UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

Delenator Stevens, individually and on behalf of all others similarly situated, Plaintiff, v. Walgreen Co., Defendant.	CASE NO. 21-cv-10603 **CLASS ACTION COMPLAINT** **JURY TRIAL DEMANDED**

Plaintiff Delenator Stevens ("Plaintiff") brings this action on behalf of himself and all others similarly situated against Defendant Walgreen Co. ("Defendant"). Plaintiff makes the following allegations pursuant to the investigation of his counsel and based upon information and belief, except as to the allegations specifically pertaining to himself, which are based on personal knowledge.

INTRODUCTION

1. This is a putative class action lawsuit on behalf of purchasers of Defendant's lidocaine patches (the "Lidocaine Patches").[1] Defendant markets, sells and distributes the Lidocaine Patches through numerous brick-and-mortar Walgreens retail locations and online through www.walgreens.com.

[1] The Lidocaine Patches include Defendant's "Pain Relieving Lidocaine Patch (5 patches)"; "Pain Relieving Lidocaine Patch (6 patches)"; "Pain Relieving Lidocaine Patches"; and "Cool n' Heat Lidocaine Patch."

2. Lidocaine is a topical anesthetic that is used to treat pain by blocking the transmission of pain signals from nerve endings in the skin to the spinal cord and brain. Specifically, lidocaine functions by blocking sodium channels located on nerve endings which prevents action potential from propagating in the nerve cell and thereby interrupting the transmission of the pain signal.

3. Although lidocaine patches are often prescribed by doctors, Defendant offers its Lidocaine Patches over-the-counter to unsuspecting consumers under false pretenses. Defendant takes advantage of these consumers by prominently displaying on the packaging of the Lidocaine Patches that the patches deliver a "Maximum Strength" dose of lidocaine while "Staying-put" for "up to 12 hours." Plaintiff and the proposed class members relied on those representations when making their purchases. To their dismay, however, Defendant's Lidocaine Patches regularly peel off their bodies within a few hours, and oftentimes minutes, after being properly applied, and do not deliver a maximum amount of lidocaine available in patch form.

4. As a result of its deceptive conduct, Defendant is, and continues to be, unjustly enriched at the expense of its customers.

JURISDICTION AND VENUE

5. This Court has original jurisdiction over the claims asserted herein individually and on behalf of the class pursuant to 28 U.S.C. § 1332, as amended by the Class Action Fairness Act of 2005. Subject matter jurisdiction is proper because: (1) the amount in controversy in this class action exceeds five million dollars, exclusive of interest and costs; (2) there are more than 100 Class members; (3) at least one member of the Class is diverse from the Defendant; and (4) the Defendant is not a governmental entity.

6. This Court has personal jurisdiction over Defendant because it conducts substantial business within New York, including the sale, marketing, and advertising of the Lidocaine Patches. Furthermore, a substantial portion of the events giving rise to Plaintiff's claims occurred in this State, including Plaintiff's purchases.

7. Venue is proper in this District pursuant to 28 U.S.C. § 1391 because Defendant does substantial business in this District and a substantial part of the events giving rise to Plaintiff's claims took place within this District.

THE PARTIES

8. Plaintiff Delenator Stevens is a citizen of New York, residing in New York, New York. Plaintiff Stevens purchased Defendant's "Pain Relieving Lidocaine Patch (5 patches)" for approximately $8.99; "Pain Relieving Lidocaine Patch (6 patches)" for approximately $11.49; "Pain Relieving Lidocaine Patches" for approximately $12.49; and "Cool n' Heat Lidocaine Patch" for approximately $9.49. Plaintiff Stevens purchased these Lidocaine Patches on various occasions within the applicable statute of limitations, with his most recent purchase taking place in July of 2021. Plaintiff Stevens made these purchases at Walgreens stores located in the Bronx and New York, New York. Prior to his purchases, Plaintiff Stevens saw that the Lidocaine Patches were labeled and marketed as "Maximum Strength" and "Stay-put flexible" and read the directions on the back label, which indicated that he could use "[o]ne patch for up to 12 hours." Plaintiff Stevens relied on Defendant's representations when he decided to purchase the Lidocaine Patches over comparable and less expensive pain-relieving patches or gels. Plaintiff Stevens saw those representations prior to and at the time of his purchases and understood them as a representation and warranty that the Lidocaine Patches would reliably adhere to his body and deliver a 4% lidocaine dose for 12 hours. Initially, Plaintiff Stevens became frustrated when

his Lidocaine Patches peeled off his body while engaging in regular activities—such as walking, sitting, stretching, and sleeping—well before the represented 12 hours, through no fault of his own. Plaintiff Stevens, nonetheless, continued to purchase other Lidocaine Patches, believing that such failures were the result of one-off manufacturing flukes. After giving the Lidocaine Patches the benefit of the doubt, however, Plaintiff Stevens stopped purchasing them altogether after realizing that the Lidocaine Patches consistently failed to "Stay-put" or deliver a 4% "Maximum Strength" lidocaine dose for "up to 12 hours." For example, on a couple of occasions, the Lidocaine Patches that Plaintiff Stevens bought peeled off his body within an hour or two after he properly applied them pursuant to the directions contained on the products—delivering little to no analgesic effect to his sore muscles. Plaintiff Stevens relied on Defendant's representations and warranties in deciding to purchase his Lidocaine Patches. Accordingly, those representations and warranties were part of the basis of his bargains, in that he would not have purchased his Lidocaine Patches on the same terms had he known those representations and warranties were false. However, Plaintiff Stevens remains interested in purchasing Defendant's Lidocaine Patches and would consider the Lidocaine Patches in the future if Defendant ensured that the products actually "[s]tay- put" and can deliver a 4% "Maximum Strength" dose of lidocaine to his body for "up to 12 hours." Additionally, in making his purchases, Plaintiff Stevens paid a substantial price premium due to Defendant's false and misleading claims regarding the qualities of its Lidocaine Patches. However, Plaintiff Stevens did not receive the benefit of his bargains because his Lidocaine Patches did not, in fact, "[s]tay-put" or deliver a 4% "Maximum Strength" dose of lidocaine to his body for "up to 12 hours."

9. Defendant Walgreen Co. ("Defendant") is an Illinois corporation with its principal place of business in Deerfield, Illinois. Defendant markets, sells, and distributes the

Lidocaine Patches and is responsible for the advertising, marketing, trade dress, and packaging of the Lidocaine Patches. Defendant marketed, distributed, and sold the Lidocaine Patches during the class period.

FACTUAL ALLEGATIONS

Defendant's False Advertising

10. Defendant markets, sells and distributes the Lidocaine Patches through numerous brick-and-mortar Walgreens retail locations and online through www.walgreens.com. On the Lidocaine Patches packaging, Defendant represents that its Lidocaine Patches are "Stay-put flexible" patches that can be applied "up to 12 hours." The Lidocaine Patches are all substantially similar, in that they all share the same adhesiveness misrepresentations:

11. By representing that Lidocaine Patches are "Stay-put flexible" patches that can be applied "up to 12 hours"[2]—a very specific number—Defendant induced Plaintiff and the proposed class members into believing that the Lidocaine Patches: (1) would continuously adhere to their bodies up to 12 hours; (2) were sufficiently flexible to withstand regular activities

[2] In the directions panel on the back label of each of the Lidocaine Patches, Defendant represents that consumer can "Use one patch for up to 12 hours." Exhibit A.

(such as walking, stretching, and sleeping) for someone who is suffering from sore muscles; and (3) would continuously relieve pain by providing a 4% lidocaine dose throughout the specified amount of time represented therein. Furthermore, by representing that the "Pain Relieving Lidocaine Patch (6 patches)" and "Pain Relieving Lidocaine Patches" (the "Maximum Strength Lidocaine Patches") provide "Maximum Strength," Defendant induced Plaintiff and the proposed class members into believing that the Maximum Strength Lidocaine Patches: (1) contain and deliver the maximum amount of lidocaine available in patch form; and (2) that they are superior, or at least equivalent, in efficacy and results to other over-the-counter and/or prescription-strength lidocaine patches.

12. Despite these representations, however, Defendant's Lidocaine Patches: (1) systematically fail to adhere to its consumers' bodies up to 12 hours; (2) are insufficiently flexible to withstand regular activities (such as walking, stretching, and sleeping); (3) fail to continuously relieve pain by providing a 4% lidocaine dose throughout the specified amount of time represented therein due to their partial or complete detachment; (4) do not provide the maximum amount of lidocaine available in patch form; and (5) are not superior, or at least equivalent, in efficacy and results to other over-the-counter and/or prescription-strength lidocaine patches.

Defendant's Knowledge of the Defective Lidocaine Patches

13. Defendant knew that its Lidocaine Patches did not live up to the adhesiveness representations contained therein based on dozens of complaints posted on its own website, www.walgreens.com, which Defendant actively monitors.

14. For example, in October of 2021, a buyer explained their issue trying to get a Lidocaine Patch to adhere to their body:

> "They don't stick to the skin well at all, the edges curl off with every movement, they're in a constant state of falling off. All the edges curl up from the moment you put them in and stick to any clothing or bedding rolling them up and pulling them off."[3]

15. In January of 2021, yet another consumer expressed their frustration using Defendant's Lidocaine Patch:

> "I bought these thinking they'd be better than they turned out to be. Scent free is about the only positive thing. They don't stick very well and if you have them under your cloths - normal moving around they fall off. Very disappointed but am unable to return them."[4]

16. Furthermore, Defendant knew, or should have known, that its Lidocaine Patches were defectively designed based on FDA reports and scientific studies regarding the efficacy of the products.

17. Specifically, Defendant's Lidocaine Patches work by delivering lidocaine through a transdermal mechanism—i.e., by delivering the analgesic chemical "through the dermis, or skin…in ointment or patch form."[5] According to FDA reports, transdermal drug delivery systems, such as the one used by Defendant, systematically fail to adhere to the body.[6] To that end, the FDA is in the process of finalizing an industry guidance on "Transdermal and Topical

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[3] https://www.walgreens.com/store/c/walgreens-lidocaine-pain-relief-patches/ID=prod6386698-product (last accessed December 10, 2021).
[4] https://www.walgreens.com/store/c/walgreens-lidocaine-patches/ID=300394242-product (last accessed December 10, 2021).
[5] https://medical-dictionary.thefreedictionary.com/transdermal (last accessed December 10, 2021).
[6] *See* Yellela S.R. Krishnaiah *FDA Perspectives on Product Quality of Transdermal Drug Delivery Systems*, PhD Division of Product Quality Research OTR/OPQ/CDER US Food and Drug Administration Silver Spring, MD, USA AAPS 2015_Sunrise Session (2015). https://healthdocbox.com/Deafness/74997073-Fda-perspectives-on-product-quality-of-transdermal-drug-delivery-systems.html (last accessed December 10, 2021).

Delivery Systems" to address, *inter alia*, "considerations for areas where quality is closely tied to product performance and potential safety issues, such as adhesion failure…"[7]

18. Even more alarming, the FDA Adverse Events Reporting System reports that approximately 70% of concerns stemming from lidocaine patches involve their poor adhesion.[8]

19. Furthermore, a peer-reviewed study published in January of 2021 by the Journal of Pain Research found that 0% of generic prescription lidocaine patches had a >90% adhesion rate to the study's subjects after 12 hours (i.e., essentially no part of the product lifting off the skin).[9] The study also found that after 12 hours, "37.5% of subjects experienced substantial detachment (to <10% adhesion) while using the generic lidocaine patch 5%, including 7 (29.1%) complete detachments." The study also found that the mean adhesiveness score of the generic lidocaine patches after 12 hours was 37.67% (where 0% reflects complete detachment and 50%

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[7] *See* 84 FR 64319 - *Transdermal and Topical Delivery Systems-Product Development and Quality Considerations; Draft Guidance for Industry*; Availability (2019) https://www.regulations.gov/document/FDA-2019-D-4447-0001 (last accessed December 10, 2021).

[8] *See* Gudin J, Nalamachu S. *Utility of lidocaine as a topical analgesic and improvements in patch delivery systems*. *Postgrad Med*. 2020;132(1):28–36. doi:10.1080/00325481.2019.1702296 https://www.tandfonline.com/doi/full/10.1080/00325481.2019.1702296 (last accessed December 10, 2021).

[9] See Gudin J, Webster LR, Greuber E, Vought K, Patel K, Kuritzky L. *Open-Label Adhesion Performance Studies of a New Lidocaine Topical System 1.8% versus Lidocaine Patches 5% and Lidocaine Medicated Plaster 5% in Healthy Subjects*. *J Pain Res*. 2021;14:513-526. Published 2021 Feb 23. doi:10.2147/JPR.S287153. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7914064/ (last accessed December 10, 2021). The study measured adhesion of the patches "immediately after application (0 hours) and at 3, 6, 9, and 12 hours (±15 minutes; before product removal) after application. Assessments in Study 1 were performed by a trained scorer using the FDA-recommended 5-point adhesion scale. The FDA scale ranges from 0 to 4, where 0 represents ≥90% of the product adhered (essentially no part of the product lifting off the skin), 1 represents 75% to <90% adhered (only some edges of the product lifting off the skin), 2 represents 50% to <75% adhered (less than half the product lifting off the skin), 3 represents >0% to <50% adhered (more than half the product lifting off the skin but not detached), and 4 represents 0% adhered (complete product detachment). The mean cumulative adhesion score was calculated by summing the scores at 3, 6, 9, and 12 hours and dividing the total by the total number of observations per subject." *Id.*

reflects half the product lifting off the skin but not detached). In contrast, the study found that a newly developed 1.8% lidocaine patch technology, which is bioequivalent to 5% lidocaine patches,[10] maintained a mean adhesion >90% across all time points (0, 3, 6, 9, and 12 h).

20. Although the study published by the Journal of Pain Research only tested generic prescription lidocaine patches, upon information and belief, Defendant's over-the-counter Lidocaine Patches—which have not undergone the rigorous approval process required by the FDA and use the same outdated and defective adhesion technology as the generic lidocaine patches[11] —fair no better.

21. Furthermore, while certain companies have innovated their technology based on clinical studies to ensure that their lidocaine patches reliably adhere to a consumer's body,[12] even while exercising,[13] upon information and belief, Defendant has not.

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[10] Gudin J, Argoff C, Fudin J, Greuber E, Vought K, Patel K, Nalamachu S. *A Randomized, Open-Label, Bioequivalence Study of Lidocaine Topical System 1.8% and Lidocaine Patch 5% in Healthy Subjects*. J Pain Res. 2020 Jun 22;13:1485-1496. doi: 10.2147/JPR.S237934. PMID: 32606914; PMCID: PMC7319520. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7319520/ (last accessed December 10, 2021).

[11] Defendant, whose Lidocaine Patches are manufactured in China, has not been approved by the FDA to market or sell its Lidocaine Patches despite being required to do so. The FDA is currently reviewing a Citizen Petition filed by Scilex Pharmaceuticals Inc. (a manufacturer of FDA-approved lidocaine patches) to remove from the market all over-the-counter lidocaine patches that lack FDA approval. *See* https://www.regulations.gov/docket/FDA-2019-P-0417/document (last accessed December 10, 2021).

[12] https://www.scilexpharma.com/scilex-presents-ztlido-data-on-superior-adhesion-over-lidocaine-patch-formulation/ (last accessed December 10, 2021).

[13] A separate study demonstrated that Scilex's lidocaine patches were able to reliably adhere when subjects engaged in moderate physical exercise (exercise bike) and heat (heating pad). *See* Fudin J, Wegrzyn EL, Greuber E, Vought K, Patel K, Nalamachu S. *A Randomized, Crossover, Pharmacokinetic and Adhesion Performance Study of a Lidocaine Topical System 1.8% During Physical Activity and Heat Treatment in Healthy Subjects*. *J Pain Res*. 2020;13:1359-1367. Published 2020 Jun 10. doi:10.2147/JPR.S238268. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7293912/#CIT0007 (last accessed December 10, 2021).

22. In complete disregard of the wealth of information to the contrary, however, Defendant continues to misrepresent that its Lidocaine Patches reliably adhere to its consumers' bodies up to 12 hours when, in fact, they do not. Defendant also failed to inform its consumers that the Lidocaine Patches are prone to even greater detachment when they engage in certain activities (such as walking, stretching, and sleeping). Nor is Defendant's representation that its Lidocaine Patches are capable of continuously relieving pain by providing a 4% lidocaine dose throughout the specified 12 hours true, given that they systematically fail to fully adhere to its consumers' bodies for that period. This is crucial because "[a]dequate adhesion is a critical quality attribute for topical delivery systems; if the product lifts or detaches during wear, dosing may be compromised and there is an increased risk of inadvertent exposure to others."[14]

23. To make matters worse, Defendant misrepresents, without providing adequate disclaimers, that its Maximum Strength Lidocaine Patches provide a "Maximum Strength" dose of lidocaine, when, in fact, there are superior lidocaine patches in the market that deliver a higher amount of lidocaine: including the previously mentioned 5% and 1.8% prescription-strength lidocaine patches.[15] Defendant compounds this problem by indicating that the Maximum Strength Lidocaine Patches are "Medicated"—thereby reinforcing the misrepresentation that its Maximum Strength Lidocaine Patches are comparable to prescription-strength lidocaine patches.

24. Furthermore, nothing in Defendant's Maximum Strength Lidocaine Patches indicates that they provide a greater dose of lidocaine in comparison to other over-the-counter lidocaine patches, including its own. Specifically, Defendant's representation that its Lidocaine Patches contain 4% lidocaine is misleading because the actual strength of a lidocaine patch is

[14] *See supra* footnote 10.
[15] *Id*.

measured by the "mass of drug relative to the mass of the adhesive per patch."[16] In other words, Defendant's representation that its Lidocaine Patches contain 4% lidocaine does not indicate the *actual* amount of lidocaine milligrams that its Lidocaine Patches deliver to a consumer's body.[17]

25. Shockingly, and by way of illustration, Defendant labels its "Pain Relieving Lidocaine Patch (6 patches)" as possessing "Maximum Strength" although it has the exact specifications and delivers the same amount of lidocaine as its non-maximum-strength "Pain Relieving Lidocaine Patch (5 patches)"—both Patches weigh 9 grams per patch and contain a lidocaine dose of 4 grams for every 100 grams.[18] Translated into milligrams, both Patches contain 360 milligrams of lidocaine per patch—although one of the Patches claims to possess "Maximum Strength," while the other one does not. Further, both of Defendant's Maximum Strength Lidocaine Patches contain less lidocaine than other over-the-counter lidocaine patches: which range from 411.4 to 4,500 milligrams.[19] Defendant's arbitrary and patently false claim regarding the strength of its Maximum Strength Lidocaine Patches goes beyond the pale.

26. Had Defendant not made the false, misleading, and deceptive misrepresentations and omissions alleged herein, Plaintiff and the proposed class members would not have

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[16] *See* Scilex Pharmaceuticals Inc.'s Citizen Petition. Exhibit B at pg. 19.

[17] "It is emphasized that most of these patch products are labeled as a percentage strength, without providing the total drug content per patch. For other topical dosage forms like creams, ointments, and lotions, the amount of drug administered can easily be determined by weighing the mass of product and applying the strength factor as illustrated in the table below. In contrast, the amount of drug applied for patch products cannot easily be determined because the exact mass of adhesive applied cannot be estimated due to the contributing mass of the backing materials. inasmuch as patches are manufactured in a variety of sizes and thicknesses, the drug exposure from patches is unknown and cannot be estimated by reviewing the product label, unless the manufacturer discloses the drug mass. Many of the patch products exclude this from their labels, and the absence of this information on unapproved OTC product labels creates a safety risk." Ex. B at pg. 20.

[18] https://www.dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=1a587e6e-88d1-4b01-abad-9a365dc64a4d (last accessed December 10, 2021).

[19] *See* Attachment 1 to Scilex Pharmaceuticals Inc.'s Citizen Petition. Exhibit C.

purchased the Lidocaine Patches or would not have paid as much as they did for those purchases. Thus, Plaintiff and the proposed class members suffered an injury in fact and lost money or property as a result of Defendant's wrongful conduct.

CLASS ACTION ALLEGATIONS

27. Plaintiff brings this action on behalf of himself and all other similarly situated persons pursuant to Federal Rules of Civil Procedure 23(a), (b)(1), (b)(2), and (b)(3).

28. The class periods shall be defined from the date of the filing of this Complaint, back to any such time the Court deems appropriate.

29. Plaintiff seeks to represent all persons in the United States who purchased Defendant's Lidocaine Patches (the "Class").

30. Plaintiff also seeks to represent a subclass of all Class members who purchased Defendant's Lidocaine Patches in New York (the "New York Subclass") (collectively with the Class, the "Classes").

31. The Classes do not include (1) Defendant, its officers, and/or its directors; or (2) the Judge to whom this case is assigned and the Judge's staff.

