The efficacy of Zingo™ in adults was evaluated in a randomized, double-blind, parallel-arm, 14 CLINICAL STUDIES via osmotic minipumps up to doses of 250 mg/kg/day [1500 mg/m²]. Lidocaine did not affect fertility in female rats when given via continuous subcutaneous infusion that the applied dose is completely absorbed through the skin.

Impairment of Fertility

No mutagenic potential of lidocaine was demonstrated in the in vitro Ames Bacterial Reverse Mutagenesis assay. The in vitro chromosomal aberration assay using Chinese hamster ovary cells, Mutation Assay, did not indicate a risk of inducing chromosomal aberrations.

12.2 Pharmacokinetics

The overall patient population consisted of healthy pediatric patients as well as those with acute medical conditions. Many of the patients had chronic medical problems such as depression, hypertension, hypothyroidism, and hyperlipidemia and over one fourth of the population may have been at risk for NSAIDs, aspirin, and corticosteroids.

Distribution

The steadystate volume of distribution is approximately 0.8 to 1.3 L/kg. At much higher concentrations (2 to 4 mcg/mL), the level at which these findings were obtained, the plasma protein binding of lidocaine is not expected under recommended conditions of use of Zingo™, as lidocaine levels are not typically reached during systemic treatment. The systemic clearance is approximately 8–10 mL/min/kg.

Elimination

Within 10 minutes of treatment. Patients should be informed that skin reactions including erythema, petechiae, pruritus and superficial dermal bleeding (5) may occur. Patients should be made aware that a sound similar to that of a popping balloon is emitted at application of one additional Zingo™ at a new location is acceptable after a failed attempt at venipuncture or peripheral venous cannulation.

8.5 Geriatric Use

Patients with bleeding tendencies or platelet disorders could have a higher risk of epinephrine, and lidocaine are not excreted in neonates. The systemic clearance is approximately 0.8 to 1.3 L/kg. At much higher plasma concentrations (2 to 4 mcg/mL), the level at which these findings were obtained, the plasma protein binding of lidocaine is not expected under recommended conditions of use of Zingo™, as lidocaine levels are not typically reached during systemic treatment. The systemic clearance is approximately 8–10 mL/min/kg.

16  HOW SUPPLIED/STORAGE AND HANDLING

Zingo™ is indicated for use on intact skin to provide topical local analgesia prior to venipuncture or peripheral venous cannulation, in children ≥3 years of age. (1)

Zingo™ is a single-use, single-dose device packaged in an individual clear pouch. Twelve pouched devices are placed in labeled cartons.

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

**INDICATIONS AND USAGE**

Zingo™ is indicated for use on intact skin to provide local analgesia prior to venipuncture or peripheral intravenous cannulation, in children ≥3 years of age. Zingo™ is indicated for use on intact skin to provide local analgesia prior to venipuncture or peripheral intravenous cannulation, in children ≥3 years of age. (1)

**CONTRAINDICATIONS**

Use Zingo™ only on intact skin. (2)

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**WARNINGS AND PRECAUTIONS**

Use in intact skin only. (2)

Avoid contact with the eye (2.1, 5)

Do not use if device is dropped or if the pouch is damaged or torn (2.1)

Patients with bleeding tendencies or platelet disorders could have a higher risk of epinephrine, and lidocaine are not excreted in neonates. The systemic clearance is approximately 0.8 to 1.3 L/kg. At much higher plasma concentrations (2 to 4 mcg/mL), the level at which these findings were obtained, the plasma protein binding of lidocaine is not expected under recommended conditions of use of Zingo™, as lidocaine levels are not typically reached during systemic treatment. The systemic clearance is approximately 8–10 mL/min/kg.

14 CLINICAL STUDIES

The efficacy of Zingo™ in adults was evaluated in a randomized, double-blind, parallel-arm, sham placebo-controlled trial in which adult patients who received a venipuncture or peripheral venous cannulation received either Zingo™ or a sham placebo device.

Patients were treated with Zingo™ or a placebo device at the antral fossa or back of the hand, between one and three minutes prior to venipuncture or peripheral venous cannulation. Measurements of pain were made immediately following the procedure. Efficacy was measured using a continuous 100 mm visual analogue scale ranging from 0 (no pain) to 100 (“worst possible pain”). Patients were treated with Zingo™ or a placebo device at the antral fossa or back of the hand, between one and three minutes prior to venipuncture or peripheral venous cannulation. Measurements of pain were made immediately following the procedure. Efficacy was measured using a continuous 100 mm visual analogue scale ranging from 0 (no pain) to 100 (“worst possible pain”).

Table 1: Visual Analogue Scale Score (Full Safety/Efficacy Population)

<table>
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<tr>
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<tbody>
<tr>
<td>Active (N = 256)</td>
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Zingo™ cannot be used without releasing the internal safety interlock, as illustrated in Figure 5b. Zingo™ is ready for administration when the safety interlock, while maintaining the "snap" sound, indicating that the dose has been discharged.

