

SYNERA®
(lidocaine and tetracaine) Topical Patch

fertility in male or female rats when given subcutaneous doses up to 7.5 mg/kg (45 mg/m² or 1-fold the SDA). Multiples of exposure are based on an SDA of 70 mg each of lidocaine and tetracaine in SYNERA patch for 30 minutes to a 60 kg person (43 mg/m²).

14 Clinical Studies
14.1 Superficial Venous Access

Three randomized, double-blind, placebo controlled clinical trials in adult and geriatric subjects evaluated the degree of dermal analgesia upon venipuncture following a 20-minute treatment with SYNERA or a placebo patch (patch with heating component but no drug). In each trial, subjects received SYNERA on one arm and placebo patch on the other. In all three studies pain was measured by a 100-mm VAS in which a lower VAS score corresponds to less pain. In the first study in 21 subjects, median VAS scores for SYNERA and placebo treatments were 1 mm and 9 mm, respectively. In the second study in 40 subjects, median VAS scores were 5 mm and 28 mm for SYNERA and placebo treatments, respectively. In the third study, in 40 subjects over the age of 65 years, median VAS scores for SYNERA and placebo treatments were 8 mm and 14 mm, respectively.

In a randomized, double-blind, placebo controlled study, 61 pediatric patients received either SYNERA or placebo for 20 minutes prior to venipuncture or IV cannulation in the antecubital fossa or dorsum of the hand. Subjects were stratified by age group (3 to 6 years and 7 to 17 years). Children in the younger group reported less pain on IV cannulation with SYNERA than with placebo, as rated using a six-point Oucher pain scale with faces. Children in the older group rated their pain using an eleven-point Oucher pain scale that contained both faces and numbers. Pain scores on IV cannulation in the older children treated with SYNERA were not significantly different from pain scores in those treated with placebo.

In a double-blind trial in 250 adults, subjects were randomized to receive either SYNERA without heating element or SYNERA with heating element, prior to venipuncture. Median VAS scores for the patch with the heating element and without the heating element were 17 mm and 22 mm, respectively.

14.2 Superficial Dermatological Procedures

In one randomized, double-blind, placebo controlled study, 94 adult subjects received either SYNERA or placebo patch for 30 minutes prior to a superficial dermatological procedure such as superficial excision, shave biopsy or electrocauterization. Median VAS scores for SYNERA and placebo treatments were 5 mm and 31 mm, respectively. In a similarly designed study in 74 subjects over the age of 65 years, less pain was reported following SYNERA treatment compared to placebo with median VAS scores for SYNERA and placebo treatments of 10 mm and 23 mm, respectively.

In a randomized, double-blind, placebo controlled study, 88 pediatric patients were stratified by age group (3 to 6 years and 7 to 17 years) to receive a 30-minute application of either SYNERA or placebo patch, prior to lidocaine injection. In younger children who used the Oucher pain scale with faces, those receiving SYNERA reported less

pain from lidocaine injection than those receiving placebo. Older children used the numerical Oucher pain scale to report pain intensity. There was no difference between treatments observed in the older children.

16 How Supplied/Storage and Handling
16.1 How Supplied

SYNERA is available as the following:
NDC 10885-002-01 One individually packaged SYNERA patch
NDC 10885-002-10 Box of 10 individually packaged SYNERA patches

16.2 Storage and Handling

Store at 25°C (77°F); excursions permitted to 15 to 30°C (59 to 86°F) [see USP Controlled Room Temperature].

Keep out of reach of children and pets.

Apply SYNERA immediately upon removal from the protective pouch.

Do not cut the patch or otherwise remove the top cover as this could cause the patch to heat to temperatures that could cause thermal injury. Do not cover the holes on the top side of the patch as this could cause the patch not to heat.

Hands should be washed after handling SYNERA, and eye contact with SYNERA should be avoided. The used patch should be disposed of immediately. The adhesive sides of the patch should be folded together and the patch should then be thrown away in a location that is out of the reach of children and pets.

