of lung tumors. 09/10/2015.

30. UpToDate. Radiofrequency ablation and cryoablation for renal cell carcinoma. 07/01/2015.

31. UpToDate.com. Management of Stage I and Stage II Non-Small Cell Lung Cancer. 02/03/2017.

32. UpToDate.com. Image-Guided Ablation of Skeletal Metastases. 11/02/2015.

33. Valerio M, Dickinson L, Ali A, et al. Nanoknife Electroporation Ablation Trial: A Prospective Development Study Investigating Focal Irreversible Electroporation for Localized Prostate Cancer. *The Journal of urology.* Mar 2017;197(3 Pt 1):647-654.

34. Valerio M, Dickinson L, Ali A, et al. A prospective development study investigating focal irreversible electroporation in men with localised prostate cancer: Nanoknife Electroporation Ablation Trial (NEAT). *Contemp Clin Trials.* Sep 2014;39(1):57-65.

35. van den Bos W, de Bruin DM, Jurhill RR, et al. The correlation between the electrode configuration and histopathology of irreversible electroporation ablations in prostate cancer patients. *World journal of urology.* Aug 22 2015.

36. van den Bos W, Jurhill RR, de Bruin DM, et al. Histopathological outcomes after irreversible electroporation in prostate cancer; Results of an ablate-and-resect study. *The Journal of urology.* Mar 19 2016.

37. Wendler JJ, Ricke J, Pech M, et al. First Delayed Resection Findings After Irreversible Electroporation (IRE) of Human Localised Renal Cell Carcinoma (RCC) in the IRENE Pilot Phase 2a Trial. *Cardiovasc Intervent Radiol.* Feb 2016;39(2):239-250.

38. Wichtowski M, Nowaczyk P, Kocur J, Murawa D. Irreversible electroporation in the treatment of locally advanced pancreas and liver metastases of colorectal carcinoma. *Contemp Oncol (Pozn).* 2016;20(1):39-44.

39. Yan L, Chen YL, Su M, et al. A Single-institution Experience with Open Irreversible Electroporation for Locally Advanced Pancreatic Carcinoma. *Chin Med J (Engl).* Dec 20 2016;129(24):2920-2925.

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Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe'é atah nílínigíí Blue Cross Blue Shield of Arizona haada yit'éego bína'ídíłkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yína'ídíłkidgo beehaz'áanii hóló díí t'áá hazaadk'ehjí háká a'doowołgo bee haz'ą doo bąąh ílínígóó. Ata' halne'ígíí kojį' bich'į' hodíilnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:
إن كان لديك أو لدى شخص تساعده أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون اية تكلفة. للتحدث مع مترجم اتصل ب 877-475-4799.

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Multi-Language Interpreter Services: (cont.)

Tagalog: Kung ikaw, o ang iyong tinutulangan, ay may mga katanungan tungkol sa Blue Cross Blue Shield of Arizona, may karapatan ka na makakuha ng tulong at impormasyon sa iyong wika ng walang gastos. Upang makausap ang isang tagasalin, tumawag sa 877-475-4799.

Korean: 만약 귀하 또는 귀하가 돕고 있는 어떤 사람이 Blue Cross Blue Shield of Arizona 에 관해서 질문이 있다면 귀하는 그러한 도움과 정보를 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 그렇게 통역사와 얘기하기 위해서는 877-475-4799 로 전화하십시오.

French: Si vous, ou quelqu'un que vous êtes en train d'aider, a des questions à propos de Blue Cross Blue Shield of Arizona, vous avez le droit d'obtenir de l'aide et l'information dans votre langue à aucun coût. Pour parler à un interprète, appelez 877-475-4799.

German: Falls Sie oder jemand, dem Sie helfen, Fragen zum Blue Cross Blue Shield of Arizona haben, haben Sie das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Um mit einem Dolmetscher zu sprechen, rufen Sie bitte die Nummer 877-475-4799 an.

Russian: Если у вас или лица, которому вы помогаете, имеются вопросы по поводу Blue Cross Blue Shield of Arizona, то вы имеете право на бесплатное получение помощи и информации на вашем языке. Для разговора с переводчиком позвоните по телефону 877-475-4799.

Japanese: ご本人様、またはお客様の身の回りの方でも、Blue Cross Blue Shield of Arizona についてご質問がございましたら、ご希望の言語でサポートを受けたり、情報を入手したりすることができます。料金はかかりません。通訳とお話される場合、877-475-4799 までお電話ください。

Farsi:
اگر شما، یا کسی که شما به او کمک میکنید ، سوال در مورد Blue Cross Blue Shield of Arizona ، داشته باشید حق این را دارید که کمک و اطلاعات به زبان خود را به طور رایگان دریافت نمایید 877-475-4799
[تماس حاصل نمایید.

Assyrian:
[illegible] Blue Cross Blue Shield of Arizona [illegible]
[illegible] 877-475-4799.

Serbo-Croatian: Ukoliko Vi ili neko kome Vi pomažete ima pitanje o Blue Cross Blue Shield of Arizona, imate pravo da besplatno dobijete pomoć i informacije na Vašem jeziku. Da biste razgovarali sa prevodiocem, nazovite 877-475-4799.

Thai: หากคณ หรอคนทคณกาลงชวยเหลอมคาถามเกยวกบ Blue Cross Blue Shield of Arizona คณมสทธทจะไดรบความชวยเหลอและขอมลในภาษา ของคณไดโดยไมมคาใชจาย พดคยกบลาม โทร 877-475-4799