Introduction to neuropathic pain

Neuropathic pain is defined as ‘pain caused by a lesion or disease of the somatosensory system’ either from the central nervous system or peripheral nervous system. Peripheral neuropathic pain is mediated through nociceptors, which are specialised, small-diameter sensory nerve endings, predominantly found in the epidermis. Nociceptors usually detect chemical, mechanical or thermal stimuli but become spontaneously active after lesion or disease due to the lowering of the activation threshold that leads to the perception of pain.

Introduction to QUTENZA™ – the capsaicin 8% patch

Localised topical therapy for peripheral neuropathic pain provides pain relief whilst avoiding the possible problems of systemic treatment such as unwanted side effects, drug–drug interactions and addictive potential. Capsaicin is a highly selective agonist for Transient Receptor Potential Vanilloid 1 (TRPV1), a ligand-gated, non-selective channel preferentially expressed in small-diameter sensory neurons (C fibres and to a lesser extent Aδ fibres). Initially, the activation of TRPV1-expressing nociceptors by capsaicin causes depolarisation, action potential initiation and pain signal transduction. Continued exposure to high concentrations of capsaicin produces a prolonged and reversible defunctionalisation of nociceptive sensory axons. This defunctionalisation of hyperactive nociceptors is thought to underlie the pain relief that follows exposure to a localised high concentration of capsaicin.

QUTENZA is an advanced application system containing 8% w/w capsaicin that is optimised for rapid dermal delivery. It is supplied as a thin, 14 x 20 cm, transparent, adhesive patch with capsaicin prepared in a microreservoir formulation that enables the patch to be cut without the risk of aerosolisation of capsaicin. QUTENZA is also supplied with a proprietary cleansing gel. The high concentration of capsaicin in this formulation results in reversible defunctionalisation of TRPV1-expressing cutaneous sensory nerve endings and reduction in nerve fibre density in the epidermis. The resulting pain relief is long lasting at up to 12 weeks and possibly longer in some patients, with a single application.

QUTENZA is a novel treatment designed to deliver prolonged pain relief direct to the source of peripheral neuropathic pain.

- QUTENZA enables rapid delivery of high-dose capsaicin to the hyperactive pain receptors.
- A single application of QUTENZA results in rapid, selective and prolonged defunctionalisation of nociceptors.
- Prolonged defunctionalisation of nociceptors may result in reduced pain for up to 12 weeks and possibly longer in some patients.

QUTENZA provides rapid, lasting efficacy from a single application.

- Patients with postherpetic neuralgia (PHN) achieved full therapeutic effect from QUTENZA within 2 days of treatment.
- Significant pain relief compared with control up to Week 12.
- 12 weeks post-treatment with QUTENZA, the majority of patients with PHN continued to experience improvement in pain.

QUTENZA re-treatments provide patients with consistent and reproducible reductions in pain levels.

- Patients receiving up to three re-treatments with QUTENZA experienced similar levels of pain reduction after each treatment.
- There was no increase in the incidence of adverse events or negative effects on sensory function with repeated treatments.
- Qutenza remains a well-tolerated treatment with each repeated application. 10, 11

**QUTENZA is an effective localised topical therapy.** 8–11

- The only commonly reported side effects are transient and related to the QUTENZA application procedure. 8–11
- Application site discomfort is usually mild to moderate in intensity and resolves within 2–3 days. 8–11
- QUTENZA has no known drug–drug interactions, allowing freedom to administer other medications.

**References:**

General handling and disposal measures
- Wear nitrile gloves at all times while handling QUTENZA and cleaning treatment areas.
- Do NOT wear latex gloves as they do not provide adequate protection.
- Do not hold patches near eyes or mucous membranes.
- Avoid direct contact with QUTENZA patch, used gauze or used cleansing gel.
- The use of a mask and protective glasses should be considered, particularly during patch removal.
- Dispose of all used and unused patches and all other materials that have been in contact with the treated area by sealing them in a polyethylene medical waste bag in an appropriate medical waste container.