32. Plaintiff reserves the right to amend the above class definitions and add additional classes and subclasses as appropriate based on investigation, discovery, and the specific theories of liability.

33. ***Community of Interest***: There is a well-defined community of interest among members of the Classes, and the disposition of the claims of these members of the Classes in a single action will provide substantial benefits to all parties and to the Court.

34. ***Numerosity***: While the exact number of members of the Classes is unknown to Plaintiff at this time and can only be determined by appropriate discovery, upon information and belief, members of the Classes number in the millions. The precise number of the members of the Classes and their identities are unknown to Plaintiff at this time but may be determined through discovery. Members of the Classes may be notified of the pendency of this action by mail and/or publication through the distribution records of Defendant and third-party retailers and vendors.

35. ***Existence and predominance of common questions of law and fact***: Common questions of law and fact exist as to all members of the Classes and predominate over any questions affecting only individuals of the Classes. These common legal and factual questions include, but are not limited to:

(a) Whether the Lidocaine Patches are defective;

(b) Whether Defendant knew of the Lidocaine Patches' defective nature;

(c) Whether Defendant breached the express warranties on the Lidocaine Patches' packaging;

(d) Whether Defendant breached the Lidocaine Patches' implied warranty of merchantability;

(e) Whether Defendant breached the Lidocaine Patches' implied warranty of fitness for use;

(f) Whether Defendant's representations that the Lidocaine Patches are "Stay-put flexible" patches that can be applied "up to 12 hours" or otherwise provide "Maximum Strength" are false and misleading in violation of New York's consumer-protection statutes;

(g) Whether Plaintiff and the members of the Classes have suffered damages as a result of Defendant's actions and the amount thereof;

(h) Whether Plaintiff and the members of the Classes are entitled to statutory damages;

(i) Whether Plaintiff and the members of the Classes are entitled to restitution;

(j) Whether Plaintiff and the members of the Classes are entitled to injunctive relief to enjoin Defendant from further engaging in these wrongful practices; and

(k) Whether Plaintiff and the members of the Classes are entitled to attorney's fees and costs.

36. ***Typicality:*** The claims of the name Plaintiff are typical of the claims of other members of the Classes in that the name Plaintiff was exposed to Defendant's false and misleading marketing, purchased Defendant's defective Lidocaine Patches, and suffered a loss as a result of those purchases.

37. ***Adequacy***: Plaintiff will fairly and adequately represent and protect the interests of the Classes as required by Federal Rule of Civil Procedure Rule 23(a)(4). Plaintiff is an adequate representative of the Classes because he has no interests which are adverse to the interests of the members of the Classes. Plaintiff is committed to the vigorous prosecution of this action and, to that end, Plaintiff has retained skilled and experienced counsel, and by providing a cure-notice to Defendant regarding the Lidocaine Patches' defects on behalf of the members of the Classes to protect their interests.

38. ***Superiority:*** A class action is superior to all other available methods of the fair and efficient adjudication of the claims asserted in this action under Federal Rule of Civil Procedure 23(b)(3) because:

(a) The expense and burden of individual litigation makes it economically unfeasible for

members of the Classes to seek to redress their claims other than through the procedure of a class action;

(b) If separate actions were brought by individual members of the Classes, the resulting duplicity of lawsuits would cause members of the Classes to seek to redress their claims other than through the procedure of a class action; and

(c) Absent a class action, Defendant likely will retain the benefits of its wrongdoing, and there would be a failure of justice.

CAUSES OF ACTION

COUNT I
Violation of New York's Warranty Act, N.Y. U.C.C. § 2-313
(On Behalf of Plaintiff and the New York Subclass)

39. Plaintiff incorporates by reference each of the allegations contained in the foregoing paragraphs of this Complaint as though fully set forth herein.

40. Defendant's Lidocaine Patches are goods as defined in N.Y. U.C.C. § 2-105(1).

41. Plaintiff and the New York Subclass members are buyers as defined in N.Y. U.C.C. § 2-103(1)(a).

42. Defendant is a seller as defined in 15 N.Y. U.C.C. § 2-103(1)(d).

43. 15 N.Y. U.C.C. § 2-607 is satisfied because Plaintiff provided Defendant a reasonable opportunity to cure the defects contained in the Lidocaine Patches by sending Defendant a cure notice outlining those defects in full via certified mail on October 20, 2021.

44. N.Y. U.C.C. § 2-313 provides a cause of action to buyers when sellers breach express warranties.

45. On the Lidocaine Patches' packaging, Defendant expressly warranted that Lidocaine Patches are "Stay-put flexible" patches capable of providing pain relief by delivering a 4% lidocaine dose for "up to 12 hours."

46. Furthermore, on the Maximum Strength Lidocaine Patches packaging, Defendant expressly warranted that those Patches provide a "Maximum Strength" dose of lidocaine in comparison to other over-the-counter and/or prescription-strength lidocaine patches.

47. Those statements became the basis of the bargains for Plaintiff and the New York Subclass members because they are factual statements that a reasonable consumer would consider material when purchasing a lidocaine patch.

48. Defendant breached these express warranties by delivering Lidocaine Patches that: (1) systemically fail to adhere to its consumers' bodies up to 12 hours; (2) are insufficiently flexible to withstand regular activities (such as walking, stretching, and sleeping); (3) fail to continuously relieve pain by providing a 4% lidocaine dose throughout the specified amount of time represented therein due to their partial or complete detachment; (4) do not provide the maximum amount of lidocaine available in patch form; and (5) are not superior, or at least equivalent, in efficacy and results to other over-the-counter and/or prescription-strength lidocaine patches.

49. In so doing, Defendant breached N.Y. U.C.C. § 2-313.

50. As a direct and proximate result of Defendant's breach of its express written warranties, Plaintiff and the New York Subclass members have been damaged in an amount to be proven at trial.

COUNT II
Violation of New York's Warranty Act, N.Y. U.C.C. § 2-314
(On Behalf of Plaintiff and the New York Subclass)

51. Plaintiff incorporates by reference each of the allegations contained in the foregoing paragraphs of this Complaint as though fully set forth herein.

52. Defendant's Lidocaine Patches are goods as defined in N.Y. U.C.C. § 2-105(1).

53. Plaintiff and the New York Subclass members are buyers as defined in N.Y. U.C.C. § 2-103(1)(a).

54. Defendant is a seller as defined in 15 N.Y. U.C.C. § 2-103(1)(d).

55. 15 N.Y. U.C.C. § 2-607 is satisfied because Plaintiff provided Defendant a reasonable opportunity to cure the defects contained in the Lidocaine Patches by sending Defendant a cure notice outlining those defects in full via certified mail on October 20, 2021.

56. N.Y. U.C.C. § 2-314(1) creates an implied warranty of merchantability when a seller "is a merchant with respect to goods of that kind."

57. Defendant is a merchant as defined in 15 N.Y. U.C.C. § 2-104(1) because it deals in goods in the kind (i.e., selling Lidocaine Patches) and holds itself out as having knowledge or skill peculiar to the practices or goods involved (i.e., selling pharmaceutical goods).

58. For goods to be merchantable, they must be "fit for the ordinary purposes for which such goods are used." N.Y. U.C.C. § 2-314(2)(c).

59. Defendant breached its implied warranties of merchantability by selling to Plaintiff and the New York Subclass members Lidocaine Patches which systematically peeled off their bodies well before they ought to be fit as an analgesic for sore muscles.

60. In so doing, Defendant breached N.Y. U.C.C. § 2-314(2)(c).

61. For goods to be merchantable, they must also "conform to the promises or affirmations of fact made on the container or label if any." N.Y. U.C.C. §§ 2-314(2)(f).

62. On the Lidocaine Patches' packaging, Defendant promised and otherwise made affirmations of fact that the Lidocaine Patches are "Stay-put flexible" patches capable of providing pain relief by delivering a 4% lidocaine dose for "up to 12 hours."

63. Furthermore, on the Maximum Strength Lidocaine Patches packaging, Defendant promised and otherwise made affirmations of fact that those Patches provide a "Maximum Strength" dose of lidocaine in comparison to other available over-the-counter and/or prescription-strength lidocaine patches.

64. Defendant's Lidocaine Patches did not conform to those promises and affirmations of fact because they: (1) systemically fail to adhere to its consumers' bodies up to 12 hours; (2) are insufficiently flexible to withstand regular activities (such as walking, stretching, and sleeping); (3) fail to continuously relieve pain by providing a 4% lidocaine dose throughout the specified amount of time represented therein due to their partial or complete detachment; (4) do not provide the maximum amount of lidocaine available in patch form; and (5) are not superior, or at least equivalent, in efficacy and results to other over-the-counter and/or prescription-strength lidocaine patches.

65. In so doing, Defendant breached N.Y. U.C.C. § 2-314(2)(f).

66. As a direct and proximate result of Defendant's breach of its implied warranties of merchantability, Plaintiff and the New York Subclass members have been damaged in an amount to be proven at trial.

COUNT III
Violation of New York's Warranty Act, N.Y. U.C.C. § 2-315
(On Behalf of Plaintiff and the New York Subclass)

67. Plaintiff incorporates by reference each of the allegations contained in the foregoing paragraphs of this Complaint as though fully set forth herein.

68. Defendant's Lidocaine Patches are goods as defined in N.Y. U.C.C. § 2-105(1).

69. Plaintiff and the New York Subclass members are buyers as defined in N.Y. U.C.C. § 2-103(1)(a).

70. Defendant is a seller as defined in 15 N.Y. U.C.C. § 2-103(1)(d).

71. 15 N.Y. U.C.C. § 2-607 is satisfied because Plaintiff provided Defendant a reasonable opportunity to cure the defects contained in the Lidocaine Patches by sending Defendant a cure notice outlining those defects in full via certified mail on October 20, 2021.

72. N.Y. U.C.C. § 2-315 provides a cause of action when "the seller at the time of contracting has reason to know any particular purpose for which the goods are required and that the buyer is relying on the seller's skill or judgment to select or furnish suitable goods."

73. Defendant knew that the Lidocaine Patches that it sold to Plaintiff and the New York Subclass members were designed for the specific purpose of providing analgesic effects to sore muscles.

74. Lacking the requisite pharmacological knowledge to evaluate the efficacy of the Lidocaine Patches, Plaintiff and the New York Subclass members relied on Defendant's skill and judgment as a reputable pharmaceutical company when they chose to buy the Lidocaine Patches.

75. Defendant breached its implied warranties of fitness for use by selling to Plaintiff and the New York Subclass members Lidocaine Patches which systematically peeled off their bodies well before they ought to be fit as an analgesic for sore muscles.

76. In so doing, Defendant breached N.Y. U.C.C. § 2-315.

77. As a direct and proximate result of Defendant's breach of its implied warranties of fitness for use, Plaintiff and the New York Subclass members have been damaged in an amount to be proven at trial.

COUNT IV
Violation Of The Magnuson-Moss Warranty Act, 15 U.S.C. § 2301, *et seq.*
(On Behalf of Plaintiff and the Class)

78. Plaintiff incorporates by reference each of the allegations contained in the foregoing paragraphs of this Complaint as though fully set forth herein.

79. 15 U.S.C. § 2310(d) is satisfied because Plaintiff properly invokes jurisdiction under the Class Action Fairness Act ("CAFA").

80. 15 U.S.C. § 2310(e) is satisfied because Plaintiff provided Defendant a reasonable opportunity to cure the defects contained in the Lidocaine Patches by sending Defendant a cure notice outlining those defects in full via certified mail on October 20, 2021.

81. 15 U.S.C. § 2310(d)(1) provides a cause of action to "a consumer who is damaged by the failure of a supplier, warrantor, or service contractor to comply with any obligation… under a written warranty, implied warranty, or service contract."

82. Defendant's Lidocaine Patches are consumer products as defined in 15 U.S.C. § 2301(1).

83. Plaintiff and the Class members are consumers as defined in 15 U.S.C. § 2301(3).

84. Defendant is a supplier and warrantor as defined in 15 U.S.C. §§ 2301(4) and (5).

85. 15 U.S.C. § 2301(6)(A) defines "written warranty" as "any written affirmation of fact or written promise made in connection with the sale of a consumer product by a supplier to a buyer which relates to the nature of the material or workmanship and affirms or promises that

such material or workmanship…will meet a specified level of performance over a specified period of time."

86. Defendant provided Plaintiff and the Class members "written warranties" within the meaning of 15 U.S.C. § 2301(6) by providing written promises and affirmations of fact on the Lidocaine Patches' packaging that the Lidocaine Patches are "Stay-put flexible" patches capable of providing pain relief by delivering a 4% lidocaine dose for "up to 12 hours."

87. Furthermore, on the Maximum Strength Lidocaine Patches packaging, Defendant provided written promises and affirmations of fact that those Patches provide a "Maximum Strength" dose of lidocaine in comparison to other over-the-counter and/or prescription-strength lidocaine patches.

88. Those statements became the basis of the bargains for Plaintiff and the Class members because they are factual statements that a reasonable consumer would consider material when purchasing a lidocaine patch.

89. Defendant breached these express warranties by delivering Lidocaine Patches that: (1) systemically fail to adhere to its consumers' bodies up to 12 hours; (2) are insufficiently flexible to withstand regular activities (such as walking, stretching, and sleeping); (3) fail to continuously relieve pain by providing a 4% lidocaine dose throughout the specified amount of time represented therein due to their partial or complete detachment; (4) do not provide the maximum amount of lidocaine available in patch form; and (5) are not superior, or at least equivalent, in efficacy and results to other over-the-counter and/or prescription-strength lidocaine patches.

90. Further, Defendant breached its implied warranties of merchantability and fitness for use due to its breaches of N.Y. U.C.C. §§ 2-314, 15, as set forth above. 15 U.S.C. § 2301(7).

91. As a direct and proximate result of Defendant's breach of its express and implied warranties, Plaintiff and the Class members have been damaged in an amount to be proven at trial.

COUNT V
Violation of New York G.B.L. § 349
(On Behalf of Plaintiff and the New York Subclass)

92. Plaintiff incorporates by reference each of the allegations contained in the foregoing paragraphs of this Complaint as though fully set forth herein.

93. New York's General Business Law § 349 prohibits deceptive acts or practices in the conduct of any business, trade, or commerce.

94. In its sale of Lidocaine Patches throughout the State of New York, at all relevant times herein, Defendant conducted business and trade within the meaning and intendment of New York's General Business Law § 349.

95. Plaintiff and the New York Subclass members are consumers who purchased the Lidocaine Patches from Defendant for their personal use.

96. By the acts and conduct alleged herein, Defendant engaged in deceptive, unfair, and misleading acts and practices, which include, without limitation, (i) misrepresenting the efficacy of the Lidocaine Patches on their packaging (i.e., that they are "Stay-put flexible" patches capable of providing pain relief by delivering a 4% lidocaine for "up to 12 hours," despite their systematic failure to do so); (ii) omitting that the Lidocaine Patches are prone to even greater detachment when consumers engage in certain activities: such as walking, stretching, or sleeping; and (iii) misrepresenting that the Maximum Strength Lidocaine Patches provide a "Maximum Strength" dose of lidocaine in comparison to other over-the-counter and/or prescription-strength lidocaine patches when, in fact, the Maximum Strength Lidocaine Patches

do not provide the maximum amount of lidocaine available in patch form and are not superior, or at least equivalent, in efficacy and results to other over-the-counter and/or prescription-strength lidocaine patches.

97. The foregoing deceptive acts and practices were directed at consumers.

98. The foregoing deceptive acts and practices are misleading in a material way because they fundamentally misrepresent the intrinsic qualities of the Lidocaine Patches.

99. As a result of Defendant's deceptive practices, Plaintiff and the New York Subclass members suffered an economic injury because (a) they would not have purchased the Lidocaine Patches had they known the veracity of Defendant's misrepresentations and omissions, and (b) they overpaid for the Lidocaine Patches on account of such misrepresentations and omissions.

100. On behalf of himself and the New York Subclass members, Plaintiff seeks to enjoin the unlawful acts and practices described herein, to recover their actual damages or fifty dollars, whichever is greater, three times actual damages, and reasonable attorneys' fees and costs.

COUNT VI
Violation of New York G.B.L. §350
(On Behalf of Plaintiff and the New York Subclass)

101. Plaintiff incorporates by reference each of the allegations contained in the foregoing paragraphs of this Complaint as though fully set forth herein.

102. New York's General Business Law § 350 prohibits false advertising in the conduct of any business, trade, or commerce.

103. Defendant violated New York General Business Law § 350 by falsely advertising on the Lidocaine Patches' packaging that they are "Stay-put flexible" patches capable of

providing pain relief by delivering a 4% lidocaine dose for "up to 12 hours," when, in fact, they systematically fail to do so.

104. Furthermore, Defendant violated New York General Business Law § 350 by omitting that the Lidocaine Patches are prone to even greater detachment when consumers engage in certain activities: such as walking, stretching, or sleeping.

105. Finally, Defendant violated New York General Business Law § 350 by misrepresenting that the Maximum Strength Lidocaine Patches provide a "Maximum Strength" dose of lidocaine in comparison to other over-the-counter and/or prescription-strength lidocaine patches when, in fact, the Maximum Strength Lidocaine Patches do not provide the maximum amount of lidocaine available in patch form and are not superior, or at least equivalent, in efficacy and results to other over-the-counter and/or prescription-strength lidocaine patches.

106. The foregoing advertising was directed at consumers and was likely to mislead a reasonable consumer acting reasonably under the circumstances.

107. Defendant's misrepresentations and omissions have resulted in consumer injury or harm to the public interest.

108. As a result of Defendant's false advertising, Plaintiff and the New York Subclass members suffered an economic injury because (a) they would not have purchased the Lidocaine Patches had they known the veracity of Defendant's misrepresentations and omissions, and (b) they overpaid for the Lidocaine Patches on account of such misrepresentations and omissions.

109. On behalf of himself and the New York Subclass members, Plaintiff seeks to enjoin the unlawful acts and practices described herein, to recover their actual damages or five hundred dollars, whichever is greater, three times actual damages, and reasonable attorneys' fees and costs.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff, individually and on behalf of all others similarly situated, seeks judgment against Defendant, as follows:

(a) For an order certifying the Classes under Rule 23 of the Federal Rules of Civil Procedure; naming Plaintiff as representative of the Classes; and naming Plaintiff's attorney as Class Counsel to represent the Classes;

(b) For an order finding in favor of Plaintiff and the Classes on all counts asserted herein;

(c) For compensatory and punitive damages in amounts to be determined by the Court and/or jury;

(d) For prejudgment interest on all amounts awarded;

(e) For an order of restitution and all other forms of equitable monetary relief;

(f) For injunctive relief as pleaded or as the Court may deem proper; and

(g) For an order awarding Plaintiff and the Classes their reasonable attorneys' fees and expenses and costs of suit.

DEMAND FOR TRIAL BY JURY

Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiff demands a trial by jury of any and all issues in this action so triable as of right.

Dated: December 11, 2021

Respectfully submitted,

GUCOVSCHI ROZENSHTEYN, PLLC

By: *__/s/ Adrian Gucovschi__*
Adrian Gucovschi

Adrian Gucovschi
630 Fifth Avenue, Suite 2000
New York, NY 10111

Telephone: (212) 884-4230
E-Mail: adrian@gr-firm.com

Attorney for Plaintiff

EXHIBIT A

"Pain Relieving Lidocaine Patch (6 patches)"[1]

Drug Facts

Active ingredient . . . . . **Purpose**

Lidocaine 4.0% . . . . . Topical anesthetic

Use Temporarily relieves minor pain.

Warnings

For external use only

Do not use ■ More than one patch on your body at a time ■ On cut, irritated or swollen skin ■ On puncture wounds ■ For more than one week without consulting a doctor ■ If you are allergic to any active or inactive ingredients ■ If pouch is damaged or opened.

When using this product ■ Use only as directed ■ Read and follow all directions and warnings on this carton ■ Do not allow contact with the eyes ■ Do not use at the same time as other topical analgesics ■ Do not bandage tightly or apply local heat (such as heating pads) to the area of use ■ Do not microwave ■ Dispose of used patch in manner that always keeps product away from children and pets. Used patches still contain the drug product that can produce serious adverse effects if a child or pet chews or ingests this patch.

Stop use and consult a doctor if ■ Condition worsens ■ Redness is present ■ Irritation develops ■ Symptoms persist for more than 7 days or clear up and occur again within a few days ■ You experience signs of skin injury, such as pain, swelling or blistering where the product was applied.

If pregnant or breastfeeding, ask a health professional before use.

Keep out of reach of children and pets. If swallowed, get medical help or contact a Poison Control Center right away.

