

First patient enrolled in a Phase III study with QUTENZA® in post-surgical neuropathic pain

- The study AV001 aims to include the treatment of post-surgical neuropathic pain (PSNP) in the U.S. label. QUTENZA® is currently approved for use in adults in 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.
- Post-surgical neuropathic pain is a debilitating complication of surgery that affects approximately 13% of all patients who undergo surgery, representing 3.3 million patients per year in the US.¹

Aachen, Germany, & Morristown, N.J., 10 August 2021 – Grünenthal announced today that its U.S. subsidiary, Averitas Pharma Inc., enrolled the first patient in the randomised, double-blind trial AV001. The Phase III study investigates the efficacy, safety, and tolerability of QUTENZA (capsaicin) 8% topical system in post-surgical neuropathic pain (PSNP) to support an extension of the U.S. label.

The trial will include over 400 patients who suffer from moderate to severe chronic PSNP for at least six months and is being carried out across more than 70 sites in Europe and the U.S. The trial aims to demonstrate a significant reduction in the average pain intensity after 12 weeks and after 42 weeks compared to baseline. In addition, the trial will assess other outcomes such as progressive response over time with repeated application, reduction of the treatment area over several applications, and quality of life aspects such as sleep interference, physical activity, anxiety, and depression. The completion and subsequent supplemental new drug application submission are expected in 2024.

“We believe that QUTENZA, a non-opioid and non-systemic topical system, is a meaningful treatment option and continuously work to increase its footprint,” says Jan Adams, M.D., Chief Scientific Officer Grünenthal. “We want to provide patients in the U.S. who suffer from PSNP access to QUTENZA and make progress towards our vision of a world free of pain.”

¹ Classifying surgeries were factored against their respective time-bound frequency of PSNP to yield the prevalence based on:

- Carroll, I. R., Hah, J. M., Barelka, P. L., Wang, C. K. M., Wang, B. M., Gillespie, M. J., ... Mackey, S. C. (2015). Pain Duration and Resolution following Surgery: An Inception Cohort Study. *Pain Medicine*, 16(12), 2386–2396. doi:10.1111/pme.12842.
- Shipton, E. (2008). POST-SURGICAL NEUROPATHIC PAIN. *ANZ Journal of Surgery*, 78(7), 548–555. doi:10.1111/j.1445-2197.2008.04569.x
- Borsook, D., Kussman, B. D., George, E., Becerra, L. R., & Burke, D. W. (2013). Surgically Induced Neuropathic Pain. *Annals of Surgery*, 257(3), 403–412. doi:10.1097/sla.0b013e3182701a7b.



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Continuous development of the QUTENZA US label

Grünenthal acquired the global rights for QUTENZA in November 2018. At this point, the U.S. label for QUTENZA comprised the treatment of neuropathic pain associated with postherpetic neuralgia. Since then, Grünenthal had worked consistently to make the product available to more people in the U.S. and achieved a significant label extension when the FDA approved QUTENZA for the treatment of neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet in adults in July 2020. Through the new study AV001, Grünenthal strives to include another major indication in the field of peripheral neuropathic pain in the U.S. label.

About QUTENZA

QUTENZA offers physicians a different way to treat neuropathic pain associated with PHN or DPN of the feet in adults. QUTENZA, a specially formulated topical system, delivers prescription-strength capsaicin directly to the skin during an in-office procedure. This way, it can reversibly desensitise and defunctionalise the TRPV1 (Transient Receptor Potential Vanilloid 1) receptor, which plays a critical role in pain signalling.

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

QUTENZA (capsaicin) 8% topical system 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. Important U.S. safety information is available below and at www.qutenza.com.

In Europe, QUTENZA is indicated for the treatment of peripheral neuropathic pain in adults either alone or in combination with other medicinal products for the treatment of pain. For further information, please visit www.grunenthalhealth.com.

About post-surgical neuropathic pain

Chronic post-surgical pain is defined as chronic pain that develops after a surgical procedure and persists beyond the healing process, i.e. at least three months after the surgery. The pain is either localised to the surgical field or area of injury, projected to the innervation territory of a nerve situated in this area, or referred to a dermatome (after surgery/injury to deep somatic or visceral tissues).³ Chronic post-surgical pain is the result of nerve damage and can be due to the surgery itself or other causes of pain including infection, malignancy, etc. It is identified by symptoms of neuropathic nerve pain such as burning, stabbing or shooting pain, numbness and changes to physical sensation or sensitivity to temperature or touch. Post-surgical neuropathic pain affects approximately 13 percent of all patients undergoing surgery, which represents 3.3 million patients per year in the US.¹

² QUTENZA® [prescribing information]. Morristown, NJ: Averitas Pharma.

³ ICD 11 - <https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/985186256>



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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 focusing 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 US. Our products are available in more than 100 countries. In 2020, Grünenthal employed around 4,500 people and achieved sales of € 1.3 bn.

More information: www.grunenthal.com

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US INDICATION

QUTENZA® (capsaicin) 8% topical system 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 US-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.



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When administering QUTENZA, it is important to follow the procedures in the Important Dosage and Administration Instructions in the US Prescribing Information.

In patients treated for neuropathic pain associated with diabetic peripheral neuropathy of the feet, 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.

Contraindications

None

Warnings and Precautions

- Unintended exposure to capsaicin can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin in healthcare professionals, patients, and others. Healthcare professionals should ensure that the recommended procedures and protective measures are used when administering QUTENZA.
- For healthcare professionals, 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.
- Do not apply QUTENZA to the patient's 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. If irritation of eyes or mucous membranes occurs, flush eyes and mucous membranes with cool water. Remove the affected individual (healthcare professional or patient) from the vicinity of QUTENZA.
- 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. Administer QUTENZA in a well-ventilated treatment area. Provide supportive medical care if shortness of breath develops. If irritation of airways occurs, remove the affected individual from the vicinity of QUTENZA. If respiratory irritation worsens or does not resolve, do not re-expose the affected healthcare professional or patient to QUTENZA.
- 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.



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- Transient increases in blood pressure may occur during and shortly after 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 $\geq 5\%$ 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 [US Prescribing Information](#).