Warnings and precautions
- QUTENZA should be used only on dry, intact (unbroken) skin and not on the face, above the hairline of the scalp, or in proximity to mucous membranes.
- For patients with unstable or poorly controlled hypertension or recent cardiovascular events, the risk of adverse cardiovascular reactions due to the potential stress of the procedure should be considered prior to initiating QUTENZA therapy.
- Blood pressure should be monitored prior to and during the procedure.
- Application site reactions, such as transient local application site pain, erythema and pruritus are common or very common.
- There have been reported cases of burns, including second degree burns in patients treated with capsaicin patches. In patients reporting severe pain, the patch should be removed and the skin examined for burns.
- Patients experiencing increased pain should be provided with supportive treatment, such as local cooling after patch removal or oral analgesics (i.e. short-acting opioids).
- QUTENZA should be used with caution in patients with pre-existing minor changes in sensory function, as they may have an increased risk of further minor and temporary changes (e.g. heat detection).
- For patients using high doses of opioids:
  - Oral opioid analgesics may not be effective when used for acute pain during and following the procedure
  - A thorough history should be reviewed before initiating therapy
  - An alternative pain-reduction strategy for possible treatment-associated discomfort should be put in place prior to QUTENZA therapy in patients with suspected high opioid tolerance.
- The cleansing gel for QUTENZA contains butylhydroxyanisole, which may cause local skin reactions (e.g. contact dermatitis) or irritation of the eyes and mucous membranes.
QUTENZA™ PRESCRIBER CHECKLIST

This checklist reminds prescribers about aspects of QUTENZA to ensure the product is prescribed appropriately. You should refer to the checklist before administering QUTENZA to your patient. For further information about QUTENZA, please refer to the Summary of Product Characteristics.

Contraindications: if the following applies to your patient, do not prescribe QUTENZA™

Does your patient have hypersensitivity to the active substance or to any of the excipients?  Yes □  No □

Warnings and precautions

Does your patient have hypertension?  Yes □  No □
Does your patient have cardiovascular disease?  Yes □  No □
Does your patient have opioid tolerance?  Yes □  No □

For patients with unstable or poorly controlled hypertension or a recent history of cardiovascular events, the risk of adverse reactions due to the potential stress of the procedure should be considered before initiating QUTENZA therapy.

Patients using high doses of opioids may not respond to oral opioid analgesics when used for acute pain during and following the procedure. A thorough history should be reviewed before initiating therapy and an alternative pain-reduction strategy for possible treatment-associated discomfort put in place before QUTENZA therapy in patients with suspected high opioid tolerance.

- Monitor your patient’s blood pressure prior to and during QUTENZA therapy
- Advise your patient prior to QUTENZA therapy about the increased risk of temporary changes in sensory function (e.g. ability to detect heat)
- Advise your patient prior to QUTENZA therapy about the increased risk of temporary local skin reactions (e.g. contact dermatitis) and irritation of the eyes and mucous membranes
- Advise your patient prior to QUTENZA therapy about the possibility that they may experience treatment-associated discomfort during and sometimes after patch application.
- Avoid direct contact with QUTENZA patch

PRACTICAL PRECAUTIONS:

- Do not hold QUTENZA patches near eyes or mucous membranes
- Do not apply QUTENZA to broken skin
- Do not apply QUTENZA to the following areas: the face, above the scalp hairline or in proximity to mucous membranes
- Wear nitrile gloves (not latex) at all times while handling QUTENZA
- Also consider using a mask and protective glasses, particularly during patch removal
- Dispose of all QUTENZA patches and associated materials appropriately in a sealed polyethylene medical waste bag

† Each patch consists of a matrix containing: silicone adhesives, diethylene glycol monoethyl ether, silicone oil, ethylcellulose N50 (E462), backing layer: polyester backing film, printing ink containing Pigment White 6, removable protective layer: polyester release liner.

Each 50 g of cleansing gel for QUTENZA contains 0.2 mg/g butylhydroxyanisole (E320), edetate disodium, sodium hydroxide (E524), purified water, carboxer, polyethylene glycol.
1. The treatment setting:
   - A treatment room that is a relaxing and quiet environment with running water available is optimal.
   - Provide a means of distraction for the patient to occupy them during the application procedure, such as a TV or reading materials, or advise the patient to bring something from home.