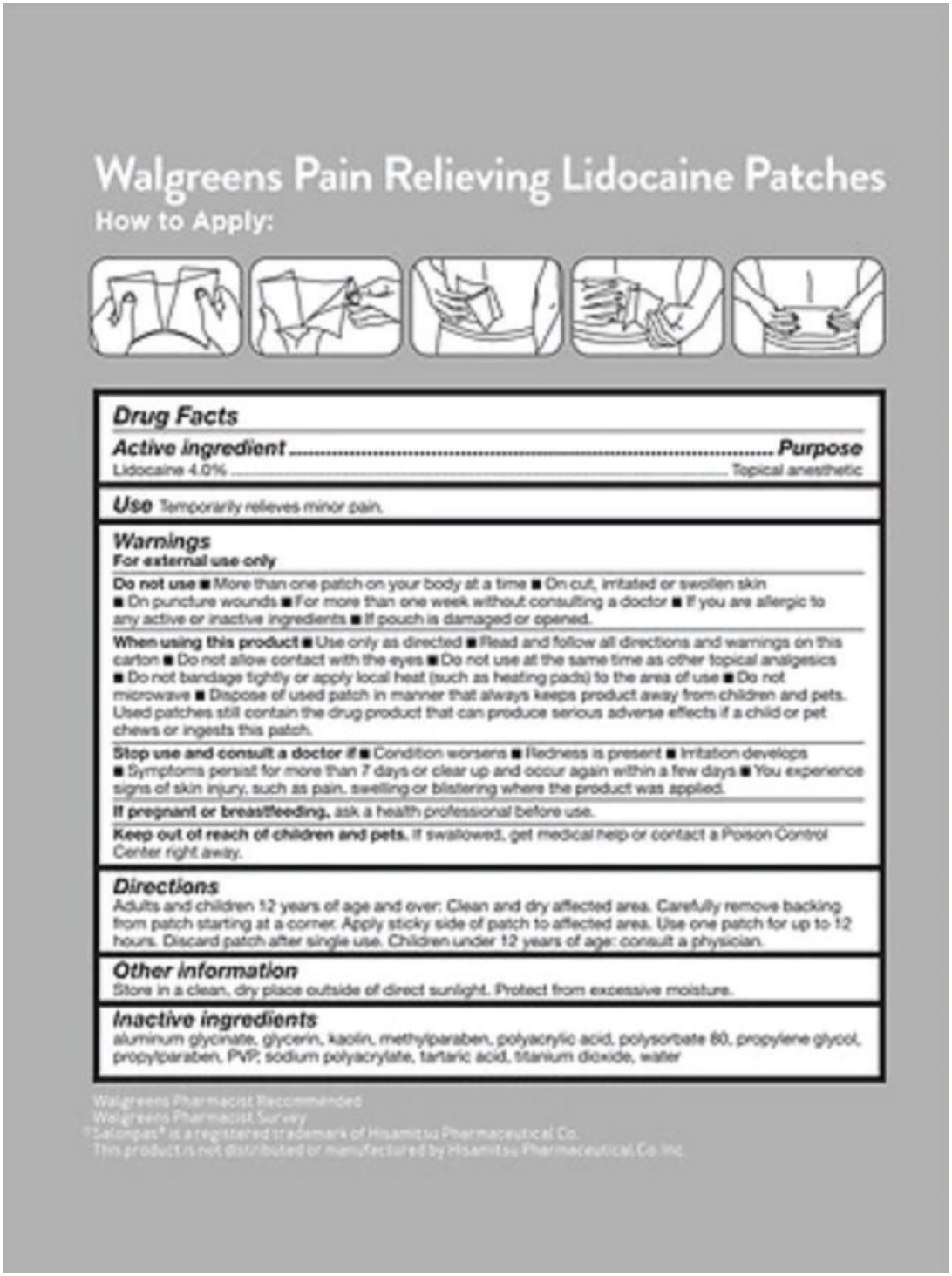
Directions Adults and children 12 years of age and over:
Clean and dry affected area. Carefully remove backing from patch starting at a corner. Apply sticky side of patch to affected area. Use one patch for up to 12 hours. Discard patch after single use.
Children under 12 years of age: consult a physician.

Other information

Store in a clean, dry place outside of direct sunlight. Protect from excessive moisture.

[1] https://www.walgreens.com/store/c/walgreens-lidocaine-pain-relief-patches/ID=prod6386698-product (last accessed November 22, 2021).

"Pain Relieving Lidocaine Patches"[2]



Walgreens Pain Relieving Lidocaine Patches

How to Apply:

Drug Facts

Active ingredient ..... **Purpose**

Lidocaine 4.0% ..... Topical anesthetic

Use Temporarily relieves minor pain.

Warnings

For external use only

Do not use ■ More than one patch on your body at a time ■ On cut, irritated or swollen skin ■ On puncture wounds ■ For more than one week without consulting a doctor ■ If you are allergic to any active or inactive ingredients ■ If pouch is damaged or opened.

When using this product ■ Use only as directed ■ Read and follow all directions and warnings on this carton ■ Do not allow contact with the eyes ■ Do not use at the same time as other topical analgesics ■ Do not bandage tightly or apply local heat (such as heating pads) to the area of use ■ Do not microwave ■ Dispose of used patch in manner that always keeps product away from children and pets. Used patches still contain the drug product that can produce serious adverse effects if a child or pet chews or ingests this patch.

Stop use and consult a doctor if ■ Condition worsens ■ Redness is present ■ Irritation develops ■ Symptoms persist for more than 7 days or clear up and occur again within a few days ■ You experience signs of skin injury, such as pain, swelling or blistering where the product was applied.

If pregnant or breastfeeding, ask a health professional before use.

Keep out of reach of children and pets. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

Adults and children 12 years of age and over: Clean and dry affected area. Carefully remove backing from patch starting at a corner. Apply sticky side of patch to affected area. Use one patch for up to 12 hours. Discard patch after single use. Children under 12 years of age: consult a physician.

Other information

Store in a clean, dry place outside of direct sunlight. Protect from excessive moisture.

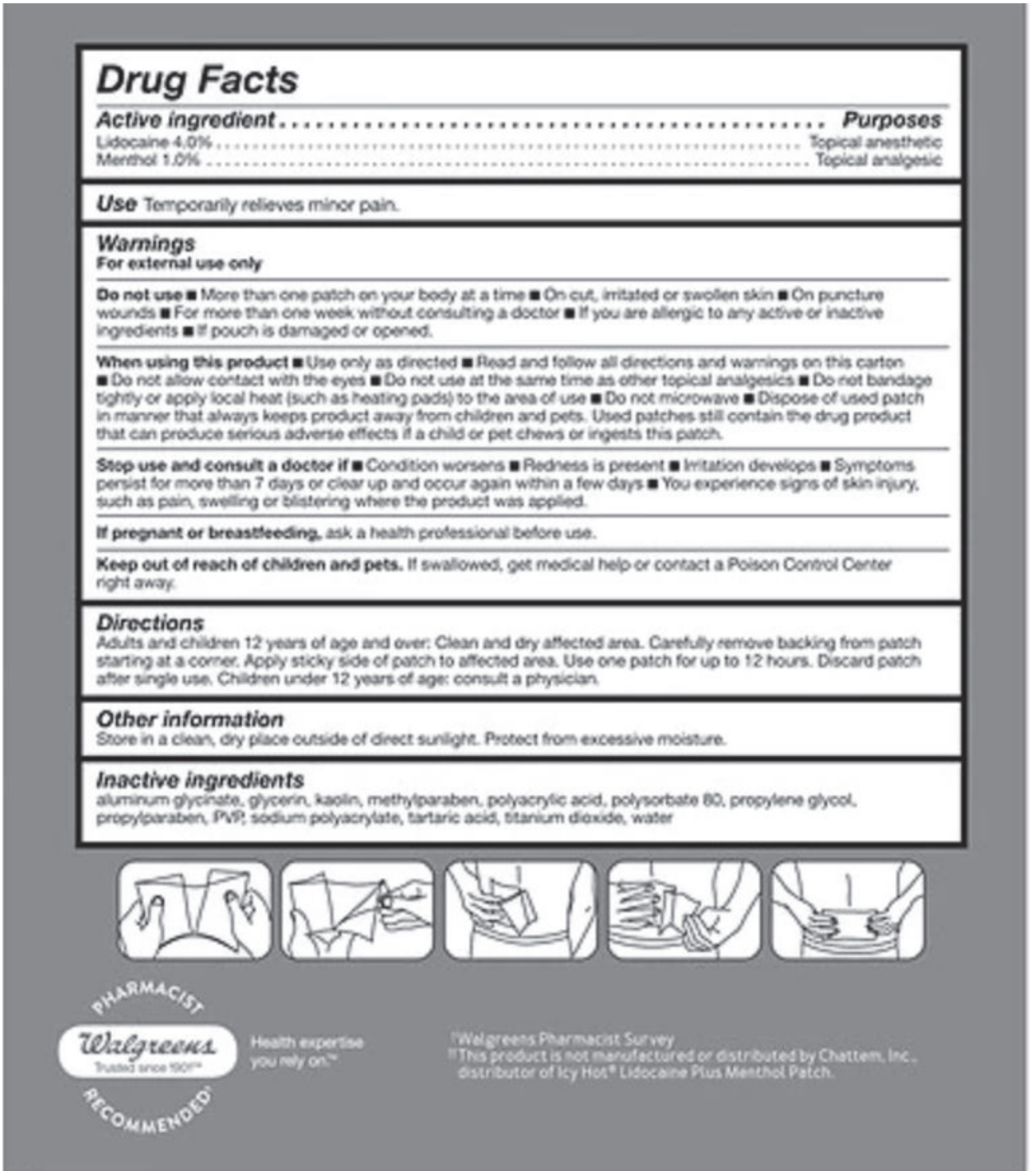
Inactive ingredients

aluminum glycinate, glycerin, kaolin, methylparaben, polyacrylic acid, polysorbate 80, propylene glycol, propylparaben, PVP, sodium polyacrylate, tartaric acid, titanium dioxide, water

Walgreens Pharmacist Recommended
Walgreens Pharmacist Survey
*Salonpas® is a registered trademark of Hisamitsu Pharmaceutical Co.
This product is not distributed or manufactured by Hisamitsu Pharmaceutical Co. Inc.

[2] https://www.walgreens.com/store/c/walgreens-lidocaine-pain-patches-assorted/ID=300394241-product (last accessed November 22, 2021).

"Cool n' Heat Lidocaine Patch"[3]



Drug Facts

Active ingredient — **Purposes**

Lidocaine 4.0% — Topical anesthetic

Menthol 1.0% — Topical analgesic

Use Temporarily relieves minor pain.

Warnings

For external use only

Do not use ■ More than one patch on your body at a time ■ On cut, irritated or swollen skin ■ On puncture wounds ■ For more than one week without consulting a doctor ■ If you are allergic to any active or inactive ingredients ■ If pouch is damaged or opened.

When using this product ■ Use only as directed ■ Read and follow all directions and warnings on this carton ■ Do not allow contact with the eyes ■ Do not use at the same time as other topical analgesics ■ Do not bandage tightly or apply local heat (such as heating pads) to the area of use ■ Do not microwave ■ Dispose of used patch in manner that always keeps product away from children and pets. Used patches still contain the drug product that can produce serious adverse effects if a child or pet chews or ingests this patch.

Stop use and consult a doctor if ■ Condition worsens ■ Redness is present ■ Irritation develops ■ Symptoms persist for more than 7 days or clear up and occur again within a few days ■ You experience signs of skin injury, such as pain, swelling or blistering where the product was applied.

If pregnant or breastfeeding, ask a health professional before use.

Keep out of reach of children and pets. If swallowed, get medical help or contact a Poison Control Center right away.

Directions

Adults and children 12 years of age and over: Clean and dry affected area. Carefully remove backing from patch starting at a corner. Apply sticky side of patch to affected area. Use one patch for up to 12 hours. Discard patch after single use. Children under 12 years of age: consult a physician.

Other information

Store in a clean, dry place outside of direct sunlight. Protect from excessive moisture.

Inactive ingredients

aluminum glycinate, glycerin, kaolin, methylparaben, polyacrylic acid, polysorbate 80, propylene glycol, propylparaben, PVP, sodium polyacrylate, tartaric acid, titanium dioxide, water

PHARMACIST RECOMMENDED

Walgreens

Trusted since 1901

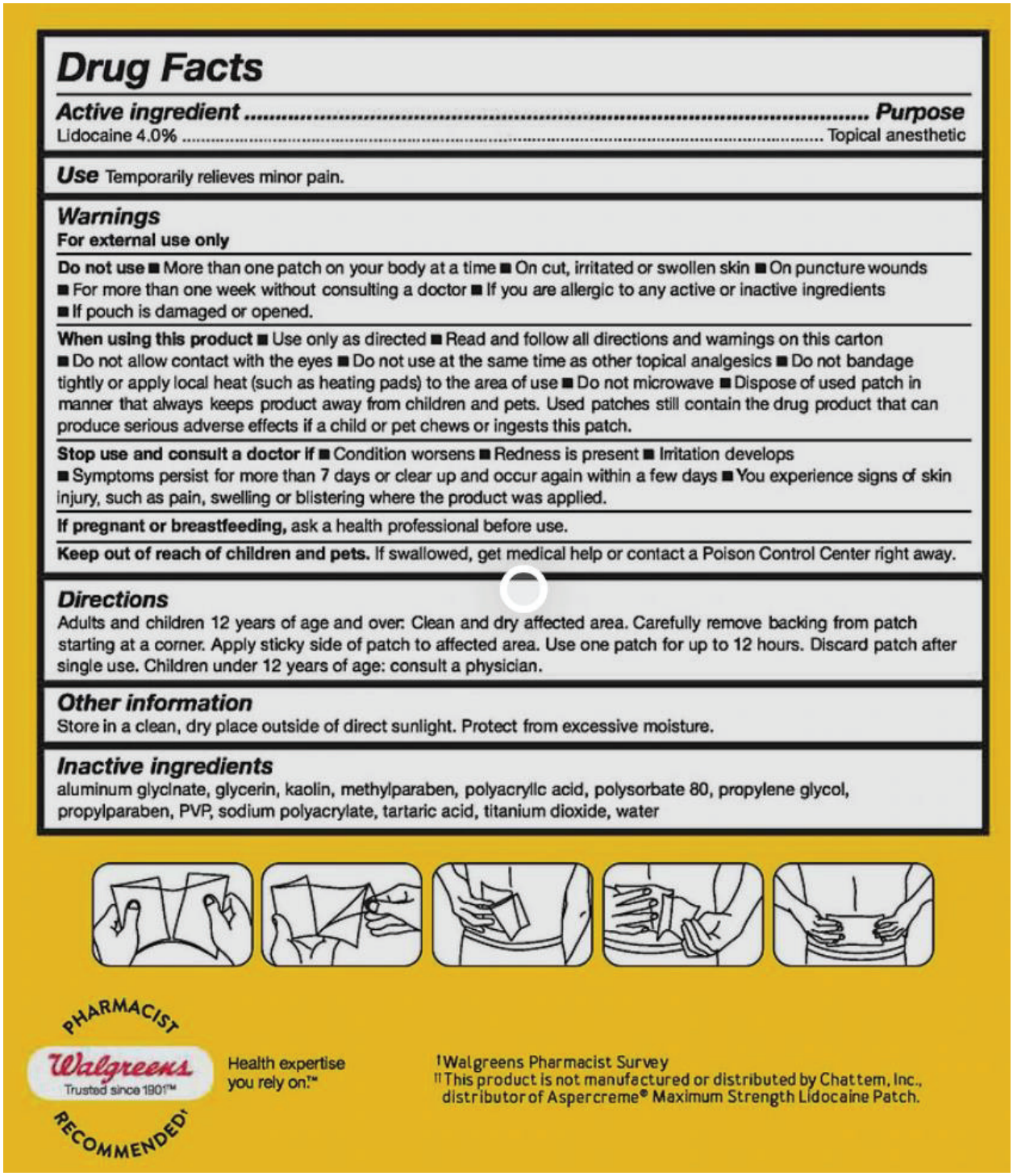
Health expertise you rely on.™

†Walgreens Pharmacist Survey

††This product is not manufactured or distributed by Chattem, Inc., distributor of Icy Hot® Lidocaine Plus Menthol Patch.

[3] https://www.walgreens.com/store/c/walgreens-cool-n'-heat-lidocaine-patches/ID=300394238-product (last accessed November 22, 2021)

"Pain Relieving Lidocaine Patch (5 patches)"[4]



Drug Facts

Active ingredient ..... **Purpose**
Lidocaine 4.0% ..... Topical anesthetic

Use Temporarily relieves minor pain.

Warnings
For external use only

Do not use ■ More than one patch on your body at a time ■ On cut, irritated or swollen skin ■ On puncture wounds ■ For more than one week without consulting a doctor ■ If you are allergic to any active or inactive ingredients ■ If pouch is damaged or opened.

When using this product ■ Use only as directed ■ Read and follow all directions and warnings on this carton ■ Do not allow contact with the eyes ■ Do not use at the same time as other topical analgesics ■ Do not bandage tightly or apply local heat (such as heating pads) to the area of use ■ Do not microwave ■ Dispose of used patch in manner that always keeps product away from children and pets. Used patches still contain the drug product that can produce serious adverse effects if a child or pet chews or ingests this patch.

Stop use and consult a doctor if ■ Condition worsens ■ Redness is present ■ Irritation develops ■ Symptoms persist for more than 7 days or clear up and occur again within a few days ■ You experience signs of skin injury, such as pain, swelling or blistering where the product was applied.

If pregnant or breastfeeding, ask a health professional before use.

Keep out of reach of children and pets. If swallowed, get medical help or contact a Poison Control Center right away.

Directions
Adults and children 12 years of age and over: Clean and dry affected area. Carefully remove backing from patch starting at a corner. Apply sticky side of patch to affected area. Use one patch for up to 12 hours. Discard patch after single use. Children under 12 years of age: consult a physician.

Other information
Store in a clean, dry place outside of direct sunlight. Protect from excessive moisture.

Inactive ingredients
aluminum glycinate, glycerin, kaolin, methylparaben, polyacrylic acid, polysorbate 80, propylene glycol, propylparaben, PVP, sodium polyacrylate, tartaric acid, titanium dioxide, water

[4] https://www.walgreens.com/store/c/walgreens-lidocaine-patches/ID=300394242-product (last accessed November 22, 2021).

EXHIBIT B

SCILEX PHARMACEUTICALS

December 28, 2018

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

CITIZEN PETITION

Scilex Pharmaceuticals, Inc. ("Scilex") submits this Citizen Petition under 21 U.S.C. §§ 321, 352, and 355 and 21 C.F.R. § 10.30 to request that the Commissioner of Food and Drugs ("FDA" or "Agency") take the following actions with respect to unapproved, lidocaine-containing drug products in patch, plaster, poultice, and comparable delivery systems (abbreviated collectively hereafter as "patches" or "patch dosage forms"). A continuing stream of such products are unlawfully distributed in interstate commerce, outside the scope of FDA's over-the-counter ("OTC") drug monograph development process for external analgesic drugs or any reasonable enforcement discretion. Most significantly, as discussed in Section B.4 of this petition, these products raise important patient and third-party safety and effectiveness questions, demand enhanced controls, and should properly be vetted as part of FDA's other current activities to apply modern regulatory science and controls to patch dosage forms and their complex delivery mechanisms.

A. ACTION REQUESTED

Scilex respectfully requests that FDA:

1. Initiate all administrative and judicial actions necessary to remove from the market, and to prevent the further marketing of, lidocaine-containing drug products in patch, plaster, poultice, or comparable delivery systems that have not been approved pursuant to a new

drug application ("NDA") or an abbreviated new drug application ("ANDA") submitted under 21 U.S.C. § 355 and implementing regulations;[1]

2. Strictly apply the provisions of 21 U.S.C. § 355, 21 C.F.R. Part 330, and related regulatory decisions, which do not allow the marketing or distribution of lidocaine-containing patch dosage form drug products that were introduced into United States ("U.S.") commerce after the OTC drug review was initiated on May 11, 1972;[2]

3. Finalize the Tentative Final Monograph for External Analgesic Drug Products for Over-the-Counter Human Use, as amended[3] (the "TFM" or "External Analgesics TFM"), which expressly excludes lidocaine-containing products in patch dosage forms from its scope because of concerns about the safety and efficacy of these products;

4. Publish an immediately applicable enforcement policy guidance document that will apply until the final OTC External Analgesics Monograph is codified, and that affirms that lidocaine-containing drug products marketed in nonprescription patch dosage forms ("OTC lidocaine patches") and that are marketed without approved NDAs or ANDAs do not conform to the terms of the External Analgesics TFM, are outside the scope of any enforcement discretion that may exist pursuant to Compliance Policy Guide 450.200[4] or

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[1] For clarity, this petition is focused on lidocaine-containing patch dosage form drug products, and does not address the lidocaine-containing cream, lotion, or ointment dosage form drug products that were reviewed as part of the OTC External Analgesic Monograph development process. This petition also does not address non-lidocaine external analgesic patch, plaster, or poultice dosage forms that may be marketed under the External Analgesics TFM, but acknowledges that the issues (and requested actions) in this petition may apply to the broader category.