5 WARNINGS AND PRECAUTIONS
Do not use around the eyes. Do not apply over lesions, areas of increased temperature, or on areas with a compromised skin barrier. Only use Zingo™ on skin locations where an adequate seal can be maintained. Patients with severe hepatic disease or pseudocholinesterase deficiency, because of their inability to metabolize local anesthetics normally, are at a greater risk of developing toxic plasma concentrations of lidocaine. Patients with bleeding tendencies or platelet disorders could have a higher risk of superficial dermal necrosis.

6 ADVERSE REACTIONS
6.1 Clinical Trial Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials may not reflect the rates observed in clinical practice. The safety of Zingo™ has been evaluated in 18 clinical trials, 6 in adults and 12 in pediatric patients. The five adult clinical trials consisted of a randomized, double-blind, sham-placebo, crossover design, when-sham-controlled Phase 1 trial that enrolled 605 patients, two randomized, double-blind, crossover design, when-sham-controlled Phase 1 trial that enrolled 605 patients, and two open-label studies that enrolled 44 patients. A total of 742 adults received an active treatment with an active treatment that delivered a 0.5 mg dose of lidocaine, while 773 received placebo. The most common adverse reactions occurring in adults were erythema (2.9% of Zingo™-treated patients), and in 0.6% of placebo-treated patients. Pruritus occurred in 9.4% of Zingo™-treated patients and in 6.2% of placebo-treated patients. Petechiae occurred in 46.4% of Zingo™-treated patients, and in 7.0% of placebo-treated patients. In adults, erythema occurred in 67.3% of Zingo™-treated patients, and in 25.0% of placebo-treated patients. Pruritus occurred in 3.8% of Zingo™-treated patients and in 0.7% of placebo-treated patients. The most common systemic adverse reactions were nausea (2%) and vomiting (1%). Adverse events occurred in more than two patients in either treatment group. The most common systemic adverse reaction was dizziness, which occurred in 0.9% of active-treated patients and in 0.1% of placebo-treated patients. Burns (0.1% active, 0.3% sham placebo), and vesicle formation (0.1% active, 2.2% sham placebo) were the most common cutaneous adverse reactions occurring in adults.

6.2 Labor and Delivery
When used in labor and delivery, the use of lidocaine for labor conversion analgesia has not been associated with an increased incidence of adverse fetal effects, other than delivery during the neonatal period. Should Zingo™ be used concomitantly with other products containing lidocaine, total doses contributed by all formulations must be considered.

8.3 Nursing Mothers
Zingo™ is contraindicated in nursing women; therefore, caution should be exercised when Zingo™ is administered to a nursing mother. Because no pharmacokinetic data of lidocaine are detected after topical administration of Zingo™, it is advisable to avoid breastfeeding during or after Zingo™ treatment. Nipple burning may occur in the breast milk of women that took lidocaine, but it is not likely to occur only by a sucking infant in order to cause adverse effects.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients below the age of 3 years has not been established.

8.5 Geriatric Use
Of the 602 patients evaluated in a Phase 3 randomized, double-blind, sham-placebo-controlled trial, 66 were 65 years or older and the safety and effectiveness of Zingo™ was similar to that of Zingo™ in adults under 65 years of age.

9 DRUG ABUSE AND DEPENDENCE
Zingo™ is not known to possess drug abuse or dependence potential.

10 OVERDOSAGE
In the event of a single administration of the Zingo™ device, the plasma levels of lidocaine were below the limit of detection (5 ng/mL). Signs of central nervous system (CNS) toxicity may be observed. Signs of CNS toxicity as low as 10 ng/mL, and the risk of cardiac toxicity increases with increasing plasma levels. Very high levels of lidocaine can cause respiratory arrest, metabolic acidosis, and mental status changes, in addition to tremors, convulsions, and cardiac arrest. The toxicity of overdosage of lidocaine is thought to be at least additive. In the absence of reversal topical overdosage or oral ingestion, other therapeutics for the effect overdosage or those from overdose of lidocaine or other therapeutic drugs should be considered. The management of overdose in a hospital setting is supportive care, including monitoring, supportive care, and symptomatic treatment. Dialysis is of negligible value in the treatment of overdose of lidocaine.

11 DESCRIPTION
Zingo™ (lidocaine hydrochloride monohydrate) powder intradermal injection system contains 0.5 mg of sterile lidocaine hydrochloride monohydrate. The chemical name is 2-diethylamino-2',6' acetoxylidide, monohydrochloride, monohydrate. The molecular formula is C14H22N2O · HCl · H2O with a molecular weight of 288.8 Da. Lidocaine hydrochloride monohydrate is a local anesthetic of the amide class, having the following structural formula:

15 14 22 2 0
\[C \cdot H \cdot N \cdot O \cdot HCl \cdot H2O\]