2. Briefing the patient:
   - Before beginning the treatment, provide the patient with relevant information and ensure they feel comfortable with the treatment process.
   - Set the correct expectations about what to expect from the application procedure.
   - Inform the patient that treatment site reactions may or may not occur.
   - The area may or may not go red and they may or may not experience a burning, deep heat-like sensation similar to that of sunburn, but without the physical damage and need for creams or lotions.
   - Ensure that the patient understands that there is no correlation between the presence or absence of treatment site reactions and the efficacy of QUTENZA.
   - Inform the patient about the possibility of a lasting effect and that one treatment may provide pain relief for up to 12 weeks, or possibly longer in some patients.

3. Identify:
   - The treatment area should be determined by identifying areas of dynamic and pinprick allodynia and any painful regions that extend beyond the area of allodynia.
   - Once identified, mark the painful area on the skin using a skin marker that will not rub off during the procedure.
   - Trace the treatment area onto a stencil/transparency or directly onto the QUTENZA patch. Use anatomical markings to ensure the patch is applied in the correct position.
4. Prepare:
- If removal of hair from the treatment area is necessary it should be clipped rather than shaved.
- The treatment area may be pre-treated with a topical anaesthetic or the patient may be administered an oral analgesic prior to application of QUTENZA to reduce potential treatment-associated discomfort.
- In clinical trials, patients were pre-treated with topical lidocaine (4%), lidocaine (2.5%)/prilocaine (2.5%) or with 50mg of tramadol.
- The topical anaesthetic or oral analgesic should be used in accordance with the product's instructions for use. If used, topical anaesthetic should be removed prior to applying QUTENZA.
- Before applying the QUTENZA patch, the skin should always be washed and dried thoroughly.

5. Apply:
- QUTENZA is a single-use transparent patch and can be cut to match the size and shape of the treatment area.
- Cut QUTENZA before the release liner is removed. Do not remove the release liner until just before application.
- There is a diagonal cut in the release liner to aid in its removal. Peel and fold a section of the release liner, then place the adhesive side of the QUTENZA patch onto the treatment area.
- Hold the patch in place then slowly and carefully peel away the release liner while simultaneously smoothing the patch onto the skin with the other hand.
- Allow the patch to remain in place for 30 minutes for the feet or 60 minutes for any other area.
- If possible, avoid leaving the patient alone during the application procedure, but if it is necessary, provide them with a means of contacting someone quickly.
- If the patient develops a burning sensation in the eyes, skin or airway, remove the patient from the vicinity of the treatment area. Flush eyes or mucous membranes with water. Provide appropriate medical care if shortness of breath develops.
Tips to aid patch adhesion

- For QUTENZA to be effective, it is critical to ensure that there is complete contact between the patch and the skin, with no air bubbles and no moisture.
- The texture of the patch is such that extra care may be needed to ensure close contact, especially in some more difficult to treat areas.
- Applying pressure to the patch during application, by using gauze or bandages to tightly wrap the treatment area, having the patient wear tight socks, using weights or sandbags or asking the patient to lie on the treatment area can all aid adhesion.
- Other techniques to improve adhesion include cutting the patch into smaller pieces or making cuts into the patch; pulling the skin taut before application; and warming the skin if necessary particularly on cold feet.

Remove:

- Slowly and gently remove the QUTENZA patch by rolling it inward to minimise the risk of aerosolisation of capsaicin.
- Dispose of all materials in the waste bag provided.
Cleanse:
- Apply cleansing gel liberally to the treatment area and leave on for at least 1 minute.
- Wipe off the cleansing gel with dry gauze then gently wash the affected area with soap and water.
- Do not let the capsaicin-contaminated water contact the surrounding skin.