[2] 21 C.F.R. § 330.13(e) (establishing that conditions for marketing ingredients recommended for OTC use under the OTC drug review "appl[y] only to conditions under consideration as part of the OTC drug review initiated on May 11, 1972, and evaluated under the [expert panel review and monograph development] procedures set forth in § 330.10." Separate regulations apply to OTC drugs initially marketed in the U.S. after the OTC drug review began in 1972. Id. (cross-referencing 21 C.F.R. § 330.14).

[3] 48 Fed. Reg. 5852, Feb. 8, 1983, amended by 68 Fed. Reg. 42324, July 17, 2003 ("FDA is amending the tentative final monograph ... to clarify the status of patch, plaster, or poultice dosage forms for OTC external analgesic drug products.... This proposed rule indicates that these dosage forms have not been determined to be generally recognized as safe and effective for any OTC external analgesic drug products at this time" (emphasis added)).

[4] FDA, Compliance Policy Guide Sec. 450.200, "Drugs – General Provisions and Administrative Procedures for Recognition as Safe and Effective" (revised March 1995), available at https://www.fda.gov/iceci/compliancemanuals/compliancepolicyguidancemanual/ucm074388.htm.

other relevant statements of enforcement discretion, and may be the subject of immediate enforcement action without further notice;[5] and

5. Initiate and regularly review drug listing and other marketplace information to identify lidocaine-containing products in patch dosage forms and take appropriate administrative and judicial action to ensure their compliance with the Federal Food, Drug, and Cosmetic Act, implementing regulations, and findings pursuant to this petition.

B. STATEMENT OF GROUNDS

1. Introduction

Patch dosage forms are complex drug delivery systems, and the biopharmaceutics are highly dependent on the formulation and material construct. Patches can deliver drugs to the stratum corneum or upper layers of the skin (as in the case of topical dermatological products); through the stratum corneum to the nerves in dermis (as in the case of topical analgesic products); or through the skin to enter systemic circulation (as in the case of transdermal products). To mediate delivery through the skin, the drug must be formulated in an appropriate vehicle, consisting of adhesives, solvents, and in some cases chemical penetration enhancers, to ensure effective delivery to the site action. This complex drug-vehicle formulation is coated on a backing material that provides an occlusive or semi-occlusive physical barrier that can help drive sustained drug delivery to the skin. The selection of formulation adhesives, active ingredient(s) and differing salt forms, permeation enhancers, and solvents have consequences for product performance both in terms of drug flux and adhesion. The physical nature of the adhesive layer(s) and thickness in combination with different types of backing materials also provide varying levels of occlusion that directly impact drug flux.

Patch technology has evolved immensely since the first patch product for scopolamine was approved by the FDA in 1979.[6] Early patch designs contained drug reservoirs in which a drug was suspended within a semisolid matrix and encapsulated within a pouch that adhered to the skin, with drug delivery controlled by a rate-controlling membrane. Newer products feature thinner, drug-in-matrix formulations manufactured by solvent casting or hot-melt

[5] The Agency recently published a similar guidance titled "Enforcement Policy – Over-the-Counter Sunscreen Drug Products Marketed Without an Approved Application; Guidance for Industry; Availability," 83 Fed. Reg. 23917, May 23, 2018.

[6] See NDA 017874.

processes.[7,8] FDA has recognized the innovations in patch drug delivery technology and manufacturing over the past several decades and the significance of patch performance characteristics to safe and effective use in human patients.[9] Recognition of these complexities has led to FDA's formation of the Center for Drug Evaluation and Research ("CDER") Transdermal Working Group that participates in the review of these product types and is involved in developing science-based regulatory standards to help industry with patch product development and manufacturing. The Generic Drug User Fee Amendments ("GDUFA"), first enacted in 2012 and recently updated, also established a regulatory science research program that has enabled FDA to develop and publish several detailed guidances for industry related to topical and transdermal product development and to fund research on how safety risks related to patches are affected by product formulation and design. These standards are being applied to new, generic, and OTC products reviewed under NDA and ANDA regulations; however, there is no regulatory mechanism to implement and enforce these important standards to products that are subject (or claim to be subject) to OTC monographs per 21 C.F.R. § 330.13. FDA is also recognizing new topical and transdermal patches (broadly categorized as topical or transdermal "system" dosage forms) as combination drug-device products requiring implementation of both drug and device quality compliance standards (see 21 C.F.R. Parts 210, 211, and 4) in their development and commercial manufacturing with supportive market application review by the Center for Devices and Radiological Health ("CDRH").

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[7] Paudel KS, Milewski M, Swadley CL, Brogden NK, Ghosh P, Stinchcomb AL. "Challenges and opportunities in dermal/transdermal delivery." *Ther. Deliv.* 2010; 1(1):109-31.

[8] Kandavilli S, Nair V, Panchagnula R. "Polymers in transdermal drug delivery systems." *Pharm. Tech.* 2002; 26(5):62-80.

[9] E.g., FDA, "Assessing Adhesion With Transdermal and Topical Delivery Systems for ANDAs; Revised Draft Guidance for Industry; Availability," 83 FR 50942, Oct. 10, 2018 (acknowledging that factors such as surface area dosed and product adherence impact drug delivery, variability, and unintentional exposure of third parties); FDA, "Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for Abbreviated New Drug Applications; Draft Guidance for Industry; Availability," 83 Fed. Reg. 50945, Oct. 10, 2018 (discussing, for example, that the components and composition of a transdermal ("TDS") formulation, including the nature of the drug substance and/or the degree to which the TDS materials occlude the transmission of water vapor from the skin, in conjunction with other factors such as environmental humidity or the condition of the skin, may have the potential to irritate the skin or lead to a sensitization reaction, and that reactions can be unpleasant, affect patient compliance, and/or adhesion of the TDS to the skin). See also FDA Public Workshop addressing current regulatory science initiatives concerning topical dermatological drug products, Oct. 20, 2017 (discussing complexity of formulations and complexity of dermatological routes of administration, among other topics); Strasinger C, Raney SG, Tran DC, Ghosh P, Newman B, Bashaw ED, Ghosh T, Shukla CG. "Navigating sticky areas in transdermal product development." *J Control. Release.* 2016; 233:1-9; Choi SH, Wang Y, Conti DS, Raney SG, Delvadia R, Leboeuf AA, Witzmann K. "Generic drug device combination products: Regulatory and scientific considerations." *Int. J. Pharm.* 2018; 544(2):443-454. The academic scholarship uses the broader term "transdermal" when addressing these dosage forms, but is addressing the scope of both topical and transdermal drug delivery.

Patches are an attractive dosage form for topical analgesic agents, because drug delivery can be localized to the affected areas for a sustained amount of time, first-pass hepatic metabolism is avoided, and systemic exposure is limited relative to other routes of administration, such as oral. Lidocaine is a small-molecule, amide-type local anesthetic agent that stabilizes neuronal membranes by inhibiting the ionic fluxes required for the initiation and conduction of impulses and is amenable to topical administration. Lidocaine has been approved for prescription use for topical and injection anesthesia, and is used intravenously in the control of cardiac arrhythmias. Several topical prescription lidocaine products have been approved pursuant to NDAs or ANDAs for anesthetic and analgesic indications, as shown in Table 1.

FDA has also considered lidocaine for nonprescription (OTC) uses. Following specific review of the available data, the ingredient lidocaine was classified as Category I (generally recognized by qualified experts as safe and effective ("GRAS/E") and not misbranded) in the final OTC monograph for anorectal drug products.[10] It was also determined to be GRAS/E and not misbranded as a male genital desensitizer in spray dosage form in accordance with the External Analgesics final monograph.[11] Lidocaine cream, ointment, and lotion dosage forms were included in the External Analgesics TFM as a treatment for temporary pain and itch relief associated with minor burns, sunburns, cuts, scrapes and minor skin irritations.[12] A comparison of the prescription and nonprescription topical lidocaine formulations and dosage forms is provided in Table 1.

Table 1 Topical Lidocaine Prescription and Over-the-Counter Drug Products*

Product	Strength	Dosage Form(s)	Indication	Regulatory Status[13] (Reference Listed Drug Application Number, if applicable)
Lidocaine	5%	Ointment	Indicated for production of anesthesia of accessible mucous membranes of the oropharynx; it is also useful as an anesthetic lubricant for intubation and for the temporary relief of pain associated with minor burns, including sunburn, abrasions of the skin, and insect bites	Prescription (ANDA 080198)

[10] 55 Fed. Reg. 31776, Aug. 3, 1990.

[11] 57 Fed. Reg. 27654, Jun. 19, 1992.

[12] 48 Fed. Reg. 5852, Feb. 8, 1983.

[13] FDA recognizes lidocaine's use in OTC drug products for oral healthcare but has determined there are inadequate data to establish general recognition of safety and effectiveness for this use. 21 C.F.R. § 310.545(a)(14).

Product	Strength	Dosage Form(s)	Indication	Regulatory Status[13] (Reference Listed Drug Application Number, if applicable)
Lidocaine HCl	4%	Solution	Indicated for the production of topical anesthesia of accessible mucous membranes of the oral and nasal cavities and proximal portions of the digestive tract	Prescription (ANDA 088803)
XYLOCAINE® (lidocaine HCl)	2%	Jelly	Indicated for prevention and control of pain in procedures involving the male and female urethra, for topical treatment of painful urethritis, and as an anesthetic lubricant for endotracheal intubation (oral and nasal)	Prescription (NDA 008816)
EMLA® (lidocaine; prilocaine)	2.5%; 2.5%	Cream	Topical anesthetic for use on: - normal intact skin for local analgesia - genital mucous membranes for superficial minor surgery and as pretreatment for infiltration anesthesia	Prescription (NDA 019941)
PLIAGLIS® (lidocaine; tetracaine)	7%; 7%	Cream	Topical local analgesia for superficial dermatological procedures such as dermal filler injection, pulsed dye laser therapy, facial laser resurfacing, and laser-assisted tattoo removal	Prescription (NDA 021717)
ZINGO™ (lidocaine HCl)	0.5 mg	Powder	Indicated for use on intact skin to provide topical local analgesia prior to venipuncture or peripheral intravenous cannulation, in children 3–18 years of age and adults	Prescription (NDA 022144)
LIDODERM® (lidocaine)	5%	Patch	Pain associated with post-herpetic neuralgia	Prescription (NDA 020612)
ZTLIDO™ (lidocaine)	1.8%	Patch	Pain associated with post-herpetic neuralgia	Prescription (NDA 207962)
SYNERA® (lidocaine; tetracaine)	70 mg; 70 mg	Patch	Local anesthetic indicated for use on intact skin to provide local dermal analgesia for superficial venous access and superficial dermatological procedures such as excision, electrodessication and shave biopsy of skin lesions	Prescription (NDA 021623)
Lidocaine	2 – 5%	Cream, Lotion, Ointment	Temporary relief of local discomfort associated with hemorrhoids	Nonprescription 21 C.F.R. § 346.10(f) Anorectal Drug Products for OTC Human Use Final Monograph
Lidocaine	10 mg	Spray	Male genital desensitizer	Nonprescription 21 C.F.R. § 348.10(a)(2) External Analgesics for OTC Human Use
Lidocaine and lidocaine HCl	0.5% - 4%	Cream, Ointment, Lotion	Temporary relief of pain and itch associated with minor burns, sunburn, minor cuts, scrapes, insect bites or minor skin irritations	Nonprescription External Analgesics Tentative Final Monograph, 1983

* Data on prescription topical lidocaine products is from the Orange Book ("Approved Drug Products with Therapeutic Equivalence Evaluations"; November 2018). Application numbers correspond to the Orange Book Reference Listed Drug; generic equivalents may also have been approved. Discontinued topical lidocaine products are not included.

While lidocaine has a long history as a prescription and nonprescription drug product dating back to the 1940s, safety issues – particularly with topical delivery – continue to be recognized, prompting several FDA public health advisories in recent years.

In 2007, FDA issued a public health advisory following reports of several serious adverse events, including the deaths of two women, aged 22 and 25 years old, who had applied topical anesthetics to their legs to lessen the pain of laser hair removal. The pharmacy-compounded cream formulations contained multiple anesthetics including lidocaine. The women wrapped their legs with plastic wrap to increase the creams' numbing effects. FDA noted that "anesthetic drugs in these products can pass through the skin into the blood stream, and if too much gets into the blood, patients can experience serious harm. More drug passes into the blood stream when the product is applied over a large area of skin, when it stays on the skin for a long time, and when the skin is covered after application of the cream. Anesthetic drugs may also pass into the blood stream if the skin is irritated or has a rash, or if the skin temperature goes up. Exercise, covering the skin with a wrap, or use of a heating pad can all increase the skin temperature."[14] In 2009, FDA again warned about potential serious adverse events associated with topical lidocaine, when it issued a public health advisory on the risks of lidocaine use during mammography or other medical procedures and warned these risks increase "after covering the skin with any type of material or dressing."[15]

In 2018, FDA issued a safety announcement on the risk of methemoglobinemia, a potentially fatal blood disorder caused by local anesthetics, and required manufacturers of all prescription local anesthetics to standardize warning information about the risk of methemoglobinemia in product labeling across this class of products.[16] While most of the adverse events were associated with oral benzocaine used for teething and mouth pain, case reports were identified in the literature where patients developed methemoglobinemia while

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[14] Public Health Advisory: Life-Threatening Side Effects with the Use of Skin Products Containing Numbing Ingredients for Cosmetic Procedures, Feb 6, 2007. Available at: https://wayback.archive-it.org/7993/20171105015424/https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm054718.htm.

[15] Public Health Advisory: Potential Hazards of Skin Products Containing Numbing Ingredients for Relieving Pain from Mammography and Other Medical Tests and Conditions, Jan. 16, 2009. Available at: https://wayback.archive-it.org/7993/20171105132310/https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm110625.htm.

[16] Safety Announcement: Risk of serious and potentially fatal blood disorder prompts FDA action on oral over-the-counter benzocaine products used for teething and mouth pain and prescription local anesthetics, May 23, 2018. Available at: https://www.fda.gov/Drugs/DrugSafety/ucm608265.htm.

using 5% topical lidocaine patches[17,18] or combination lidocaine/prilocaine creams.[19] Patients with glucose-6-phosphate dehydrogenase deficiency, congenital or idiopathic methemoglobinemia, cardiac or pulmonary compromise, infants under 6 months of age, and patients with concurrent exposure to oxidizing agents or their metabolites are more susceptible to developing clinical manifestations of the condition. Prescription topical anesthetics are labeled with warnings related to methemoglobinemia along with guidance to closely monitor for associated symptoms and signs of the effect, and the fact that the products and other oxidizing agents should be discontinued in specific circumstances. The warnings also note that patients may warrant supportive care (i.e., oxygen therapy or hydration) with severe clinical presentation requiring treatment with methylene blue, exchange transfusion, or hyperbaric oxygen. The prescription labels also outline risks associated with concomitant use of other drugs associated with methemoglobinemia.

OTC lidocaine product manufacturers (subject to the 1983 External Analgesics TFM) were not required to update their labeling to warn about the risk of methemoglobinemia or the risks associated with concomitant use with other drugs associated with the condition. Manufacturers voluntarily adding warnings or administration modifications not included in the External Analgesics TFM (unless otherwise subject to an Agency directive) may result in the product being out of compliance with the monograph and ultimately considered a misbranded drug product.

Although lidocaine is generally considered to be a safe and effective drug ingredient for many purposes, these recent safety issues highlight that, when lidocaine is applied topically, a significant amount of drug can be absorbed that can result in serious, sometimes life-threatening, adverse events. While the products leading to these advisories were not patch products, they all showed that drug concentration, vehicle, occlusion, and area of exposure are factors that can contribute to this risk. Patch products, by their nature, are occlusive, as the skin is covered by a physical barrier consisting of an adhesive layer, or layers, on a backing material. FDA recognized this potential safety issue comparing lidocaine patches versus cream/lotion OTC formulations in its review of the NDA for prescription lidocaine patch, Lidoderm®: "Topical lidocaine 0.5% to 4% is recognized as an effective topical analgesic for

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[17] Weingarten TN, Gleich SJ, Craig JR, Sprung J. "Methemoglobinemia in the Setting of Chronic Transdermal Lidocaine Patch Use." *Pain Medicine*. 2012; 13: 976-977.

[18] Acevedo FA, Kim EJ, Chyatte DA, Nielsen VG. "Rare cause of delirium and hypoxemia after coronary bypass surgery: transdermal lidocaine patch-associated methemoglobinemia." *Int. J. Legal Med.* 2018; 132: 767 – 769.

[19] Shamriz O, Cohen-Glickman I, Reif S, Shteyer E. "Methemoglobinemia Induced by Lidocaine-Prilocaine Cream." *IMAJ* 2014; 16:250-254.

purposes of the external analgesic tentative final monograph. Either increasing the concentration to 5% or adding an occlusive dressing should be considered to provide at least much as much efficacy (**but would raise questions of safety**)" [emphasis added].[20]

While the External Analgesics TFM concerns OTC lidocaine products in cream, ointment, or lotion dosage forms, unfortunately, OTC lidocaine patches have been marketed under the guise of being compliant with the TFM in recent years (Attachment 1). Of particular concern, these patches can differ significantly in design, drug load, residual drug, product size and shape, and heat effects, all of which present safety and efficacy issues that should be evaluated against all applicable regulatory standards established for these products, prior to marketing. The NDA and ANDA approval processes consider product characteristics and performance on a product-specific basis, taking into account the latest developments in regulatory science, and safeguarding against ineffective and/or unsafe products in the market. The present, unapproved marketing of OTC lidocaine patches *undermines the applicable regulatory process and subverts FDA's role in protecting public health*, exposing consumers to products that have not demonstrated clinical benefit and may pose significant safety risks.

FDA previously proposed and should affirm for several reasons discussed herein – the most significant of which is safety – that lidocaine-containing patch dosage form drug products are outside the scope of the External Analgesics TFM. Indeed, given current and future advancements in patch technology for improving drug delivery (i.e., amount of delivered drug and level of percutaneous absorption), these safety risks require and deserve careful consideration.

2. Lidocaine-Containing Patch Dosage Form Drug Products Are Outside the Scope of the External Analgesics TFM

FDA created the OTC drug review program in 1972 "to evaluate the safety and effectiveness of OTC drug products marketed in the United States before May 11, 1972."[21] In fact, the Agency regulations governing the OTC drug review expressly state: "This section applies only to conditions under consideration as part of the OTC drug review initiated on May 11, 1972, and evaluated under the procedures set forth in § 330.10."[22]

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[20] NDA 020612 Summary Basis of Approval, Deputy Director's Review, Dec 2, 1998.

[21] FDA, "Over-the-Counter (OTC) Drug Monograph Process," available at https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/ucm317137.htm.

[22] 21 C.F.R. § 330.13(e).

