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Press Release

Grünenthal and Averitas Pharma Announce U.S. FDA Approval of QUTENZA® for the Treatment of Neuropathic Pain Associated with Diabetic Peripheral Neuropathy of the Feet

- Neuropathic pain associated with diabetic peripheral neuropathy is a progressive and debilitating complication of diabetes that will affect approximately more than 5 million Americans in 2020[1].
- QUTENZA® is the first and only topical, non-systemic, non-opioid pain treatment of its kind to deliver prescription strength capsaicin directly into the skin.

Aachen, Germany & Morristown, N.J. – 21 July 2020 – Grünenthal announced today that its U.S. subsidiary Averitas Pharma, Inc. received U.S. Food and Drug Administration (FDA) approval for QUTENZA® (capsaicin) 8% patch for the treatment of neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet in adults.[2] QUTENZA® is a topical, non-systemic, non-opioid pain treatment delivered in the form of a patch and is the first and only treatment of its kind to deliver prescription strength capsaicin directly into the skin.

"Pain associated with diabetic neuropathy is an extremely challenging condition to diagnose, treat and manage effectively, which has a significant quality of life impact for many patients," said David M. Simpson, MD, principal investigator and Professor of Neurology at the Icahn School of Medicine at Mount Sinai. "In addition, patients are dissatisfied with unresolved pain and the side effects associated with current systemic treatments."

Neuropathic pain associated with diabetic peripheral neuropathy (DPN), or diabetic nerve pain, is a progressive and debilitating complication of diabetes that will affect approximately more than 5 million Americans in 2020[1] and is expected to double by 2030.[3] Patients with diabetic nerve pain typically experience symptoms of numbness, tingling, as well as shooting or stabbing sensations that most often affect the lower extremities.[4]

"Painful diabetic peripheral neuropathy has a significant impact on the day-to-day lives of millions of individuals, and we believe QUTENZA® can be a much-needed non-opioid treatment option for these patients," said Jan Adams, Chief Scientific Officer, Grünenthal. "This expanded indication of QUTENZA® in the U.S. is an exciting milestone in our efforts to make QUTENZA® available to even more patients in need worldwide."

QUTENZA® offers physicians a different way to effectively treat neuropathic pain associated with diabetic peripheral neuropathy. QUTENZA®, a specially formulated patch, delivers prescription strength capsaicin directly to the skin during an in-office procedure. Thereby, it can reversibly desensitize and defunctionalize the TRPV1 (Transient Receptor Potential Vanilloid 1) receptor, which plays a critical role in pain signaling.

QUTENZA® can provide sustained relief that lasts for up to three months. QUTENZA® has no known drug-drug interactions. The most common adverse reactions include application site reactions, such erythema, pain, and pruritus. The majority of application site reactions were transient and self-limited.[2]

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QUTENZA® (capsaicin) 8% patch has been approved in the U.S. for the management of neuropathic pain associated with postherpetic neuralgia since 2009. The full U.S. prescribing information for QUTENZA® in both indications is available at www.qutenza.com/pdfs/Qutenza_Prescribing_Information.pdf.

About Neuropathic Pain Associated with Diabetic Peripheral Neuropathy

More than 34 million Americans – just over 1 in 10 – have diabetes[5], and diabetic peripheral neuropathy, or nerve damage caused by diabetes, is one of its most common complications.[6] Diabetic peripheral neuropathy (DPN) affects around 28% of all patients diagnosed with diabetes and approximately half of those with DPN will experience the debilitating manifestations of painful DPN in their lifetime.[7-13] It is a progressive and debilitating condition in which patients experience symptoms of numbness, tingling, as well as shooting or stabbing sensations that most often affect the lower extremities.[4] Its consequences can be devastating and may result in foot ulcers, lower limb amputations and other poor outcomes.[7] In the U.S., one fourth of the health expenditure on diabetes is spent on diabetic peripheral neuropathy and is estimated to be more than $10 billion annually.[7,14,15]

About QUTENZA®

QUTENZA® (capsaicin) 8% patch is approved in the US for the treatment of neuropathic pain associated with postherpetic neuralgia and for the treatment of neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet in adults. A single localized procedure with QUTENZA® may provide up to 3 months of relief. Important U.S. safety information is available below and at www.qutenza.com.

QUTENZA® is also approved in Europe. For further information please visit www.grunenthalhealth.com.

About Averitas Pharma, Inc.