Advise:
- Inform the patient that the treated area may be sensitive (to heat, hot showers/baths, direct sunlight, vigorous exercise, etc.) for a few days.
- In particular, it is important to ensure that the patient understands that the burning sensation may increase at night if the treatment area becomes hot, under bedclothes for example, but that they may use cooling measures or oral analgesics to manage any discomfort, as described under section 9.
- All ongoing treatment for neuropathic pain should be continued as prescribed.
- Capsaicin can continue to leach out of the skin following cleansing; therefore advise the patient not to touch the contaminated area in the days following treatment. Patients receiving treatment to the hands could be advised to wear gloves for 1–2 days following treatment.
- If possible, provide patients with an information sheet to take home with them, detailing the advice given, as a reminder.

Managing treatment-associated discomfort:
- Cooling provides an effective way of managing any treatment-related discomfort and local cooling after patch removal should be used along with oral analgesics (e.g. short-acting opioids), if necessary, to treat acute pain during and following the procedure.
- Cooling should only be initiated after patch removal; however, if absolutely necessary, cooling measures may be initiated towards the end of the QUTENZA application if this will ensure patients complete the full duration of treatment.
- The use of wet compresses during the QUTENZA application should be avoided as moisture can impact on patch adhesion.
- Use chilled (not frozen) cool packs on the treated area after the QUTENZA application. Wrap the cool packs in material to avoid direct contact with the skin.
- Provide patients with cool packs to manage the pain at home. Advise of other cooling measures such as walking on cold floor tiles and applying tepid water.
Patient follow-up:
- **Follow-up is recommended** at least once 2-3 weeks post treatment. New users of Qutenza should follow-up with patients more frequently until adequate experience with the application procedure is established.
- Patients should be **provided with a number to call** if they need any assistance.
- Inform the patient that they **should not reduce their concomitant pain medications** without the guidance of the healthcare professional responsible for prescribing these medications.

**Identify & Prepare**

**Apply**

**Improve adhesion**

**Remove**

**Cleanse**
CHECKLIST FOR HEALTHCARE PROFESSIONALS
ADMINISTERING QUTENZA™

The following list can be used to determine whether the patient has been given all relevant information needed regarding post-treatment care. This list could be provided to the patient in a leaflet to take away with them.

- Continue all analgesics as prescribed
- Do not touch or scratch the treatment area
- Do not let children or animals touch the treatment area
- The treatment area may or may not be red
- On the day of treatment, use only lukewarm water for bathing/showering
- The burning sensation may increase again at night if the treatment area becomes hot
- Use localised cooling or over-the-counter analgesics, suitable for that individual patient, to manage any discomfort. This must also take into account any other tablets that they may be on. Patients should contact their GP if they are unsure if a medication is suitable.
- Side effects, such as increased sensitivity or inflammation are not unexpected and should wear off over the first 7 days
- If the pain worsens considerably, ring the pain centre
- You can complete the provided pain diary if you wish
- A copy of the treatment procedure and plan of care will be sent to your primary care physician
- Resume normal daily activities
- A follow-up appointment will be made for you, or we will follow up by phone
- QUTENZA treatment can be repeated every 3 months as necessary

The patient may wish to take their information sheet to their primary care physician for information.
QUTENZA™ Prescribing Information

PRESCRIBING INFORMATION: QUTENZA™ 179 mg capsaicin cutaneous patch.

ACTIVE INGREDIENT: Capsaicin (640 mcg/cm²).

PHARMACEUTICAL FORM AND CONTENTS: Each carton contains 1 or 2 sachets each containing 1 cutaneous patch and 1 tube of cleansing gel (50 g). Each patch is 14 cm × 20 cm (280 cm²).

LIST OF EXCIPIENTS: Each patch consists of a matrix containing: silicone adhesives, diethylene glycol monoethyl ether, silicone oil, ethylcellulose N50 (E462); backing layer: polyester backing film, printing ink containing Pigment White 6; removable protective layer: polyester release liner; each 50 g of cleansing gel for QUTENZA contains 0.2 mg/g butylhydroxyanisole (E320), disodium edetate, sodium hydroxide (E524), purified water; carbomer; macrogol 300.

THERAPEUTIC INDICATIONS: QUTENZA is indicated for the treatment of peripheral neuropathic pain in non-diabetic adults either alone or in combination with other medicinal products for pain.