The Agency and the courts have both recognized that the OTC drug review was a retrospective approach to apply 1962 statutory amendments to the Federal Food, Drug, and Cosmetic Act to a large number of OTC products, with a common group of active ingredients, that were already in the marketplace:

> In 1962, Congress amended the definition of "new drugs" to include all drugs "not generally recognized among experts ... as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof." Drugs first marketed before 1938 were exempted from both the safety and efficacy requirements of the Act provided that they were not subsequently relabeled. Similarly, drugs marketed between 1938 and 1962 as GRAS, and thus without an NDA, were exempted from the newly-imposed efficacy requirement as long as the conditions for use suggested by the labeling remained unchanged.
>
> ...The efficacy requirement became operative immediately for drugs not classified as "new drugs." For such drugs to be classified as GRAS/E, there must be an "expert consensus ... founded upon 'substantial evidence'" of the drug's effectiveness and safety.
>
> ...In 1972, upon completion of the [Drug Efficacy Study Implementation (DESI) Review of products that had been marketed pursuant to new drug applications], FDA turned its attention to pharmaceuticals marketed under the Act's GRAS/E exemption, which include primarily over-the-counter drugs.... A drug efficacy study undertaken by the National Academy of Science-National Research Council (NAS-NRC) had concluded, after reviewing 420 drugs broadly representative of the OTC market that only one-fourth of the drugs reviewed were actually effective. In response, FDA began a comprehensive review of all OTC drugs to determine whether they were properly marketable under the GRAS/E exemption. Instead of evaluating each of the hundreds of thousands of those drugs individually, however, FDA classified the medications according to their comparatively few active ingredients, and directed the OTC drug review to be conducted in four phases. First, advisory panels of qualified experts are appointed to *analyze existing test data* and make recommendations in the form of monographs establishing the conditions under which each OTC drug could be marketed without an NDA. In Phase II, FDA reviews these monographs and publishes them in the Federal Register for public comment on the *safety and effectiveness of the products under examination*. The third stage of the program obligates FDA to review comments, to publish a tentative final monograph, and to offer the public the opportunity to object formally ... to the *findings made*

> *with respect to individual drugs*. In the fourth and final part of the OTC review, FDA promulgates a final monograph containing the agency's conclusive and legally binding determinations on the conditions under which a drug is considered GRAS/E.[23]

Both the 1979 Advanced Notice of Proposed Rulemaking ("ANPR") entitled "External Analgesic Drug Products Monograph for Over-The-Counter Human Use; Establishment of a Monograph and Notice of Proposed Rulemaking,"[24] and 1983 External Analgesics TFM identified multiple active ingredients – including lidocaine -- that were found to be GRAS/E at specified concentrations and labeling for use as OTC topical analgesics in cream, ointment, and lotion dosage forms. Analgesic patches were not, however, originally considered by FDA during the 1979 ANPR, nor were they included in the External Analgesics TFM published in 1983.[25] In 2003, FDA affirmatively considered the coverage of patch dosage forms when responding to an industry request to market counterirritant products pursuant to the External Analgesics TFM. Following review, FDA explained that the expert panel had discussed poultices and plasters with respect to only one counterirritant active ingredient (allyl isothiocynate), and further explained that the Agency had "surveyed several standard texts that listed currently marketed topical drug products containing counterirritants and did not find any plaster or poultice dosage forms listed therein."[26]

Scilex has been unable to identify evidence that the expert panel or FDA considered lidocaine-containing patch products in the course of developing the TFM. No relevant products have been identified in more recent submissions to FDA.[27]

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[23] Cutler v. Hayes, 818 F.2d 879 (D.C. Cir. 1987; emphasis added).

[24] 44 Fed. Reg. 69768, Dec 4, 1979.

[25] 48 Fed. Reg. 5852, Feb. 8, 1983.

[26] 68 Fed. Reg. at 42325. Cf. Letter from William Gilbertson, Pharm.D., Director, Monograph Review Staff, Office of OTC Evaluation, Center for Drug Evaluation and Research to AAC Consulting Group (Dec. 10, 1993) (Attachment 2) (Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products "was especially concerned about vehicles that could increase absorption. ... Ointments, pastes, creams, and oleaginous vehicles were discussed..., but not gels. In fact, a gel dosage form was not marketed at the time the Panel evaluated this ingredient. Based on that discussion, we do not currently find a gel dosage form to be acceptable for 1 percent hydrocortisone drug products without further information.").

[27] For example, the Consumer Healthcare Products Association ("CHPA") has continued to submit information concerning counterirritant patch dosage forms to the docket; however, these submissions do not provide information or attempt to argue that lidocaine-containing patch products are within the scope of the TFM. E.g., Letter from CHPA to Docket No. 78N-0301, Feb. 27, 2012 (Attachment 3).

Attachment 1 identifies drug listings and initial marketing dates for currently marketed lidocaine-containing patch dosage form products purportedly compliant with the External Analgesics TFM identified from FDA's current DailyMed database.[28] Although we acknowledge that this database may not be comprehensive, it includes information prepared by product sponsors. From the sponsors' submitted information, it seems clear that lidocaine OTC patch products have been introduced into the U.S. market decades after 1972.

3. Lidocaine-Containing Patch Dosage Form Drug Products Are "New Drugs" Within the Scope of the Federal Food, Drug, and Cosmetic Act and Require Product-Specific Evaluations and Approval

The External Analgesics TFM does not include conditions under which lidocaine-containing OTC patch drug products might be generally recognized as safe and effective and not misbranded. For example, the directions for use in the TFM do not address how to apply and remove a patch, and the dosage forms covered by the monograph do not address patches. In fact, the considerations below show that there is lack of consensus about the safety or effectiveness of patches, and they must be regulated as "new drugs" in accordance with 21 U.S.C. § 321(p).[29]

The inclusion of only cream, ointment, and lotion dosage forms was challenged after the publication of the TFM, with ***requests from manufacturers to include alternate dosage forms like gels or patches; however, FDA maintained the inclusion of select dosage forms was***

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[28] Available at dailymed.nlm.nih.gov.

[29] The term "new drug" includes "any drug ... the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a 'new drug' if at any time prior to June 25, 1938, it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use." It also includes "any drug ... the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions." 21 U.S.C. §321(p). Any contention that a drug product is generally recognized as safe and effective within the meaning of 21 U.S.C. § 321(p) is required to be supported by submission of the same quantity and quality of scientific evidence that is required to obtain approval of a new drug application for the product. 21 C.F.R. § 314.200(e)(1). Scilex is aware that FDA adopted a regulation setting forth criteria and procedures by which certain OTC drugs initially marketed in the U.S. after the OTC drug review began in 1972 might be considered within the OTC drug monograph system (i.e., time and extent applications). However, that regulation requires both (1) a determination that a condition appears to be generally recognized as safe and effective for OTC use in the U.S., and (2) a subsequent public process, with opportunity for interested parties to submit comments and data. To Scilex's knowledge, neither of these events has occurred (nor could they be justified).

purposeful because only dosage forms marketed at the time the TFM was drafted were considered in determining whether the ingredient was GRAS/E for OTC human use.[30,31] In 2003, FDA reopened the Administrative Record of the External Analgesics TFM to classify patches, poultices, and plasters as Category III conditions (more data needed) and to expressly exclude them – *with respect to all products, not only counterirritants* – from the monograph. In the 2003 revision to the External Analgesic TFM, FDA proposed amending the introductory language in 21 C.F.R. §§ 348.10 and 348.12 to include the following language:

> The active ingredients of the product consist of any of the following, within the established concentration for each ingredient, *but not for use in a patch, plaster, or poultice dosage form.*[32]

In the proposed rule preamble, FDA was explicit with its rationale relative to safety and effectiveness:

> FDA stated (Ref. 5) that in order for poultice and plaster dosage forms to be generally recognized as safe and effective and to develop any additional labeling that may be needed for such dosage forms, it is necessary to obtain more information, specifically:
>
> 1. The safe and effective concentration of the drug ingredient(s), especially under the occlusion of a plaster.
> 2. Data on percutaneous absorption under occlusion.
> 3. The length of contact time that it is safe to leave the poultice or plaster on the skin; how often the plaster or poultice needs to be changed for effective use.
> 4. The frequency of application that is considered safe and effective.
> 5. Whether or not directions and a warning are necessary regarding checking the area at specified intervals for erythema to prevent blistering, and what time intervals are recommended.

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[30] Letter from William Gilbertson, Pharm.D., Director, Monograph Review Staff, Office of OTC Evaluation, CDER, FDA to AAC Consulting Group Inc. on excluding a hydrocortisone gel dosage form for OTC use (Dec. 10, 1993) (see n. 26, *supra*). See also 68 Fed. Reg. 42324, 42325, July 17, 2003 (specific to the External Analgesic TFM, FDA description of the Panel's limited discussion of a poultice or plaster with respect to a single counterirritant active ingredient, and further explaining that the Agency had "surveyed several standard texts that listed currently marketed topical drug products containing counterirritants and did not find any plaster or poultice dosage forms listed therein.").

[31] 68 Fed. Reg. at 42326.

[32] Id. (emphasis added).

6. The age groups for whom poultices and plasters are recommended for safe use.
7. Labeling of currently marketed products.[33]

FDA's concerns about patch dosage forms in 2003 can be supplemented with additional factors that are now appreciated to contribute to safety and efficacy of products delivered percutaneously. Beside factors related to dosing such as drug concentration, duration, surface area, frequency of use, and patient age that FDA outlined above, there are other factors that influence percutaneous absorption[34,35,36] and should be considered in determining whether a patch product may be considered safe and effective, namely:

- Vehicle-related factors: Drug concentration in a patch dosage form, by itself, does not inform on the percutaneous absorption potential. The solubility of the drug within the chosen adhesive matrix and effects of the vehicle on the skin integrity are known to affect drug bioavailability.

- Exposure and application-related factors: Drug absorption from patches may be affected by climate (heat and humidity); use during exercise; and where on the body the patch is applied, as it is appreciated that there is anatomical regional variation in absorption.

- Patient-related factors: In addition to age of the patient, general health, genetic differences, and differences in hair and pore density will contribute to population variability in drug absorption.

All of these factors are considered by FDA during their assessments of drug products in order to balance the risks against the benefit of a product. There is nothing inherent in OTC lidocaine patch products that suggest that these factors are benign to the consumers. Rather, the only formulation constraint for these products is the product strength (up to 4%), which

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[33] Id.

[34] Wester RC, Maibach HI. "Cutaneous pharmacokinetics: 10 steps to percutaneous absorption." *Drug Metab. Rev.* 1983; 14:169-205.

[35] Ngo MA, Maibach HI. "15 Factors of percutaneous penetration of pesticides." In: Knaak JB, Timchalk C, Tonero-Velez R, editors. Parameters for pesticide QSAR and PBPK/PD models of human risk assessment. Vol. 1099. Danvers (MA): Oxford University Press; 2012, p. 67-86.

[36] Li BS, Cary JH, Maibach HI. "Should we instruct patients to rub topical agents into skin? The evidence" *J. Dermatolog. Treat.* 2018; 19:1-5.

does not reconcile any of these factors relative to the amount of delivered drug, and the level and rate of percutaneous absorption of the drug.

There is precedent for treating OTC patch products pursuant to the NDA – rather than the monograph – process. In 2008, FDA approved NDA 022029 for Salonpas Pain Relief Patch (containing TFM ingredients methyl salicylate and menthol). The Deputy Division Director Review and Basis for Action explained FDA's findings:

> The active ingredients in this product were reviewed in 1979 by an Expert Panel for Over-the-Counter (OTC) Topical Analgesic Drug Products, and were found to be generally recognized as safe and effective (GRAS/E) (Category 1). However, the Tentative Final Monograph (TFM) for OTC External Analgesic Drug Products published by FDA in 1983 ... provides for topically applied ointments, lotions, or creams containing methyl salicylate in the range of 10%-60% and menthol in the range of 1.25%-16% ... but does not include this dosage form of topical patch. Hence, a New Drug Application was required to obtain approval for marketing.[37]

It appears that some of the OTC lidocaine patch manufacturers have recognized and tried to avoid the designation of the patch dosage form -- for example by labeling a product as a "pain relieving ointment on a breathable adhesive pad" [e.g., IcyHot Lidocaine Patch Plus Menthol; emphasis added].[38] The inference is that the product is actually an "ointment" in conformance with the External Analgesics TFM; however, the designation is undermined by the inclusion of "patch" in the formal product nomenclature and the notation of the number of "patches" included in the secondary packaging.

These product formulations identified as an "ointment on a breathable pad" do not meet the regulatory definition of an ointment. In accordance with the CDER Data Standards Manual (Dosage Form), an ointment is described as[39]:

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[37] NDA 022029, Memorandum from Sharon Hertz, M.D., Feb. 29, 2008, available at https://www.accessdata.fda.gov/drugsatfda_docs/nda/2008/022029TOC.cfm. See also Summary Review at 2. Despite containing active ingredients at levels allowed by the External Analgesics TFM and claiming an indication provided for by the TFM, formal review and approval of both clinical and nonclinical data on this formulation were required by the FDA before commercialization. The Summary Basis of Approval for Salonpas® Pain Relief Patch discusses the regulatory pathway for patches, noting, "Analgesic patch formulations are subject to approval via an NDA."

[38] See example labeling in Attachment 4.

[39] CDER Data Standards Manual (Dosage Form) available at: http://wayback.archive-it.org/7993/20171115111312/https://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/DataStandardsManualmonographs/ucm071666.htm.

> A semisolid dosage form, usually containing <20% water and volatiles and >50% hydrocarbons, waxes, or polyols as the vehicle. This dosage form is generally for external application to the skin or mucous membranes.

Whereas a patch is described as:

> A drug delivery system that often contains an adhesive backing that is usually applied to an external site on the body. Its ingredients either passively diffuse from, or are actively transported from, some portion of the patch. Depending upon the patch, the ingredients are either delivered to the outer surface of the body or into the body. A patch is sometimes synonymous with the terms "extended release film" and "system."

By their nature, these OTC patch formulations are not ointments, as ointments lack the necessary adhesive properties for the product to function properly (i.e., hydrocarbons, waxes and polyols lack these adhesive properties). Because the vehicle is adhesive, and applied to a backing material, these products are indeed "patches" as labeled in the product names.

Despite FDA's determination that patches should be excluded from the External Analgesics TFM in 2003, in the past ~5 years, approximately 100 patch products have been listed on DailyMed as OTC lidocaine patches. According to the self-reported drug product listing information, these drug products contain between 11-5000 mg lidocaine/patch.

At a minimum, current safety considerations demonstrate the questionable state of unapproved, marketed drug products. Specific issues regarding the safe and effective use of these products are described below.

4. <u>Safety and Effectiveness of OTC Lidocaine Patches Have Not Been Established</u>

a. Questions of Efficacy

i. Are OTC lidocaine patches effective for pain relief[40]?

As FDA discussed in the 2003 proposed rule to amend the External Analgesics TFM, safe and effective concentrations of active drug ingredients under occlusion need to be

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[40] Indication outlined in the External Analgesics TFM proposed 21 C.F.R. § 348.50(b)(2).

demonstrated before it can be determined whether external analgesic drugs are GRAS/E in this kind of dosage form with their specific labeling. Most of the currently marketed OTC lidocaine patch products contain lidocaine content of up to 4%, which was presumably chosen based on the acceptable concentration range of 0.5% to 4% in creams, lotions, and ointments, allowed under the External Analgesics TFM. However, the percentage of drug in a cream or ointment may not correlate with the percentage of drug per mass adhesive needed to be effective in a patch. Creams, lotions, and ointments are applied differently than patch products, typically by rubbing into the skin. FDA noted this in its review of the development program for the Salonpas® Pain Relief Patch, for example, which was formulated with l-menthol and methyl salicylate at concentrations allowed for creams, ointments, and lotions per the TFM:

> There is a concern about the efficacy of the proposed patch product because of the difference in the way of drug application between patch and cream/ointment products. The cream/ointment products have been massaged into the painful area to demonstrate analgesic efficacy, where the patch is applied directly to the painful area. The equivalence in systemic absorption alone is not considered sufficient to provide a bridge between the efficacy of these different formulation. ... Therefore, additional clinical studies to demonstrate efficacy of the drug combination patch against placebo patch are required. [41]

OTC lidocaine creams, ointments, and lotions also are applied by rubbing into the skin versus a patch application, which sits on top of the skin. As such, there are questions as to whether, and to what extent, lidocaine patch products formulated at concentrations contemplated by the external analgesic TFM would be effective for temporary pain relief. One recently appreciated phenomenon is that rubbing/massaging drugs into the skin can enhance percutaneous absorption of some drugs and is another factor that should be studied when formulating topical drug products.[42] How drug bioavailability compares from patch versus rubbed-in cream, lotion, and ointment dosage forms has not been characterized, and this

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[41] NDA 022029 Summary Basis of Approval, Administrative Comments. We note that the NDA process yielded pediatric study data leading FDA to find Salonpas Pain Patch ineffective in children, with exclusionary labeling required pursuant to the NDA ("Children under 18 years of age: Do not use; this product has not been shown to work in children."). In uncomfortable juxtaposition, multiple, unapproved Salonpas patches with similar formulation continue to be affirmatively labeled as appropriate for use in children 12 years of age and older. See FDA, Pediatric Postmarketing Pharmacovigilance Review for NDA 022029 (July 1, 2016), available at https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/PediatricAdvisoryCommittee/UCM519748.pdf.

[42] Li BS, Cary JH, Maibach HI. "Should we instruct patients to rub topical agents into skin? The evidence" *J. Dermatolog. Treat.* 2018; 19:1-5.

distinction in the method of application warrants further investigation because it may have consequences in determining whether patch products have the same safety and efficacy as OTC TFM-compliant dosage forms (i.e., creams, ointments and lotions).

ii. Are OTC lidocaine patch dosing regimens supported by adhesive performance?

One of the key differences between creams, ointments, and lotions versus topical patches is that patches are drug/device combination products. The efficacy of a patch product is inherently tied to its device performance characteristics; that is, its ability to remain adhered to the skin throughout the entire labeled wear period. FDA has recognized the criticality of adhesion to efficacy and safety of the patches[43] and in 2018 issued a draft guidance to industry emphasizing the relationship between adhesion and efficacy in patch development:

> The amount of drug delivered into and through the patient's skin from a TDS [transdermal or topical delivery system] is dependent, in part, on the surface area dosed. It is expected that entire contact surface area of a TDS should remain consistently and uniformly adhered to the patient's skin throughout the duration of wear under the conditions of use included in the product labeling. When a TDS loses its adherence during wear, the amount of drug delivered to the patient may be reduced.[44]

While this guidance is for generic topical systems (including patches) subject to an ANDA, the regulatory standard and underlying basis have been applied to new drug products subject to an NDA. The assessment of adhesion performance is expected to be evaluated under normal-wear conditions and exercise. Likewise, the Agency has required that the use of reinforcement measures (e.g., tape reinforcement and overlays) be characterized relative to their effects on biopharmaceutic performance.

As FDA stated in its 2003 External Analgesics amended TFM on patch dosage forms, in order to determine if patches, plasters and poultices are effective, more information is needed on the length of contact time the product needs to be placed on the skin and the frequency of application. Most of the patch products listed in Attachment 1 are labeled for 8 to 12 hours of

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[43] Wokovich AM, Prodduturi S, Doub WH, Hussain AS, Buhse LF. "Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute." *Eur. J. Pharm. Biopharm.* 2006; 64(1): 1-8.

[44] Guidance for Industry: Assessing Adhesion With Transdermal and Topical Systems for ANDAs, October 2018. Available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM504157.pdf.

wear, presumably based on the External Analgesics TFM that allows application of cream, ointment and lotion products not more than 3 or 4 times daily. It should be demonstrated that patch products are effective when used as directed and that the patch remains in contact with the skin throughout this period.

b. Questions of Safety

i. Is the drug load in OTC lidocaine patches safe?

While most OTC lidocaine patches claim a strength of up to 4% lidocaine, the total drug load in the patch can vary greatly. Strength is expressed as a mass of drug relative to the mass of the adhesive per patch; however, there are no uniform standards on the size or thickness of a patch. According to the DailyMed database, current or recently marketed OTC lidocaine patches contain between 11 and 5000 mg (a 500x greater drug load) lidocaine on a per unit basis (see Attachment 1), self-reported by the respective manufacturers. There are also varying sizes of OTC lidocaine patches up to 12 cm x 20 cm (e.g., Odor Free Aspercreme® Lidocaine Patch XL), which is nearly a two-fold increase in surface area exposure of prescription Lidoderm® 5% and associated generics (10 cm x 14 cm).

Patches containing hundreds of milligrams of lidocaine present a significant risk of overexposure, particularly if the patches are applied when skin temperature is elevated, for example, because a heating pad/blanket is used, or the patch is worn while using a sauna or hot tub. FDA has recognized that patch design and formulation may affect drug exposure in response to heat and has recently funded research efforts to better understand the effects of heat on generic patch products. Recent data from that initiative show application of heat enhanced drug delivery from prescription lidocaine patches, as serum lidocaine concentrations increased by up to ~5-7 fold after applying heating pad to the patch for 90 minutes.[45] Many of the OTC lidocaine patch products do not warn against heat exposure – although this is not surprising because the External Analgesics TFM did not review or provide coverage for patch products; therefore, the warnings in the TFM do not address unique aspects of this dosage form. Some manufacturers have voluntarily included warnings associated with heat exposure; however, these label additions are not contemplated by the External Analgesic TFM and consequentially may render these products misbranded.

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[45] Thomas S, Shukla S, Hammell D, Hazem H, Stinchcomb A. "In Vitro and In Vivo Evaluation of Two Lidocaine Topical Delivery Systems With or Without the Influence of Transient Heat Exposure." AAPS PharmSci360, Washington DC, Nov 4-7, 2018.

Patch drug load also presents safety risk for use during exercise. Exercise has been shown to increase skin perfusion of some transdermal patch products, likely due to vasodilation and increased blood circulation. The effects of exercise may be product-specific; for example, percutaneous absorption from nicotine and nitroglycerin patches increased during exercise;[46,47] however, no effect on pharmacokinetics was observed with norelgestromin and ethinyl estradiol patches.[48] Because biopharmaceutic performance for patch dosage forms is a function of the drug chemistry and formulation, each product should be individually evaluated for these effects. Most of the OTC lidocaine patches do not caution against exercising while wearing the product, and changing the TFM labeling relative to exercise exposure may render the product misbranded.