Averitas Pharma is a specialty pharmaceutical company dedicated to delivering innovative, effective, non-opioid pain management options to patients in the U.S. The company was formed in 2018, as a subsidiary of GRT U.S. Holding, Inc. and member of the Grünenthal Group. For more information, visit www.averitaspharma.com.

About Grünenthal

Grünenthal is a global leader in pain management and related diseases. As a science-based, privately-owned pharmaceutical company, we have a long track record of bringing innovative treatments and state-of-the-art technologies to patients worldwide. Our purpose is to change lives for the better – and innovation is our passion. We are focussing all of our activities and efforts on working towards our vision of a world free of pain.

Grünenthal is headquartered in Aachen, Germany, and has affiliates in 29 countries across Europe, Latin America and the U.S. Our products are available in more than 100 countries. In 2019, Grünenthal employed around 4,700 people and achieved sales of € 1.4 bn.

More information: www.grunenthal.com

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IMPORTANT U.S. SAFETY INFORMATION

INDICATION

QUTENZA® (capsaicin) 8% patch is indicated in adults for the treatment of neuropathic pain associated with postherpetic neuralgia (PHN) and for neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet.

IMPORTANT SAFETY INFORMATION

Do not dispense QUTENZA to patients for self-administration or handling. Only physicians or healthcare professionals under the close supervision of a physician are to administer and handle QUTENZA.

Unintended exposure to capsaicin can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin in healthcare providers and others. When administering QUTENZA, it is important to follow these procedures:

- Administer QUTENZA in a well-ventilated treatment area.
- Wear only nitrile gloves when handling QUTENZA or any item that makes contact with QUTENZA, and when cleaning capsaicin residue from the skin. Do not use latex gloves as they do not provide adequate protection.
- Use of a face mask and protective glasses is advisable for healthcare providers.
- Keep QUTENZA in the sealed pouch until immediately before use.
- Use QUTENZA only on dry, intact (unbroken) skin.
- In patients treated for neuropathic pain associated with diabetic peripheral neuropathy, a careful examination of the feet should be undertaken prior to each application of QUTENZA to detect skin lesions related to underlying neuropathy or vascular insufficiency.
- During administration, avoid unnecessary contact with any items in the room, including items that the patient may later have contact with, such as horizontal surfaces and bedsheets.
- Aerosolization of capsaicin can occur upon rapid removal of QUTENZA. Therefore, remove QUTENZA gently and slowly by rolling the adhesive side inward.
- Immediately after use, clean all areas that had contact with QUTENZA and properly dispose of QUTENZA, associated packaging, Cleansing Gel, gloves, and other treatment materials in accordance with local biomedical waste procedures.
- If QUTENZA is cut, ensure unused pieces are properly disposed of.

Contraindications

None

Warnings and Precautions

- Unintended exposure to capsaicin can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin.

- Do not apply QUTENZA to the face, eyes, mouth, nose, or scalp to avoid risk of exposure to eyes or mucous membranes. Accidental exposure to the eyes and mucous membranes can occur from touching QUTENZA or items exposed to capsaicin and then touching the eyes and mucous membranes. Wear nitrile gloves when administering QUTENZA and avoid unnecessary contact with items in the room, including items that the patient may later have contact with, such as horizontal surfaces and bedsheets. If irritation of eyes or mucous membranes occurs, remove the affected individual from the vicinity of QUTENZA and flush eyes and mucous membranes with cool water.
- Aerosolization of capsaicin can occur upon rapid removal of QUTENZA. Therefore, remove QUTENZA gently and slowly by rolling the adhesive side inward. Inhalation of airborne capsaicin can result in coughing or sneezing. If irritation of airways occurs, remove the affected individual from the vicinity of QUTENZA. Provide supportive medical care if shortness of breath develops.
- If skin not intended to be treated is exposed to QUTENZA, apply Cleansing Gel for one minute and wipe off with dry gauze. After the Cleansing Gel has been wiped off, wash the area with soap and water.
- Patients may experience substantial procedural pain and burning upon application and following removal of QUTENZA. Prepare to treat acute pain during and following the application procedure with local cooling (such as a cold pack) and/or appropriate analgesic medication.
- Transient increases in blood pressure may occur during and shortly after the QUTENZA treatment. Blood pressure changes were associated with treatment-related increases in pain. Monitor blood pressure and provide adequate support for treatment-related pain. Patients with unstable or poorly controlled hypertension, or a recent history of cardiovascular or cerebrovascular events, may be at an increased risk of adverse cardiovascular effects. Consider these factors prior to initiating QUTENZA treatment.
- Reductions in sensory function have been reported following administration of QUTENZA. Decreases in sensory function are generally minor and temporary. All patients with pre-existing sensory deficits should be clinically assessed for signs of sensory deterioration or loss prior to each application of QUTENZA. If sensory deterioration or loss is detected or pre-existing sensory deficit worsens, continued use of QUTENZA treatment should be reconsidered.