17 Patient Counseling Information

- Advise patients to read the FDA-approved patient labeling (Instructions for Use).
- Advise patients that SYNERA is a patch containing two medicines (lidocaine and tetracaine) that are known as local anesthetics, and a heating component. These medicines are used to lessen the pain associated with superficial venous access and superficial dermatological procedures such as excision, electrocauterization and shave biopsy of skin lesions.
- Advise patients that SYNERA should be applied immediately after opening the pouch. Instruct patients to not cut or remove the top cover of the patch as this could result in thermal injury.
- Advise patients that keeping a patch on longer than recommended or applying multiple patches simultaneously or sequentially could result in systemic absorption sufficient to result in serious adverse effects that are typical of drugs in this class.
- Advise patients that the patch must be removed before magnetic resonance imaging.
- Advise patients that SYNERA is contraindicated in patients with a known history of sensitivity to lidocaine, tetracaine, local anesthetics of the amide or ester type, or any other component of the product and in patients with para-aminobenzoic acid (PABA) hypersensitivity.

- Advise patients that SYNERA should be used with caution in patients who may be more sensitive to the systemic effects of lidocaine and tetracaine, including the acutely ill, the debilitated, and those with compromised hepatic function. Patients with severe hepatic disease or pseudocholinesterase deficiency are at greater risk of developing toxic plasma concentrations.
- Advise patients that SYNERA should be used with caution in patients receiving class I antiarrhythmics and/or other local anesthetics, because the systemic toxic effects may be additive and potentially synergistic with lidocaine and tetracaine.
- Advise patients not to use SYNERA if they have a history of methemoglobinemia.
- Advise patients to avoid contact of SYNERA with the eyes due to potential irritation or abrasion. If contact occurs, immediately wash the eye with water or saline, and protect it until sensation returns.
- Advise patients that SYNERA should only be applied to intact skin. Inform patients that exposure of the skin to SYNERA may result in erythema, blanching and edema; these reactions are generally mild, resolving spontaneously soon after the patch is removed.
- Advise patients that SYNERA is not for use on mucous membranes or on areas with broken skin.
- Advise patients that if skin irritation or a burning sensation occurs during application, the product should be removed.
- Inform patients of the signs of an allergic or anaphylactoid reaction (urticaria, angioedema, bronchospasm, and shock). Instruct patients to seek immediate emergency help if these occur.
- Advise patients that SYNERA may lead to diminished or blocked sensation in the treated skin; therefore, patients should avoid inadvertent trauma (rubbing, scratching, or exposure to heat or cold) before complete sensation returns.
- Advise patients to contact their healthcare professional if they don't recall where to apply the patch.
- Instruct patients to store SYNERA and to discard used patches out of the reach of children and pets.
- The effect of SYNERA on intradermal injections of live vaccines has not been determined.

GALEN

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For medical information about SYNERA, call 1-866-949-9277.



INSTRUCTIONS FOR USE

Leave the patch in the foil pouch until you read this leaflet

WHAT THE PATCH DOES:

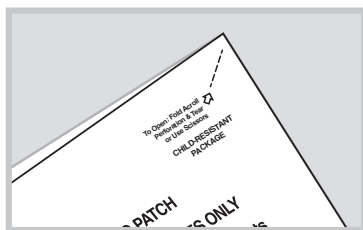
The medicine on this patch is used to numb the skin that it covers. The safety and effectiveness of Synera® have been established in adults and children 3 years of age and older.

FOLLOW THE INSTRUCTIONS BELOW, AND THESE SAFETY TIPS:

- **Do not put the patch on your lips or near your eyes.** If you get medicine from the patch in your eye, rinse your eye with water and protect it until the numbness goes away.
- **Do not cut or tear the patch.**
- **Do not get water on the patch.**
- **Keep the patch away from children and pets at all times.**

STEP 1:

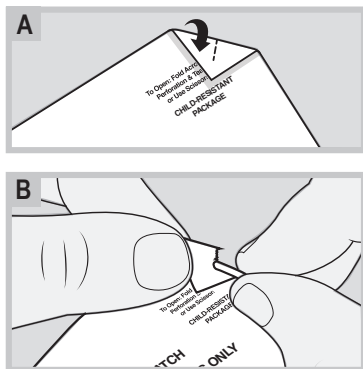
Check the skin where the patch will be worn