It is emphasized that most of these patch products are labeled as a percentage strength, without providing the total drug content per patch. For other topical dosage forms like creams, ointments, and lotions, the amount of drug administered can easily be determined by weighing the mass of product and applying the strength factor as illustrated in the table below. In contrast, the amount of drug applied for patch products cannot easily be determined because the exact mass of adhesive applied cannot be estimated due to the contributing mass of the backing materials. Inasmuch as patches are manufactured in a variety of sizes and thicknesses, the drug exposure from patches is unknown and cannot be estimated by reviewing the product label, unless the manufacturer discloses the drug mass. Many of the patch products exclude this from their labels, and the absence of this information on unapproved OTC product labels creates a safety risk.

Dosage Form	**Strength**	**Amount Applied**	**Applied Dose [Strength x Amount Applied]**
Cream, ointment, lotion	4%	1 g	40 mg
Patch	4%	Unknown (Mass of adhesive not specified on product labeling)	Unknown

[46] Barkve TF, Langseth-Manrique K, Bredesen JE, Gjesdal K. "Increased uptake of transdermal glyceryl trinitrate during physical exercise and during high ambient temperature." *Am. Heart J.* 1986; 112: 537-541.

[47] Klemsdal TO, Gjesdal K, Zahlsen K. "Physical Exercise Increases Plasma Concentrations of Nicotine During Treatment with a Nicotine Patch." *Br. J. Clin. Pharmacol.* 1995; 39:677-679.

[48] Abrams LS, Skee D, Natarajan J, Wong FA. "Pharmacokinetic overview of Ortho Evra/Evra." *Fertil. Steril.* 2002; 7(2 Suppl 2): S3-12.

Because there are no constraints on patch dimensions or adhesive thickness, the amount of drug in the product can be arbitrarily, and significantly, increased by increasing the patch size or adhesive thickness while maintaining the drug-to-adhesive ratio at 4%.

ii. How does patch design and formulation affect systemic exposures?

When lidocaine is applied topically to provide pain relief, its site of action is not the skin, but the nerve endings beneath the surface of skin and can be considered a "topical product for transdermal treatment of local tissue sites."[49] Because of this, lidocaine patches are formulated to allow the drug to penetrate through the stratum corneum. Because blood capillaries extend into the upper layers of dermis and are near the nerve endings on which lidocaine acts, there is significant systemic absorption of lidocaine from topical application, so much so that FDA recommends pharmacokinetic bioequivalence studies to evaluate generic versions of Lidoderm® 5%, rather than clinical endpoint studies, as is the case typically the case for topically-acting products.[50]

One of the key features that distinguish patch dosage forms from other topical dosage forms is that patches provide an occlusive physical barrier that covers the applied dose during wear. Occlusion is a widely recognized means to enhance percutaneous absorption of drugs. Occlusion can increase skin hydration, raise skin temperature, alter pH, and prevent the accidental removal or evaporation of an applied compound, which in effect results in a higher applied dose.[51] Occlusion has been shown to triple the serum concentrations of a topical 4% lidocaine anesthetic cream applied to the face.[52] Interestingly, in this study, the authors noted high inter-subject variability in lidocaine absorption that was not related to dose or exposure. While it was not possible to predict who would be sensitive to topical lidocaine, the authors

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[49] Paudel KS, Milewski M, Swadley CL, Brogden NK, Ghosh P, Stinchcomb AL. "Challenges and opportunities in dermal/transdermal delivery." *Ther. Deliv.* 2010; 1(1):109-31.

[50] FDA Draft Guidance on Lidocaine, October 2018. Available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm086293.pdf.

[51] Wester RC, Maibach HI. "Cutaneous pharmacokinetics: 10 steps to percutaneous absorption." *Drug Metab. Rev.* 1983; 14:169-205.

[52] Oni G, Brown S, Burrus C, Grant L, Watkins J, Kenkel M, Barton F, Kenkel J. "Effect of 4% Topical Lidocaine Applied to the Face on Serum Levels of Lidocaine and Its Metabolite, Monoethylglycinexylidide." *Aesthetic Surgery J.* 2010; 30(6): 853-858.

note: "these findings have important ramifications for *unsupervised patient application*, particularly in conjunction with occlusive dressings."[53]

The adhesive layer can also be occlusive and influence percutaneous absorption depending on the adhesive components and thickness. Because there are no constraints on the backing materials or adhesive components/thickness used for these patches, there is no standardization of their occlusion as it pertains to drug absorption. While some of these OTC lidocaine patch products incorporate a "breathable" backing cloth, these materials still remain potentially occlusive, especially as they contain and hold the adhesive layer (also with varying levels of occlusiveness) on top of the skin.

In addition to occlusive backings that can promote drug diffusion through the skin, topical lidocaine products are formulated with the inactive ingredients that can help to drive drug delivery. The formulation is critical in determining the systemic exposure to lidocaine, as was illustrated by a study by Oni, et al.[54], in which 25 subjects were treated with one of five different lidocaine creams (three OTC creams and two prescription preparations); and serum levels of lidocaine and its metabolite monoethylglycinexylidide (MEGX) were measured 90, 120, 150, 240, and 480 minutes after cream application. The creams included LMX-4 (4% lidocaine; Biopelle/Ferndale Laboratories, Ferndale, Michigan), Topicaine (4% lidocaine; Ebsa Laboratories, Jupiter, Florida), 2.5% lidocaine/2.5% prilocaine (generic EMLA preparation; High Tech Pharmaceuticals, Amityville, New York), LET (4% lidocaine, 1:2000 epinephrine, and 0.5% tetracaine), and BLT (20% benzocaine, 6% lidocaine, and 4% tetracaine) and were applied to the subject's face and neck and covered with an occlusive dressing for 60 minutes. The results showed the OTC products were associated with *greater* levels of lidocaine in the bloodstream than the prescription preparations. Interestingly, although three of the tested products contained 4% lidocaine, they had very different absorption profiles. This is likely due to formulation: one of the drugs was formulated with alcohol, another was liposomal drug-delivery system, and the third was an emollient-based product. It is known that alcohols and lipids can act as skin permeation enhancers and to increase drug absorption profiles. The authors also noted that the 2.5% lidocaine-containing formula had greater absorption than the 4% and 6% formulations.

The effect of formulation differences on biopharmaceutics also occurs with patch dosage forms. For example, Lidoderm® 5% has 700 mg lidocaine/patch with 700 mg being the

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[53] Id. (emphasis added).

[54] Oni G, Brown S, Kenkel J. "Topical Anesthetics and Their Effect on Serum Levels of Lidocaine and Its Metabolite Monoethylglycinexylidide (MEGX)." *Aesthetic Surgery Journal*. 2012; 32(4):495-503.

"administered" amount of drug, but only delivers a small fraction of the administered drug (i.e., the Lidoderm® 5% Prescribing Information states a bioavailability of 3 ± 2%).[55] In contrast, ZTLIDO™ 1.8% has 36 mg drug contained within a thinner adhesive layer (consequently a lower strength of 1.8%) but has a bioavailability of ~50% due to its biopharmaceutic efficiency of the formulation, and delivers the same amount of drug to the skin as Lidoderm® 5%, despite the difference in strength.[56] It is emphasized that ZTLIDO™ 1.8% and Lidoderm® 5% have comparable (bioequivalent) pharmacokinetics, but ZTLIDO™ 1.8% is less than half the strength of Lidoderm® 5%. This is solely a function of the product formulations and confirms that patch product strength (expressed as a percentage) does not identify the amount of delivered drug for these products. However, this nuance is likely lost to consumers who have a reasonable expectation that product strength inherently confers a standardized delivered drug dose with correlation between strength and apparent dose (i.e., higher strength products deliver more drug). This standardization is maintained for drugs subject to formal FDA review as represented by Mylan's Lidocaine Patch 5% that is a generic (bioequivalent) version of Lidoderm® 5%, but with significantly less drug load (140 versus 700 mg). The Mylan generic product notably contrasts with Lidoderm® 5% in adhesive formulation (i.e., polyisobutylene polymer system versus a hydrogel system), adhesive thickness (i.e., 0.27 versus 1.59 mm), and backing material (i.e., film versus nonwoven cloth), which presumably led to the improved biopharmaceutic efficiency allowing for the reduced drug load while maintaining the same product strength (5%) and rate/extent of delivered drug.[57]

Attachment 1 shows that OTC lidocaine patches have manufacturer-self-reported drug levels ranging from 11 to 5000 mg, but the amount of delivered drug is unknown as it is contingent on the biopharmaceutic properties of the adhesive/patch systems. Conceivably, an 11 mg lidocaine adhesive formulation with superior biopharmaceutic efficiency could deliver comparable levels of drug to the 5000 mg formulation with far inferior biopharmaceutic efficiency. This broad variability alone is reason enough why patches should not be allowed dosage forms in a final External Analgesics OTC Monograph. However, the significant safety risk is the prospect of a 5000 mg OTC lidocaine patch with a high bioavailability, which can deliver toxic levels of drug to the system (i.e., it is established that topically applied lidocaine results in systemic exposure). The application of heat and exercise can also dramatically exacerbate these safety risks. Patch product formulations have evolved over time with significant improvements in percutaneous absorption of the drugs (e.g., ZTLIDO™ 1.8% versus Lidoderm®

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[55] Lidoderm® Prescribing Information, November 2018.

[56] ZTLIDO™ Prescribing Information, November 2018.

[57] Lidocaine Patch 5% Prescribing Information, November 2018; http://lidocainepatch.mylan.com/en/health-care-professionals.

5%), and should be anticipated to continue to evolve, to the extent that OTC lidocaine patch manufacturers should be required to characterize and qualify safety and efficacy.

It is noted that the difficulty of determining what strength means in terms of efficacy for patch product has been used to promote nonprescription products as "similar" to the prescription strength lidocaine products. This raises questions about disincentives to follow well-established regulatory processes. As one reported example, Hisamitsu was developing a lidocaine 5% patch as a generic to Lidoderm® 5% but decided instead to pursue an OTC lidocaine 4% patch because it was a faster way to the market.[58] Since then, Hisamitsu has promoted the similarity of its OTC Salonpas Lidocaine Patch 4% to the prescription strength lidocaine products: "Salonpas has engineered this patch to be as close as possible to the prescription Lidocaine patch. We use the same hydrogel technology, same patch size and shape. We use the same type of individual, child resistant pouches and use the maximum concentration you can get without a prescription."[59] Highlighting the similarity of OTC and prescription lidocaine patch products can be misleading to consumers, because the safety and efficacy of the OTC products have not been reviewed by FDA, nor has the bioavailability, adhesion, or irritation potential of these products been assessed in comparison to the FDA-approved reference product that is being promoted as having near similarity in strength. Given the safety issues associated with topical lidocaine use and uncertainty of what strength means relative to systemic exposure, safety and efficacy data for each unique formulation should be reviewed before marketing.

These risks are compounded by the direct-to-consumer advertising that sometimes includes high-profile celebrities (e.g., Shaquille O'Neal (The Shaq) for IcyHot Lidocaine Patches Plus Menthol) to promote the product. Such promotion highlights the efficacy of the product, but essentially understates potential safety considerations. Admittedly, the risks of lidocaine overexposure should be less for Mr. O'Neal (due to his size) versus the average adult or children ≥12 years of age for which the product is labeled.

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[58] Spicer M. "With OTC Lidocaine, Salonpas Takes Path of Less Resistance to Market." *Ton Sheet*, 21 Oct 2016. Available at: https://pink.pharmaintelligence.informa.com/PS119368/With-OTC-Lidocaine-Salonpas-Takes-Path-Of-Less-Resistance-To-Market (Attachment 5). Significantly, FDA has acknowledged: "[I]t has become clear that one unintended consequence of [its TFM] enforcement approach is that it creates negative incentives for those who manufacture or market these OTC drugs to conduct studies or otherwise respond to safety concerns as to do so may hasten a determination that their product is not GRAS/GRAE." 81 Fed. Reg. 84465, Dec. 23, 2016. The failure to complete the process likewise creates a major loophole enabling drug manufacturers to launch unapproved new drugs into the market without important FDA review or expectation of agency reaction.

[59] Salonpas Product Description. Available at: https://www.walmart.com/ip/Salonpas-Lidocaine-Pain-Relieving-Gel-Patch-Pack-of-16/320482334 (Attachment 6).

iii. Are the inactive ingredients in lidocaine OTC patches safe?

Because patch dosage forms are not within the scope of the External Analgesics TFM review, the question of patch bioavailability and appropriate vehicles were not considered by the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (the "Expert Panel" or "Panel") or FDA. However, the concern that new vehicles could be introduced in the future that have better percutaneous absorption characteristics was not lost on the Panel. In a May 1976 meeting, the Expert Panel "expressed concern regarding the use of the new vehicles, with properties similar to DMSO [dimethylsulfoxide], which may increase the absorption of ingredients beyond what the Panel determined to be safe and effective. The Panel concluded at that meeting that, 'Ingredients reviewed by this Panel were categorized on the basis of their use in currently employed topical vehicles,' (Ref. 78)."[60]

The use of novel excipients is not compliant with 21 C.F.R. § 330.1(e), which requires OTC product to contain only suitable inactive ingredients that are safe in the amounts administered and do not interfere with the effectiveness of the preparation or with suitable tests or assays to determine if the product meets its professed standards of identity, strength, quality, and purity. FDA's Inactive Ingredient ("IIG") Database lists suitable excipients and their maximum potency delineated by routes of administration and dosage form. Ingredients that do not have a prior history of safety and suitability in a product type are subject to pre-market approval by FDA through NDA procedures.[61,62] FDA has also been very consistent in noting to industry that inclusion of an ingredient qualified as safe for cosmetic products and 21 C.F.R. Part 182 as GRAS (or direct/indirect food ingredients per 21 C.F.R. Parts 172-186) are not sufficient alone to qualify safety of these ingredients for use in pharmaceutical products. Furthermore, FDA has informed Scilex that the inclusion of an excipient in the IIG database alone for the same product form and route of administration does not necessarily qualify the safety of that excipient for its specific topical system as the dosage form may impart biopharmaceutical properties and exposure levels (dermal and systemic) that are not qualified by the underlying safety studies supporting their inclusion and maximum potencies listed in the IIG database for comparable or same dosage forms and routes of administration. In these

[60] 55 Fed. Reg. 6947, Feb. 27, 1990.

[61] FDA Small Business Assistance. "Bringing an Over-the-Counter (OTC) Drug to Market: Choosing a Regulatory Pathway for Your Drug, Factor #5 Make sure your product's inactive ingredients are safe and suitable." Available at: https://www.accessdata.fda.gov/scripts/cder/training/OTC/topic5/images/factor%205.pdf.

[62] Guidance for Industry: Determining Whether to Submit an ANDA or 505(b)(2) Application, Draft Guidance, October 2017. Available at:
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM579751.pdf.

cases, dermal toxicology studies are warranted for the safety qualification of the excipient. Furthermore, systemic toxicology studies may be warranted unless data are generated demonstrating that the novel excipients (or components of the excipient in the case of polymers) do not present risk of systemic exposure.

It is often the case that topical patches require sophisticated formulation excipients that allow for homogenous distribution of the drug, and allow the product to adhere to the skin and be easily removed after the administration period. These patch formulation challenges may require the use of excipients that are considered novel or novel for a topical patch formulation. This is especially the case for the newer products coming onto the market that involve novel adhesive polymers that not only allow for product adhesion but can also improve on the product's bioavailability. Adhesive polymers, in particular, represent a safety concern as many adhesives are not available with a defined pharmaceutical grade and differences in rheological properties, impurities, and lot-to-lot variability may affect their biocompatibility and performance. Adhesive polymers may contain impurities such as initiators, crosslinkers, solvents, or monomeric/dimeric species that need to be characterized for safety. Because of the high variability of quality of adhesives, FDA has suggested that changing adhesive suppliers would warrant comparative clinical endpoint studies for (A)NDA products.[63] OTC manufacturers should be held to the same standards regarding adhesive excipient safety characterization, performance, and control of suppliers.

Although monograph products are only allowed to use qualified, suitable excipients, there is no effective basis to verify that excipients in unapproved OTC lidocaine patches are qualified and suitable. As a case in point, Attachment 7 lists the inactive ingredients for the OTC lidocaine patch products and surveys them against FDA's IIG database. Of the 115 formulation excipients used in these products, 45 are novel (i.e., are not included in FDA's IIG Database) and 38 are novel to topical/transdermal drug delivery systems or films. Therefore, more than half of the inactive ingredients manufacturers have selected to formulate OTC lidocaine patches are novel for the dosage form and warrant safety qualification via animal toxicology studies. At a minimum, dermal toxicology studies are warranted, and systemic toxicology studies may be warranted unless data are available confirming that the excipient (or components of the excipient) do not present risk of systemic exposure. Many of the OTC lidocaine products listed in the DailyMed database have at least one novel excipient identified for the patch dosage form.

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[63] Berendt, R. "How to Resolve Current Challenges in ANDAs in Transdermal Delivery Systems (TDS): Complex Generic Drug Product Development Workshop," Sep. 13, 2018.

iv. Are lidocaine combination drug patch products safe?

The External Analgesics TFM allows manufacturers to combine lidocaine with other active ingredients; however, manufacturers have taken liberty in addressing: acceptable combination of active ingredients (i.e., lidocaine in combination with other active ingredients); combining with active ingredients that are identified as Category III; or exceeding the allowable product strength for lidocaine and/or combined active ingredient. Specific examples are provided below.

Acceptable combination of active ingredients: According to the 1983 External Analgesics TFM (Proposed 21 C.F.R. § 348.20: permitted combinations of external analgesic active ingredients), any active ingredient identified in Proposed 21 C.F.R. § 348.10(a) (including lidocaine) may be combined with an active ingredient in 21 C.F.R. § 348.10(b) (benzyl alcohol, camphor, camphorated metacresol, juniper tar, menthol, phenol, phenolate sodium, and resorcinol) or 21 C.F.R. § 348.10(c) (diphenhydramine hydrochloride, tripelennamine hydrochloride). It is further noted that the TFM does not allow for combination of active ingredients listed in 21 C.F.R. § 348.10(a) (including lidocaine) with active ingredients listed in 21 CFR § 348.12 (including capsaicin and methyl salicylate).

The most common combination for the OTC lidocaine patch products is lidocaine 4% with menthol 1%, which conforms to the permitted ingredient combinations per 21 C.F.R. § 348.20 (i.e., although not the patch dosage form, which is not a recognized dosage form by the External Analgesic TFM). Exception product combinations exist, however, including the following:

- LidoPro Patch (lidocaine 4%, menthol 5%, methyl salicylate 4%)
- 1st Medex Patch (capsaicin 0.0375%, lidocaine 4%, menthol 5%, methyl salicylate 20%)
- Medi-Sulting Topical Pain Relief Patch (capsaicin 0.035%, lidocaine 0.5%, menthol 5%, methyl salicylate 20%)
- Permavan External Patch (trolamine salicylate 10%, dextromethorphan hydrobromide 4%, lidocaine 4%)
- Velma Pain Relief Patch (lidocaine 4%, menthol 2%, methyl salicylate 2%)
- Zims Max Freeze Patch (menthol 5%, lidocaine 4%, methyl salicylate 0.04%)

None of these products conform to 21 C.F.R. § 348.20 in that they combine more than one active ingredient with lidocaine. In some cases, the product combines lidocaine with active ingredients from 21 C.F.R. § 348.10(c) (Permavan with dextromethorphan hydrobromide, and the dextromethorphan hydrobromide strength (4%) exceeds the monograph highest accepted strength (2%)). Permavan also includes trolamine salicylate, which is designated as a Category

III drug in the External Analgesics TFM. Except for Permavan, these products all include methyl salicylate (i.e., counterirritant from 21 C.F.R. § 348.12), which is not a permitted combination with lidocaine. Capsaicin (counterirritant listed in 21 C.F.R. § 348.12) is included in the 1st Medex and Medi-Sulting, which is again not a permitted combination with lidocaine.

Because lidocaine is not permitted to be combined with counterirritant active ingredients in 21 C.F.R. § 348.12, LidoPro, 1st Medex, Medi-Sulting, Velma, and Zims all exceed the allowable strength for menthol (1%).

It is important to note that the combination of lidocaine with other active ingredients in a patch dosage form may increase percutaneous absorption in ways that were not appreciated when the External Analgesics TFM was promulgated in 1983. Menthol, for example, is a vasodilator that has been shown to enhance lidocaine permeation when formulated as a eutectic lidocaine-menthol mixture in vitro models of skin permeation.[64] Addition of menthol and ethanol in a tetracaine gel formulation also enhanced in vivo absorption of a tetracaine.[65] There are several lidocaine combination patch OTC products on the market (see Appendix 1). While the combination of lidocaine with menthol is allowed in accordance with the External Analgesics TFM, its potential effect on percutaneous absorption of lidocaine (and other drugs) was not considered along with the other contributing factors such as formulation components and occlusion of the patch products.

v. What is the dermal irritation and sensitization potential of OTC lidocaine patches?