Adverse Reactions

In all controlled clinical trials, adverse reactions occurring in ≥5% of patients in the QUTENZA group and at an incidence at least 1% greater than in the control group were application site erythema, application site pain, and application site pruritus.

Adverse Event Reporting

Physicians, other healthcare providers, and patients are encouraged to voluntarily report adverse events involving drugs or medical devices. To make a report you can:

- In the U.S., visit www.fda.gov/medwatch or call 1-800-FDA-1088; or
- For QUTENZA, you may also call 1-877-900-6479 and select option 1, or press zero on your keypad to talk to an operator to direct your call.

Please see full Prescribing Information at

https://www.qutenza.com/pdfs/Qutenza_Prescribing_Information.pdf.

References

1. LTP 2020-2030: ADDRESSABLE POPULATIONS BY CONDITION (PDPN, PSNP, PHN, CINP). Company data on file. April 30, 2020.
2. QUTENZA® [prescribing information]. Morristown, NJ: Averitas Pharma.
3. Gore, M., Brandenburg, N. A., Dukes, E., Hoffman, D. L., Tai, K.-S., & Stacey, B. (2005). Pain Severity in Diabetic Peripheral Neuropathy is Associated with Patient Functioning, Symptom Levels of Anxiety and

Depression, and Sleep. Journal of Pain and Symptom Management, 30(4), 374-385. doi:10.1016/j.jpainsymman.2005.04.009
https://www.cdc.gov/media/releases/2017/p0718-diabetes-report.html.
4. Vinik, Aaron I., et al. Repeat treatment with capsaicin 8% patch (179mg capsaicin cutaneous patch): Effects on pain, quality of life, and patient satisfaction in painful diabetic peripheral neuropathy: an open-label, randomized controlled clinical trial; Journal of Current Medical Research and Opinion 2.12 (2019): 388-401.
5. CDC Division of Diabetes Translation, National Diabetes Statistics Report, 2020. https://www.cdc.gov/diabetes/library/features/diabetes-stat-report.html#:~:text=New%20in%202020%2C%20the%20report,1%20in%203%E2%80%94have%20prediabetes. Accessed July 6, 2020.
6. University of Chicago Center for Peripheral Neuropathy. Types of Peripheral Neuropathy. http://peripheralneuropathycenter.uchicago.edu/learnaboutpn/typesofpn/diabetes/diabetes.shtml. Accessed July 6, 2020.
7. Hicks, C. W., & Selvin, E. (2019). Epidemiology of Peripheral Neuropathy and Lower Extremity Disease in Diabetes. Current diabetes reports, 19(10), 86. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6755905/#!po=48.3333. Accessed July 6, 2020.
8. Iqbal, Z., et al. (2018). *Clinical Therapeutics, 40(6), 828–849.* doi:10.1016/j.clinthera.2018.04.001.
9. Sadosky, A., et al. (2013). *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 79.* doi:10.2147/dmso.s37415.
10. Boulton, A. J. M. (2005). *Management of Diabetic Peripheral Neuropathy. Clinical Diabetes, 23(1), 9–15.* doi:10.2337/diaclin.23.1.9.
11. Franklin, G. et. al. (1990). *American Journal of Epidemiology, 131(4), 633–643.* doi:10.1093/oxfordjournals.aje.a115547.
12. Boomershine, C., Ormseth, M. J., & Scholz, B. A. (2011). *Patient Preference and Adherence, 343.* doi:10.2147/ppa.s16358.
13. Young, M. J., et al (1993). Diabetologia, 36(2), 150–154. doi:10.1007/bf00400697.
14. Economic Costs of Diabetes in the U.S. in 2017. Diabetes Care, 41(5), 917–928. doi:10.2337/dci18-0007.
15. Gordois, A., Scuffham, P., Shearer, A., Oglesby, A., & Tobian, J. A. (2003). *The Health Care Costs of Diabetic Peripheral Neuropathy in the U.S. Diabetes Care, 26(6), 1790–1795.* doi:10.2337/diacare.26.6.1790.