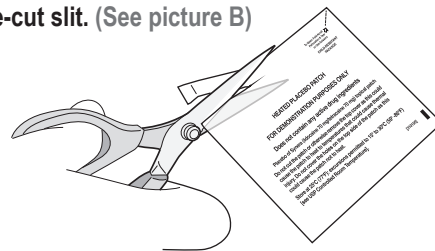
- **Keep the patch in the unopened foil pouch until you are ready to put it on.**
- **Check the skin where your doctor or health care professional told you to wear it.**
- **Do not put the patch on skin that is cut, scratched or red (like a rash).**
- **Do not shave the area or you may hurt the skin.**

STEP 2:

Open the foil pouch and remove the patch. Save the foil pouch.

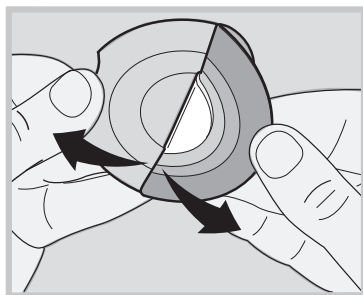


- **TO TEAR OPEN THE FOIL POUCH - fold the upper right corner toward you. (See picture A)**
- **Press the corner flat to form a small triangle.**
- **Tear the foil pouch in the middle of the fold along the pre-cut slit. (See picture B)**
- **TO CUT OPEN WITH SCISSORS - cut carefully along the edge of the package.**
- **SAVE THE FOIL POUCH.**

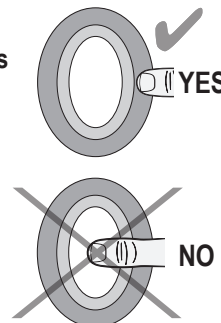


STEP 3:

Put the patch on your skin

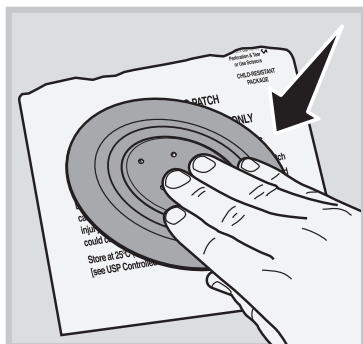


- **DO NOT TOUCH THE MEDICINE IN THE MIDDLE - touch only the sticky edges of the patch. Never touch the center area.**
- **Peel the patch off of the hard plastic backing.**
- **Put the sticky side of the patch on your skin, where you were told to wear it. Press the edges to make sure the patch will stick to your skin.**
- **Wash your hands.**

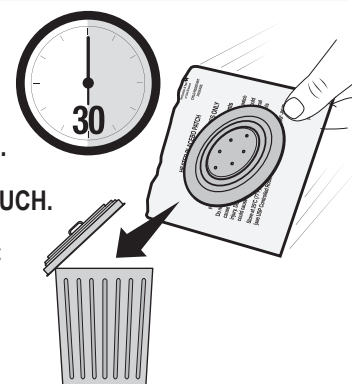


STEP 4:

IMPORTANT — How to remove and discard the patch



- **Do not leave the patch on the skin for longer than 30 minutes.**
- **Carefully peel the patch off your skin, touching only the sticky edges of the patch - DO NOT TOUCH THE MEDICINE IN THE MIDDLE.**
- **PRESS THE STICKY SIDE OF THE USED PATCH ONTO THE FOIL POUCH.**
- **THROW FOIL POUCH WITH PATCH ATTACHED, AND HARD PLASTIC BACKING, IN THE GARBAGE so children and pets cannot reach it.**
- **Wash your hands.**



While wearing the patch:

- **Do not put the patch on your lips or near your eyes.** If you get medicine from the patch in your eye, rinse it with water until the numbness goes away.
- **Do not cut or tear the patch.**
- **Do not get water on the patch. Keep the patch dry. Do not cover the small holes on the outside of the patch.** If you applied the patch to the back of your hand, wash your hands carefully.
- **If your skin hurts or burns too much, you should take the patch off.** It is normal for the skin to feel warm, but it should not burn.

After the patch is removed:

Be careful with your skin after the patch is removed. The skin that was covered by the patch stays numb and you won't be able to feel pain right away. Do not scratch or let this skin touch hot or cold things.