Unlike creams, ointments, and lotions where application site reactions and hypersensitivities can be visually observed when they occur, patches are occlusive, and these adverse events are not readily observed until after patch removal (typically labeled 8-12 hours). The External Analgesics TFM does not require label warning against dermal safety risks specific to patches or means to mitigate the risk (e.g., periodic observations). Because companies marketing products under a monograph may not deviate from the warnings in the rulemaking (unless formally directed by FDA), these OTC lidocaine patch products consequently lack very important product-specific warning language. Some OTC lidocaine patch manufacturers include

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[64] Kang L, Jun HW, McCall JW. "Physicochemical studies of lidocaine-menthol binary systems for enhanced membrane transport." *Int. J. Pharm.* 2000; 206(1-2):35-42.

[65] Fang C, Liu Y, Ye X, Rong ZX, Feng XM, Jiang CB, Chen HZ. "Synergistically enhanced transdermal permeation and topical analgesia of tetracaine gel containing menthol and ethanol in experimental and clinical studies." *Eur. J. Pharm. Biopharm.* 2008; 68:735-40.

dermal safety warnings on their product label – using varied wording – not contemplated by the TFM, and this is another reason that they may be misbranded.

When FDA determined that patch dosage forms should be excluded from the External Analgesics TFM in 2003, part of the reasoning was that there not sufficient information on how often to check the application area for erythema to prevent blistering and what time intervals are recommended. The risks for local skin reactions and the directions for safe use will often be specific to the formulation. Local tolerance is typically a function of the inactive ingredients involved in the adhesive formulation (versus the drug itself). Separate from the formulation, there is also potential mechanical irritation associated with adhesion relative to application and removal of the product as a function of the adhesive strength.

The need to study dermal irritation/sensitization for each formulation was highlighted in a recent FDA Draft Guidance for ANDA applicants[66]:

> The components and composition of a TDS formulation, including the nature of the drug substance and/or the degree to which the TDS materials occlude the transmission of water vapor from the skin, in conjunction with other factors such as the environmental humidity or the condition of the skin, may have the potential to irritate the skin or lead to a sensitization reaction. Such reactions can be unpleasant to the patient and may affect patient compliance, skin permeability, and/or adhesion of the TDS to the skin. The collective consequence of these potential effects could create uncertainty about the resulting drug delivery profile and uncertainty about the rate and extent of drug absorption from the TDS. Therefore, applicants should perform a comparative assessment of the T [test] and R [reference] TDS products using an appropriately designed skin I/S [irritation and sensitization] study with human subjects to demonstrate that the potential for a skin irritation or sensitization reaction with the T TDS is no worse than the reaction observed with the R TDS.

Because of the formulation-specific nature of dermal sensitization and irritation, FDA requires each manufacturer of a generic topical delivery system to characterize the irritation and sensitization potential of the product against the reference product, even though dermal irritation and sensitization were well-characterized for the reference product containing the same active ingredient. For generic products, this necessitates a careful balance between adhesion performance and sensitization/irritation potential while maintaining bioequivalence

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[66] Draft Guidance to Industry: Assessing the Irritation and Sensitization Potential of Transdermal and Topical Delivery Systems for ANDAs, October 2018. Available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM622672.pdf.

and product strength. It is not currently mandated, and highly unlikely that manufacturers have voluntarily undertaken studies to ensure, that OTC lidocaine patch products have adequately undergone clinical/nonclinical dermal safety evaluation/characterization. There also lacks a standard reference product or general benchmark against which to standardize the sensitization/irritation profiles of these products.

c. Risk of Inadvertent Exposure

i. How much residual drug remains in used patches and what risk does this pose?

FDA has recently expressed concern with inadvertent exposures to children or pets from patch products and has encouraged designing patches to minimize residual drug after use.[67] In FDA's 2018 Guidance for Industry on adhesion, the Agency notes:

> During the product's labeled wear period, a TDS is reasonably expected to encounter torsional strains arising from body movements, changes in environmental temperature or humidity such as the daily exposure to water (e.g., during routine showering), and contact with clothing, bedding or other surfaces. TDS products that do not maintain consistent and uniform adhesion with the skin during the labeled wear period can experience varying degrees of TDS detachment, including complete detachment, at different times during the product wear. ... When the potential for complete detachment of the TDS increases, the risk of unintentional exposure of the drug product to an unintended recipient (e.g., a household member who may be a child) also increases.[68]

Residual drug in lidocaine patches that have detached or patches that are not properly disposed after use present a significant safety concern relative to accidental exposure. Lidoderm® 5% and the associated generics have bolded text relative to the safety risks of the high level of residual drug remaining in the product after use.[69] For prescription

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[67] Guidance for Industry: Residual Drug in Transdermal and Related Drug Delivery Systems, August 2011, available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM220796.pdf.

[68] Guidance for Industry: Assessing Adhesion With Transdermal and Topical Systems for ANDAs, October 2018, available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM504157.pdf.

[69] Lidoderm® Prescribing Information, November 2018.

products the residual drug levels after use are determined and included in the labeling; however, the External Analgesics TFM is silent on this risk and many OTC lidocaine patch products do not recognize residual drug risks or provide instructions of safe disposal.[70] This is a particular concern for OTC lidocaine patch products with a combination of a higher level of drug and low bioavailability.

ii. Is the packaging for OTC lidocaine patches safe?

In accordance with 16 C.F.R. § 1700.14(a)(23), products containing more than 5 mg of lidocaine in a single package (i.e., retail unit) shall be packaged in accordance with the provisions of § 1700.15(a) and (b) that require child-resistant packaging to protect children under 5 years of age from serious personal injury or serious illness resulting from ingesting lidocaine. Some of the OTC lidocaine patch products listed in the attached table note the use of resealable pouches, which pose particular concerns about child-resistance. Most of the products do not acknowledge or note the presence of child-resistant packaging. If a drug and its packaging are in violation of applicable regulations under the Poison Prevention Packaging Act, that drug is misbranded under the Federal Food, Drug, and Cosmetic Act.[71]

5. OTC Labeling and Monograph Compliance

The foregoing discussion identifies several patch-specific labeling deficiencies burdening the current process (e.g., lack of product-appropriate directions for how to apply and remove patches; monitoring for potential dermal irritation; lack of provisions to warn about residual drug in the product; lack of provisions to warn about the effects of heat or other conditions of use (e.g., exercise) on safety and efficacy). As discussed, the TFM did not provide for patch-specific labeling for these products because the dosage form was not contemplated at the time the TFM was being promulgated. This has lead manufacturers to undergo some level of labeling contortions to attempt to adapt their lidocaine OTC patch product labeling to TFM-specific requirements.

Even more generally, the TFM is outdated with respect to current lidocaine safety information that may affect the labeling of all lidocaine-containing dosage forms. For example, lidocaine prescription products are labeled with contraindications to patients with known history of sensitivity to local anesthetics of the amide type. OTC lidocaine patch products present the same risk and potentially the same drug exposure as prescription lidocaine

[70] Products that attempt to voluntarily include cautionary language run into separate compliance considerations vis-à-vis restrictions against the TFM labeling.

[71] 21 U.S.C. § 352(p).

products. However, the monograph labeling is without these contraindications. Other labeling issues that also should be considered for lidocaine-containing OTC products include risks related to methemoglobinemia; pregnancy; lactation; risks in pediatrics; and concomitant medication use. OTC lidocaine patch products are inconsistent in the way they address these risks. It also is conceivable that the risks could affect the conclusions of qualified experts about safety of particular products, and whether and how labeling might enable consumers to understand and manage risks. At the same time, OTC lidocaine patch manufacturers may not broadly update or modify the safety warnings of the product (however well-intentioned) as they may then be out of compliance with the External Analgesics TFM and considered misbranded.

6. Conclusions

Percutaneous drug delivery is complex, and the science and technologies have evolved over the past ~35 years since the External Analgesics TFM was first drafted. Scilex agrees with FDA's 2003 determination that patch dosage forms are properly excluded from the final External Analgesics OTC monograph. The dosage form-specific concerns raised were based on sound regulatory science, and understanding of the complexity of patch dosage forms has only increased in the 15 years since the TFM was first amended to exclude these products.

In the meantime, innovation has led to a proliferation of lidocaine OTC patches being introduced to the market. These lidocaine OTC patch products do not conform to the 1983 TFM for external analgesics. Most significantly, for reasons set forth in detail herein, the advancements in technology present the potential safety risks identified by FDA when designating the dosage form as Category III in 2003.

How lidocaine OTC patch products are designed and formulated; the degree of occlusion; the selection of adhesives and penetration enhancers all impact the safety and efficacy of the lidocaine OTC patch products. There are numerous complex scientific issues to consider in developing lidocaine OTC patch products, including consistency of adhesion characteristics, amount of residual drug after use, effects of heat/exercise, and potential for dermal irritation/sensitization, all of which necessitate a thorough review of the safety and efficacy of each patch formulation prior to marketing. It cannot be assumed that these safety risks are not present with the current products based on their pharmacovigilance. Post-marketing surveillance reports to document marketing experience, adverse events, and complaints, while of interest, are plagued by underreporting[72] and are not in and of themselves

[72] Food and Drug Administration, Center for Drug Evaluation and Research, Summary Minutes of the Nonprescription Drugs Advisory Committee (NDAC) Meeting, September 4-5, 2014.

sufficient evidence to confirm the safety and efficacy (let alone GRAS/E status) of an OTC drug product. It is reasonable to assume that there will be continuous advancement of OTC lidocaine patch technology that will consequently and increasingly affect the safety risks of these products.

Given the widespread availability of OTC lidocaine patch products, it is likely that the average consumer may perceive these products as "safe," may not follow directions presented on maximum numbers of patches to use or how long to leave products on; be aware of proper administration, removal, and disposal of the product; or be properly warned of potential adverse effects. Some manufacturers seem to be aware and concerned of these issues with emphasized labeling on the administration, removal, disposal, and additional safety warnings on patch products; however, this attempt to reconcile the dosage form labeling to the 1983 External Analgesics TFM paradoxically places the product out of compliance with the monograph making them misbranded. Rather than continuing to allow the number of unproven and risky OTC lidocaine patch products to proliferate, Scilex asks FDA to use its full regulatory and enforcement authorities to ensure that only legally marketed lidocaine patch products are available to the American public.

C. ENVIRONMENTAL IMPACT

The actions requested in this Citizen Petition are subject to the categorical exclusion under 21 C.F.R. § 25.31.

D. ECONOMIC IMPACT

Scilex will provide information on the economic impact of this petition at the request of the Commissioner of Food and Drugs.

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https://wayback.archiveit.org/7993/20170404152726/https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/NonprescriptionDrugsAdvisoryCommittee/UCM421304.pdf.

E. CERTIFICATION

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Sincerely,

Kip Vought
Vice President, Global R&D
Scilex Pharmaceuticals, Inc.
Telephone: 949.441.2270
Fax: 949.916.3010
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Attachments

EXHIBIT C

ATTACHMENT 1

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
Absorbine Jr. Lidocaine	69693-414	2017	Lidocaine 4%	Duration not labeled While number of patches is not labeled, it states do not use on a large area of body with multiple patches, particularly over raw or blistered area 3-4 patches daily Maximum 7 days	246	10 cm x 14 cm	Not labeled to keep from heat exposure Does not restrict use with other topical analgesic products
Aspercreme Lidocaine Patch	62168-0584	2016	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Number of patches daily not labeled, but states 1 patch/12 hours Maximum 7 days	246	10 cm x 14 cm	
Aspercreme Lidocaine Patch Odor Free	41167-0584	2016	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Number of patches daily not labeled, but states 1 patch/12 hours Maximum 7 days	246	10 cm x 14 cm	
Aspercreme Lidocaine Patch XL	62168-0585	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Number of patches daily not labeled, but states 1 patch/12 hours Maximum 7 days	411.4	12 cm x 20 cm	
Aspercreme Lidocaine Patch XL Odor Free	41167-0585	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Number of patches daily not labeled, but states 1 patch/12 hours Maximum 7 days	422	12 cm x 20 cm	
Assured Pain Relief	69159-100	2017	Lidocaine 4%	NMT 8 hours NMT 1 patch at a time 3-4 times daily Maximum 7 days	4000 in 100,000	10 cm x 14 cm	
Avalin External Analgesic Patch	33358-901	2015	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time 3-4 times dailyMaximum 5 days	40 in 1,000	Not labeled	Allows for administration to children ≥2 years Does not restrict exposure to heat

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							Does not restrict use with other topical analgesic products
Benepatch	69418-002	2015	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	Not labeled	Does not restrict exposure to heat Does not restrict use with other topical analgesic products
CareOne Maximum Strength Lidocaine Pain Relief Patch	60000-911	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 13.97 cm	
Coralite Lidocaine Pain Relief	65923-159	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	560	10 cm x 14 cm	
Coralite Odor Free Pain Relief Lidocaine Patch	65923-149	2018	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40 in 1,000	10 cm x 14 cm	
CVS Hot and Cold	66902-218	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40	10 cm x 14 cm	
CVS Pain Relief Patch	66902-203	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40	10 cm x 14 cm	
Discount Drug Mark Pain Relief Patches	53943-911	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 13.97 cm	
Dollar General Pain Relieving Patch	55910-912	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 14 cm	
Elite Pain Relief Patch	69418-004	2015	Lidocaine 4% Allantoin 2% Petrolatum 30%	NMT 8 hours NMT 1 patch at a time NMT 4 patches/daily Maximum 5 days	4000 in 100,000	Not labeled	Does not restrict use with other topical analgesic products Does not restrict exposure to heat
Endoxcin	45861-006	2014	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time NMT 4 patches/daily Maximum 5 days	4000 in 100,000	8.5 cm x 12.5 cm	Does not restrict use with other topical analgesic products Does not restrict exposure to heat
Family Wellness Pain Relief Lidocaine Patch	55319-959	2018	Lidocaine 4%	NMT 12 hours 1 patch at a time Maximum 7 days	40 in 1,000	10 x 14 cm	

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
FirstDoc Cold and Hot Pain Relief Patch	70355-001	2015	Lidocaine 4% Menthol 5% Methyl Salicylate 4%	Duration not labeled 1 patch at a time NMT 4 times/day Maximum 7 days	4000 in 100,000	Not labeled	Product exceeds menthol strength allowed by 21 CFR 348.10(b) Notes that package is not child resistant Does not restrict use with other topical analgesic products
Good Neighbor Pharmacy Maximum Strength Lidocaine Pain Relief Patch	46122-450	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 13.97 cm	
Harris Teeter 4% Lidocaine Pain Relief Patch	72036-911	2018	Lidocaine 4%	NMT 8 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 13.97 cm	
Hot and Cold Lidocaine with Menthol Pain Relief Patch	71318-001	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch at a time NMT 1 patch/day Maximum 7 days	40	Not labeled	Does not restrict use with other topical analgesic products
Hot and Cold Lidocaine with Menthol	69159-004	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40	Not labeled	
Hot and Cold Lidocaine with Menthol Pain Relief Patch	76168-099	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch/daily Maximum 7 days	40	10 cm x 14 cm	Does not restrict use with other topical analgesic products
IcyHot Lidocaine Patch Plus Menthol	62168-1720	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch at a time NMT 2 patch/daily (implied) Maximum 7 days	240	10 cm x 14 cm	
IcyHot Lidocaine Patch Plus Menthol	41167-1720	2018	Lidocaine 4% Menthol 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	240	10 cm x 14 cm	
LenzaPro Patch	70512-011	2018	Lidocaine 4% Menthol 4%	Duration not labeled NMT 1 patch at a time, but does not restrict multiple patches NMT 2 times/day Maximum patches/day not labeled Maximum 7 days	40 in 1,000	Not labeled	Product exceeds menthol strength allowed by 21 CFR 348.10(b) Multiple patches/pouch (does not comply with child-resistance requirements) Does not restrict use with other topical analgesic products

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							Does not restrict exposure to heat
LenzaPatch	45861-017	2013	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	8.5 cm x 12.5 cm	Does not restrict use with other topical analgesic products Does not restrict exposure to heat
	63187-162					Not labeled	
LidAll Lidocaine Patch	64533-000	2013	Lidocaine 4% Menthol 1%	Duration not labeled No restriction to number of patches in a single administration, but does state do not use on a large area of body with multiple patches, particularly over raw or blistered area NMT 3 applications/day Maximum 7 days	4000 in 100,000	8.5 cm x 12.5 cm	Multiple patches/pouch (does not comply with child-resistance requirements) Does not restrict use with other topical analgesic products Does not restrict exposure to heat
Lidenza Patch	69329-017	2013	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	Not listed	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) Does not restrict use with other topical analgesic products Does not restrict exposure to heat
Lidocare Lidocaine (Arm, Neck, and Leg) Patch	69993-450	2016	Lidocaine 4%	8-12 hours No restriction to number of patches in a single administration NMT 3 applications/day Maximum 7 days	11	3.175 cm x 15.24 cm	
Lidocare Lidocaine (Back and Shoulder) Patch	69993-400				4000	6.35 cm x 15.24 cm	
Lido-Flex Shoulder Patch	69313-636	2014	Lidocaine 4%	8-12 hours No restriction to number of patches in a single administration, but does say not to apply excessive quantity of patches within a 24 hour period NMT 3 applications/day Maximum 7 days	25.3 in 0.24	Not labeled (various sizes and shape for each product)	Label notes that the packaging is not child resistant Does not restrict use with other topical analgesic products
Lido-Flex Elbow Patch	69313-633				21.5 in 0.24		
Lido-Flex Back Patch	69313-632				29 in 0.24		
Lido-Flex Knee Patch	69313-635				25.8 in 0.24		
Lido-Flex Heel Patch	69313-634				22.7 in 0.24		
Lido-Flex Strip Double Patch	69313-637				28.1 in 0.24		

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
Lidonexe	69329-002	2014	Lidocaine 4% Menthol 1%	NMT 8 hours 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	Not labeled	Does not restrict use with other topical analgesic products Does not restrict exposure to heat
LidoPatch	10882-528	2015	Lidocaine 3.6% Menthol 1.25%	NMT 12 hours NMT 1 patch/day Maximum 7 days	505	10 cm x 14 cm	Product exceeds menthol strength allowed by 21 CFR 348.10(b) Restricts to adult use only, but does not identify excluded pediatric age groups Does not restrict use with other topical analgesic products Does not warn against heat exposure
LidoPatch	10882-527 70267-001	2016	Lidocaine 3.6% or 3.99% depending on packaging configuration Menthol 1.25%	NMT 12 hours NMT 1 patch/day Maximum 7 days	0.36 or 40, depending on packaging configurations 0.36	10 cm x 14 cm	Product exceeds menthol strength allowed by 21 CFR 348.10(b) Restricts to adult use only, but does not identify excluded pediatric age groups Does not restrict use with other topical analgesic products
LidoPatch	50682-527	2012	Lidocaine 3.99% Menthol 1%	NMT 12 hours NMT 1 patch/daily Maximum 7 days	40	10 cm x 14 cm	Restricts to adult use only, but does not identify excluded pediatric age groups Does not restrict use with other topical analgesic products
LidoPatch	10882-527	2012	Lidocaine 3.99% Menthol 1.25%	NMT 12 hours NMT 1 patch/daily Maximum 7 days	40	10 cm x 14 cm	Product exceeds menthol strength allowed by 21 CFR 348.10(b) Restricts to adult use only, but does not identify excluded pediatric age groups

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Aspercreme Lidocaine Patch	62168-0584	2016	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Number of patches daily not labeled, but states 1 patch/12 hours Maximum 7 days	246	10 cm x 14 cm	
Aspercreme Lidocaine Patch Odor Free	41167-0584	2016	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Number of patches daily not labeled, but states 1 patch/12 hours Maximum 7 days	246	10 cm x 14 cm	
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Avalin External Analgesic Patch	33358-901	2015	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time 3-4 times dailyMaximum 5 days	40 in 1,000	Not labeled	Allows for administration to children ≥2 years Does not restrict exposure to heat