DO NOT USE: If the patient is allergic (hypersensitive) to capsaicin, chilli peppers or any other ingredients in the QUTENZA cutaneous patch. Do not use QUTENZA on any part of the patient’s head or face. Do not use QUTENZA on broken skin or open wounds. Do not touch QUTENZA or any other materials that have come into contact with treated areas as it may cause burning and stinging. Do not touch your eyes, mouth or other sensitive areas. Sniffing or inhaling close to the QUTENZA patches may cause coughing or sneezing.

USE IN CHILDREN AND ADOLESCENTS: QUTENZA is not recommended for treatment in patients under 18 years of age.

PREGNANCY AND LACTATION: Caution should be exercised when prescribing to pregnant women. Breastfeeding should be discontinued during treatment with QUTENZA.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: QUTENZA has no or negligible influence on the ability to drive and use machines.

DOSAGE AND METHOD OF USE: QUTENZA should be administered by a healthcare professional. The treatment area may be pre-treated with a topical anaesthetic or the patient might be administered an oral analgesic prior to application of QUTENZA to reduce potential application-related discomfort. QUTENZA should be applied to the most painful skin areas (using up to a maximum of 4 patches). QUTENZA must be applied to intact, non-irritated dry skin, and allowed to remain in place for 30 minutes for the feet (e.g. HIV-associated neuropathy) and 60 minutes for other locations (e.g. post-herpetic neuralgia). QUTENZA treatments may be repeated every 90 days, as warranted by the persistence or return of pain. Full details of QUTENZA administration are given in the Summary of Product Characteristics.

ADVERSE REACTIONS: The most commonly reported adverse reactions were transient local application site burning, pain, erythema and pruritis. Adverse reactions were transient, self-limiting and usually mild to moderate in intensity. There have been reported cases of burns, including second degree burns, in patients treated with capsaicin patches. In patients reporting severe pain, the patch should be removed and the skin examined for chemical burn.

PRECAUTIONS FOR USE: In case of unstable or poorly controlled high blood pressure or recent heart problems, the physician should consider risk of adverse reactions to heart or blood pressure as a result of procedure. Nitrile gloves should be worn at all times while handling QUTENZA and cleaning treatment areas. QUTENZA patches should not be held near eyes or mucous membranes. Direct contact with QUTENZA, used gauze or
used cleansing gel should be avoided. The cleansing gel for QUTENZA contains butylhydroxyanisole which may cause local skin reactions, e.g. contact dermatitis or irritation of the eye and mucous membranes.

**CONTRAINDICATIONS:** Hypersensitivity to the active substance or any of the excipients.

**INTERACTIONS:** No formal interaction studies with other medicinal products have been performed as only transient low levels of systemic absorption have been known to occur with QUTENZA.

**PACKAGE SIZE:** Each QUTENZA carton contains 1 or 2 QUTENZA treatment sachets and 1 tube of cleansing gel (50 g). Not all pack sizes may be marketed.

**SPECIAL STORAGE CONDITIONS:** Store flat in original sachet and carton. Store below 25°C.

**SPECIAL PRECAUTIONS FOR DISPOSAL:** Dispose of unused patches, gauze wipes and all other materials placed in contact with treated area immediately after use by sealing in a polyethylene bag and placing in an appropriate medical waste container.

**SPECIAL WARNINGS:** Keep out of the sight and reach of children.

**EXPIRY DATE:** 4 years. After opening sachet: apply QUTENZA within 2 hours.

**LEGAL CATEGORY:** Prescription Only Medicine POM / S1A.

**MARKETING AUTHORISATION NUMBERS:** EU/1/09/524/001-002.

**FURTHER INFORMATION AVAILABLE FROM:** Astellas Pharma Co Ltd, 5 Waterside, Citywest Business Campus, Naas Road, Dublin 24.

Tel No: 01 4671555

DATE OF REVISION: 17 September 2014.

FOR FULL PRESCRIBING INFORMATION REFER TO THE SUMMARY OF PRODUCT CHARACTERISTICS.

Available @www.medicines.ie

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via: HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel +353 1 6764971; Fax: +353 1 6762517. Website: www.hpра.ie; E-mail: medsafety@hpра.ie

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