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CareOne Maximum Strength Lidocaine Pain Relief Patch	60000-911	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 13.97 cm	
Coralite Lidocaine Pain Relief	65923-159	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	560	10 cm x 14 cm	
Coralite Odor Free Pain Relief Lidocaine Patch	65923-149	2018	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40 in 1,000	10 cm x 14 cm	
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Endoxcin	45861-006	2014	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time NMT 4 patches/daily Maximum 5 days	4000 in 100,000	8.5 cm x 12.5 cm	Does not restrict use with other topical analgesic products Does not restrict exposure to heat
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Good Neighbor Pharmacy Maximum Strength Lidocaine Pain Relief Patch	46122-450	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 13.97 cm	
Harris Teeter 4% Lidocaine Pain Relief Patch	72036-911	2018	Lidocaine 4%	NMT 8 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 13.97 cm	
Hot and Cold Lidocaine with Menthol Pain Relief Patch	71318-001	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch at a time NMT 1 patch/day Maximum 7 days	40	Not labeled	Does not restrict use with other topical analgesic products
Hot and Cold Lidocaine with Menthol	69159-004	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40	Not labeled	
Hot and Cold Lidocaine with Menthol Pain Relief Patch	76168-099	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch/daily Maximum 7 days	40	10 cm x 14 cm	Does not restrict use with other topical analgesic products
IcyHot Lidocaine Patch Plus Menthol	62168-1720	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch at a time NMT 2 patch/daily (implied) Maximum 7 days	240	10 cm x 14 cm	
IcyHot Lidocaine Patch Plus Menthol	41167-1720	2018	Lidocaine 4% Menthol 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	240	10 cm x 14 cm	
LenzaPro Patch	70512-011	2018	Lidocaine 4% Menthol 4%	Duration not labeled NMT 1 patch at a time, but does not restrict multiple patches NMT 2 times/day Maximum patches/day not labeled Maximum 7 days	40 in 1,000	Not labeled	Product exceeds menthol strength allowed by 21 CFR 348.10(b) Multiple patches/pouch (does not comply with child-resistance requirements) Does not restrict use with other topical analgesic products

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							Does not restrict exposure to heat
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	63187-162					Not labeled	
LidAll Lidocaine Patch	64533-000	2013	Lidocaine 4% Menthol 1%	Duration not labeled No restriction to number of patches in a single administration, but does state do not use on a large area of body with multiple patches, particularly over raw or blistered area NMT 3 applications/day Maximum 7 days	4000 in 100,000	8.5 cm x 12.5 cm	Multiple patches/pouch (does not comply with child-resistance requirements) Does not restrict use with other topical analgesic products Does not restrict exposure to heat
Lidenza Patch	69329-017	2013	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	Not listed	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) Does not restrict use with other topical analgesic products Does not restrict exposure to heat
Lidocare Lidocaine (Arm, Neck, and Leg) Patch	69993-450	2016	Lidocaine 4%	8-12 hours No restriction to number of patches in a single administration NMT 3 applications/day Maximum 7 days	11	3.175 cm x 15.24 cm	
Lidocare Lidocaine (Back and Shoulder) Patch	69993-400				4000	6.35 cm x 15.24 cm	
Lido-Flex Shoulder Patch	69313-636	2014	Lidocaine 4%	8-12 hours No restriction to number of patches in a single administration, but does say not to apply excessive quantity of patches within a 24 hour period NMT 3 applications/day Maximum 7 days	25.3 in 0.24	Not labeled (various sizes and shape for each product)	Label notes that the packaging is not child resistant Does not restrict use with other topical analgesic products
Lido-Flex Elbow Patch	69313-633				21.5 in 0.24		
Lido-Flex Back Patch	69313-632				29 in 0.24		
Lido-Flex Knee Patch	69313-635				25.8 in 0.24		
Lido-Flex Heel Patch	69313-634				22.7 in 0.24		
Lido-Flex Strip Double Patch	69313-637				28.1 in 0.24		

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							Does not restrict use with other topical analgesic products
LidoPlus Maximum Strength Pain Relief Patch	70372-724	2016	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch/daily Maximum 7 Days Warns that should be discontinued if symptoms clear and occur again within a few days	600	10.16 cm x 15.24 cm	Does not restrict use with other topical analgesic products Does not warn against heat exposure Makes numerous label claims that are inconsistent with the TFM 21 CFR 348 monograph, including (under patient medical information): - States that studies support that the two active ingredients significantly reduce pain and inflammation. - Notes MOA of both drugs including lidocaine's ability to not just preventing pain signals from propagating to the brain, but by stopping them before they begin. - Menthol MOA improves efficacy over other topical applications due to its vasodilation properties. - Superior therapy to oral analgesics such as NSAIDs and opioids (due to safety) - Suggests that the product can be used in a multimodal pain treatment setting – including chronic pain indications - States that the drugs only act locally and do not enter the bloodstream, but later notes that the drugs penetrate to deeper tissues (joints and muscles) - Lists several off-label indications that the product
Lidosport Pain Relief Patch	70372-725	2016					

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							can be used: low back pain, dermal procedures, laser treatments, body hair removal, body art, cosmetic procedures, other conditions/procedures where topical anesthetics are medically necessary
LidoPro Patch	68788-9975	2015	Lidocaine 4% Menthol 5% Methyl salicylate 4%	8-12 hours 1 patch at a time NMT 2 patches/day	0.04 (units not provided)	Not labeled	21 CFR 348.20 does not permit combination of lidocaine with active ingredients listed in 21 CFR 348.12 (methyl salicylate) Product exceeds menthol strength allowed by 21 CFR 348.10(b) Multiple patches/pouch (does not comply with child-resistance requirements) Does not restrict use with other topical analgesic products
LidoPro Patch	53225-1023	2014			4 in 100		
Lidothal Relief Medicated Patch	71437-463 69561-463	2017	Lidocaine 4% Menthol 1%	NMT 8 hours 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	Not labeled	Does not warn against heat exposure Does not restrict use with other topical analgesic products
Lidothol Medicated Patch	68788-7405 53225-1025	2018	Lidocaine 4.5% Menthol 5%	8-12 hours 1 patch at a time NMT 2 patches/daily	4500	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) Exceeds lidocaine and menthol strengths allowed by 21 CFR 348.10(a) and 21 CFR 348.10(b) respectively Multiple patches/pouch (does not comply with child-resistance requirements)

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							Does not warn against heat exposure Product exceeds lidocaine strength allowed by 21 CFR 348.10(a)
Lidozen Patch	63187-917 71574-400	2017	Lidocaine 4% Menthol 1%	NMT 8 hours 1 patch at a time NMT 4 patches/day Maximum 5 days	40 in 1000	Not labeled 12.5 cm x 8.5 cm	Does not warn against heat exposure Does not restrict use with other topical analgesic products
Limencin Patch	50488-1201	2014	Lidocaine 4% Menthol 4%	Duration not labeled 1-2 patches daily No maximum duration	40	Not labeled	Product exceeds menthol strength allowed by 21 CFR 348.10(b) Multiple patches/pouch (does not comply with child-resistance requirements) Does not restrict use with other topical analgesic products Does not warn against heat exposure Makes significant label claims similar to those made for LidoPlus
Lorenza Pain Relief Patch	69379-014	2015	Lidocaine 4% Menthol 1%	8 hours NMT 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) Does not restrict use with other topical analgesic products
Maximum Strength Lidocaine Patch	76168-067	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40	10 cm x 14 cm	Does not warn against heat exposure
Maximum Strength Lidocaine Patch	71318-002	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40	Not labeled	

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
1st Medex Patch with Lidocaine 4%	72137-555 72137-113	2018	Lidocaine 4% Capsaicin 0.0375% Menthol 5% Methyl salicylate 20%	Duration not labeled 1-2 patches daily No maximum duration	Not provided in mass	Not labeled	21 CFR 348.20 does not allow for combination of lidocaine with counterirritants listed in 21 CFR 348.12 (capsaicin and methyl salicylate) Product exceeds menthol strength allowed by 21 CFR 348.10(b) Multiple patches/pouch (does not comply with child-resistance requirements) Does not restrict use with other topical analgesic products Does not warn against heat exposure NDC 72137-113 is listed as an RX product, but with no NDA reference (or identified in the Orange Book) and has an OTC type label (i.e., drug facts panel)
Medi-Patch and Lidocaine	76074-153 76074-163	2012	Lidocaine 0.5% Capsaicin 0.035% Menthol 5% Methyl salicylate 20%	Duration lot listed NMT 3 times a day Maximum 7 days	250	Not listed	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) Product exceeds menthol strength allowed by 21 CFR 348.10(b) Does not restrict use with other topical analgesic products
Medi-Sulting Topical Pain Relief	63187-067 76074-123	2012	Lidocaine 0.5% Capsaicin 0.035% Menthol 5% Methyl salicylate 20%	Duration not labeled Number of patches in single administration not labeled NMT 4 patches daily Maximum 7 days	500 in 100,000	Not labeled	21 CFR 348.20 does not allow for combination of lidocaine with counterirritants listed in 21 CFR 348.12 (capsaicin and methyl salicylate)

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							Product exceeds menthol strength allowed by 21 CFR 348.10(b) Does not restrict use with other topical analgesic products
Meijer Maximum Strength Lidocaine Patch Plus Menthol	41250-841	2018	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4,000 in 100,000	10 cm x 14 cm	
Meijer Pain Relief Patches	41250-972	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 13.97 cm	
Mencaine	53225-1090	2017	Lidocaine 4.5% Menthol 5%	8-12 hours 1 patch at a time NMT 2 patches/day	4.5 in 100	Not labeled	Product exceeds menthol strength allowed by 21 CFR 348.10(b) Product exceeds lidocaine strength allowed by 21 CFR 348.10(a)
MTX Topical Pain	69889-026	2016	Lidocaine 4% Menthol 1%	NMT 8 hours 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	12.5 cm x 8.5 cm	Does not warn against heat exposure
Nulido Lidocaine Patch Plus Menthol	53149-2200	2018	Lidocaine 4% Menthol 1%	NMT 12 hours 1 patch at a time Number of patches daily not labeled Maximum 7 days	4000 in 100,000	10 cm x 14 cm	Multiple patches/pouch (does not comply with child-resistance requirements)
Odourless Lidocaine Pain Relieving Patch	69159-003	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40	Not labeled	
Odynia-R Regular	69647-001	2015	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 3 patches/day Maximum 7 days	4000 in 100,000	Not labeled	Does not restrict use with other topical analgesic products
Odynia-U Ultra Patch	69647-002 69647-003	2015	Lidocaine 4 % Capsicum 0.03 %	NMT 8 hours NMT 3 patches/day Maximum 7 days	4000 in 100,000	Not labeled	Does not restrict use with other topical analgesic products
Pain Relief Patches			Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4,000 in 100,000	10 cm x 13.97 cm	

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
Permavan External Patch	69379-010	2015	Lidocaine 4% Trolamine salicylate 10% Dextromethorphan hydrobromide 4%	8 hours 1 patch at a time Maximum 4 patches/daily Maximum use 5 days	4000 in 100,000	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) 21 CFR 348.20 does not permit the combination of lidocaine with antihistamines listed in 21 CFR 348.10© (dextromethorphan hydrobromide 4%) Product exceeds menthol strength allowed by 21 CFR 348.10(b) Trolamine salicylate is listed as a Category III drug by the Panel and Agency in 21 CFR 348.
Point Relief Lidospot	51452-727	2016	Lidocaine 4% Menthol 1%	NMT 12 hours 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	10.16 cm x 15.24 cm	Does not restrict use with other topical analgesic products Does not warn against heat exposure
Point Relief Lidospot with Menthol	51452-912	2018	Lidocaine 4% Menthol 1%	NMT 12 hours 1 patch at a time Maximum 7 days	4,000 ion 100,000	10 cm x 15 cm	
Premier Value Pain Relief Patches	68016-066	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4,000 in 100,000	10 cm x 13.97 cm	
Premier Scar Patch	69512-020	2015	Lidocaine 4 % Allantoin 2 % Petrolatum 30 %	NMT 8 hours 1 patch at a time Maximum 5 days	5,000 in 100,000 (incorrectly labeled)	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) Does not restrict use with other topical analgesic products Does not warn against heat exposure

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
Pure-Aid Maximum Strength Lidocaine Patch	67510-0280	2018	Lidocaine 4%	2 patches for up to 24 hours NMT 1 patch at a time Maximum 7 days	240	10 cm x 14 cm	
Pure-Aid Maximum Strength Lidocaine Plus Menthol Patch	67510-0284	2018	Lidocaine 4% Menthol 1%	2 patches for up to 24 hours NMT 1 patch at a time Maximum 7 days	240	10 cm x 14 cm	
Quality Choice Pain Relief Patches	63868-309	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4,000 in 100,000	10 cm x 13.97 cm	
Re-Lieved Lidocaine Pain Patch	71662-000	2017	Lidocaine 4%	NMT 12 hours 1 patch at a time (implied) 1-2 patches daily Maximum 7 days	18	7.62 cm x 15.24 cm	
Releevia LM Patch	69329-032	2013	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time NMT 4 patches/day Maximum 5 days	4000 in 100,000	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) Does not restrict use with other topical analgesic products Does not warn against heat exposure
Remaxazon External Patch	69379-285	2015	Lidocaine 4% Glucosamine 5% Chondroitin Sulfate Sodium 3% Capsaicin 0.0285%	NMT 8 hours NMT 1 patch at a time Maximum 5 days	4000 in 100,000	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) 21 CFR 348.20 does not allow for combination of lidocaine with counterirritants listed in 21 CFR 348.12 (capsaicin) Does not restrict use with other topical analgesic products
Renuu Patch	69329-012	2014	Allantoin 2 % Lidocaine 5 % Petrolatum 30 %	NMT 8 hours NMT 1 patch at a time Maximum 7 days	5,000 in 100,000 (Incorrectly labeled)	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel)

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							Does not restrict use with other topical analgesic products Does not warn against heat exposure
Ricora	69418-006	2015	Lidocaine 4% Menthol 1%	NMT 8 hours NMT 1 patch at a time Maximum 5 days	4 in 1,000	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label (i.e., drug facts panel) Does not restrict use with other topical analgesic products Does not warn against heat exposure
Rite Aid Hot and Cold Lidocaine with Menthol Pain Relief Patch	76168-302 76168-304	2017	Lidocaine 4% Menthol 1%	NMT 12 hours NMT 1 patch at a time NMT 1 patch/daily Maximum 7 days	40	10 cm x 14 cm	Does not restrict use with other topical analgesic products
Rite Aid Maximum Strength Lidocaine Patch	76168-305 76168-308	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	40	10 cm x 14 cm	Does not warn against heat exposure
SalonPas Lidocaine 4% Pain Relieving Gel-Patch	46581-830	2016	Lidocaine 4%	NMT 8 hours 1 patch at a time 3-4 patches/day Maximum of 7 days	560	10 cm x 14 cm	Does not restrict use with other topical analgesic products
Scadexe	69329-040	2015	Allantoin 2 % Lidocaine 4 % Petrolatum 30 %	NMT 8 hours NMT 1 patch at a time NMT 4 patches/day Maximum 7 days	4000 in 100,000	Not labeled	Does not restrict use with other topical analgesic products Does not warn against heat exposure
Silvera Pain Relief Patch	69379-037	2014	Lidocaine 1% Menthol 5% Capsaicin 0.0375%	8 hours 1 patch at a time Maximum 4 patches/daily Maximum use 5 days	1000 in 100,000	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label 21 CFR 348.20 does not allow for combination of lidocaine with counterirritants listed in 21 CFR 348.12 (capsaicin)

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							Product exceeds menthol strength allowed by 21 CFR 348.10(b) Does not restrict use with other topical analgesic products
Siterol	69440-007	2015	Lidocaine 3.99% Menthol 1%	NMT 8 hours NMT 1 patch at a time NMT 4 patches/day Maximum 5 days	3,990 in 100,000	12 cm x 7.6 cm	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label Does not restrict use with other topical analgesic products Does not warn against heat exposure
Solmara	69833-011	2015	Lidocaine 4% Menthol 5%	NMT 2 times/day Duration not listed	4000	Not listed	Product exceeds menthol strength allowed by 21 CFR 348.10(b) Multiple patches/pouch (does not comply with child-resistance requirements) Does not restrict use with other topical analgesic products Does not warn against heat exposure
Soothee Patch	69592-001	2014	Lidocaine 0.5% Menthol 5% Capsaicin 0.0375% Methyl Salicylate 2%	NMT 8 hours in 24 hour period NMT 4 patches/day Apply NMT 3 times/day	0.5 in 10,000	Not listed	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label Product exceeds menthol strength allowed by 21 CFR 348.10(b) 21 CFR 348.20 does not allow for combination of lidocaine with counterirritants listed in 21 CFR 348.12 (capsaicin)

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							Multiple patches/pouch (does not comply with child-resistance requirements) Does not warn against heat exposure
Soundbody Lidocaine Patch	67510-0283	2018	Lidocaine 4%	NMT 12 hours 2 patches for up to 24 hours Maximum 7 days	240	10 cm x 14 cm	
Soundbody Lidocaine with Menthol Patch	67510-0636	2018	Lidocaine 4% Menthol 1%	NMT 1 patch at a time 2 patches for up to 24 hours Maximum 7 days	40	10 cm x 14 cm	
TDS Pharm Lidocaine Maximum Strength Patch	42912-0150	2017	Lidocaine 4%	1 patch at a time NMT 12 hours Maximum 6 days	246	10.3 cm x 14.5 cm	
Terocin Lidocaine, Menthol Patch	50090-3538 50488-1001 55700-0048 68071-4593 68788-9555	2013	Lidocaine 4% Menthol 4%	Duration not labeled Number of patches in single administration not labeled 1 to 2 patches daily Maximum use not labeled	600	Not labeled	Multiple patches are provided in the pouch (not compliant with child resistance requirements) Product exceeds menthol strength allowed by 21 CFR 348.10(b) Elaborate label that far exceeds 21 CFR 348 including suggestions of opioid sparing Does not restrict use with other topical analgesic products Does not warn against heat exposure
Thera Care Pain Therapy	71101-911	2018	Lidocaine 4%	NMT 8 hours NMT 1 patch at a time Maximum 7 days	4000 in 100,000	10 cm x 14 cm	
Topcare Pain Relief Patches	36800-156	2017	Lidocaine 4%	NMT 12 hours NMT 1 patch at a time Maximum 7 days	4,000 in 100,000	10 cm x 14 cm	
Ultimate Lidocaine Pain Relief Patch	69159-920	2016	Lidocaine 4% Menthol 1%	8 hours Number of patches at a time not labeled Number of patches daily not labeled Maximum 7 days	4000 in 100,000	Not labeled	

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
Velma Pain Relief Patch	69379-016	2014	Lidocaine 4% Menthol 2% Methyl salicylate 2%	8 hours 1 patch at a time Maximum 4 patches/daily Maximum use 5 days	4000 in 100,000	Not labeled	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label 21 CFR 348.20 does not allow for combination of lidocaine with counterirritants listed in 21 CFR 348.12 (methyl salicylate) Product exceeds menthol strength allowed by 21 CFR 348.10(b) Does not restrict use with other topical analgesic products
Venia Premium Pain Patch	69512-700	2015	Lidocaine 4% Menthol 1%	NMT 2 applications per day	4 in 100	Not listed	Multiple patches are provided in the pouch (not compliant with child resistance requirements) Does not restrict use with other topical analgesic products Does not warn against heat exposure
Vexa	49430-053	2015	Lidocaine 4% Allantoin 2% Petrolatum 30%	NMT 8 hours NMT 4 patches/day	4	12.5 cm x 8.5 cm	Listed as an RX product, but with no NDA reference (or identified in the *Orange Book*) and has an OTC type label Does not warn against heat exposure
Viva Patch	53225-1030	2016	Lidocaine 2.5% Camphor 2% Methyl Salicylate 4%	8 – 12 hours NMT 2 patches/day NMT 1 patch at a time	2.5 in 100	Not labeled	Multiple patches are provided in the pouch (not compliant with child resistance requirements) Does not restrict use with other topical analgesic products

Product	NDC Code	Marketing Start Date	Strength	Administration	mg Lidocaine/ Patch	Patch Dimensions	Notes
							Does not list inactive ingredients; only onion and alpha-tocopherol
Walgreens Maximum Strength Pain Relief Patch	0363-9110	2018	Lidocaine 4%	NMT 8 hours NMT 1 patch at a time Maximum 7 days	4,000 in 100,000	10 cm x 14 cm	
Zims Max Freeze	66902-213	2016	Lidocaine 4% Menthol 1%	Duration not labeled Number of patches in single administration not labeled 1 to 2 patches daily Maximum use 7 days	40	7.6 cm x 12.7 cm (M) 10.2 cm x 14 cm (L) 10.2 cm x 20.3 cm (XL)	
Zims Max Freeze Patch	66902-113	2016	Menthol 5% Lidocaine 4% Methyl salicylate 0.04%	Duration not labeled Number of patches in single administration not labeled 1 to 2 patches daily Maximum use not labeled	40	7.6 cm x 12.7 cm (M) 10.2 cm x 14 cm (L) 10.2 cm x 20.3 cm (XL)	21 CFR 348.20 does not allow for combination of lidocaine with counterirritants listed in 21 CFR 348.12 (methyl salicylate) Product exceeds menthol strength allowed by 21 CFR 348.10(b)