

September 6, 2023



# **Tonix Pharmaceuticals Announces Commitment to Supply Tosymra® (sumatriptan Nasal Spray) 10 mg for Treatment of Acute Migraine to Meet Potential Increased Demand Following GSK's Planned Discontinuation of Imitrex® (sumatriptan) Nasal Spray After January 2024**

*Tosymra Nasal Spray 10 mg is a Proprietary Acute Migraine Treatment Approved Under the 505(b)2 Pathway Based on Bioequivalence to Imitrex (sumatriptan) Injection 4 mg*

*GlaxoSmithKline Recently Notified FDA that it will Discontinue Imitrex Nasal Spray 5 mg and 20 mg Products after January 2024*

CHATHAM, N.J., Sept. 06, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a biopharmaceutical company with marketed products and a pipeline of development candidates, today announced that it is committed to meeting potential increased demand for Tosymra® (sumatriptan) nasal spray 10 mg after GlaxoSmithKline's (GSK) planned discontinuation of Imitrex (sumatriptan) nasal spray 5 mg and 20 mg products after January, 2024.

On August 8, 2023, GSK informed the U.S. Food and Drug Administration (FDA) of its plan to discontinue Imitrex nasal spray 5 mg and 20 mg doses after January 31, 2024. The notification is posted on the FDA Drug Shortages website.<sup>1</sup> Tonix is preparing for potential increased demand for Tosymra (sumatriptan nasal spray) 10 mg to help avoid possible drug shortages for patients who suffer from migraines. Tosymra nasal spray is approved on the basis of bioequivalence to Imitrex injection 4 mg.

Drug shortages have presented an ongoing challenge for the U.S. healthcare system, reaching near-record levels<sup>2</sup> in recent months, causing treatment delays and rationing. Tonix is ready to step in to alleviate potential shortages in sumatriptan, a widely used treatment option for acute migraine.

"In response to FDA outreach, we have confirmed our commitment to meet potential increased demand for sumatriptan nasal spray from patients who suffer from migraines," said Seth Lederman, M.D., President and Chief Executive Officer of Tonix. "While Tosymra

nasal spray and Imitrex nasal spray are not substitutable at the pharmacy, we plan to alert providers to the possibility of prescribing Tosymra for patients who may benefit from a nasal spray formulation of sumatriptan.”

The American Headache Society Consensus Statement on migraine treatments recommends that “a non-oral formulation should be used in patients whose attacks are associated with severe nausea or vomiting, who do not respond well to traditional oral treatments, or who have trouble swallowing orally administered medications.”<sup>3</sup> Approximately 73% of migraine patients have been reported to experience nausea with or without vomiting during their attacks.<sup>4</sup>

“Intranasal sumatriptan is an important therapy for those who suffer from migraines. We believe Tosymra is differentiated from other intranasal formulations of sumatriptan, which are generic equivalents to Imitrex nasal spray because of its proprietary Intravail® absorption enhancer technology,” said James Hunter, Executive Vice President of Commercial Operations at Tonix Pharmaceuticals and President of Tonix Medicines. “Intravail technology helps the medication absorb into the bloodstream so it can work quickly, providing migraine pain relief in as little as 10 minutes for some patients.”<sup>5,6,7</sup>

## **About Migraine**

Nearly 40 million people in the United States suffer from migraine<sup>8</sup> and it has been recognized as the second leading cause of disability in the world.<sup>9</sup> Migraine is characterized by debilitating attacks lasting four to 72 hours with multiple symptoms, including pulsating headaches of moderate to severe pain intensity often associated with nausea or vomiting, and/or sensitivity to sound (phonophobia) and sensitivity to light (photophobia).

## **Tonix Pharmaceuticals Holding Corp.\***

Tonix is a biopharmaceutical company focused on commercializing, developing, discovering and licensing therapeutics to treat and prevent human disease and alleviate suffering. Tonix Medicines, our commercial subsidiary, markets Zembrace® SymTouch® (sumatriptan injection) 3 mg and Tosymra® (sumatriptan nasal spray) 10 mg under a transition services agreement with Upsher-Smith Laboratories, LLC from whom the products were acquired on June 30, 2023. Zembrace SymTouch and Tosymra are each indicated for the treatment of acute migraine with or without aura in adults. Tonix’s development portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix’s CNS development portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix’s lead development CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia, having completed enrollment of a potentially confirmatory Phase 3 study in the third quarter of 2023, with topline data expected in the fourth quarter of 2023. TNX-102 SL is also being developed to treat fibromyalgia-type Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a Phase 2 proof-of-concept study has been completed, and topline results were reported in the third quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily oral formulation being developed as a treatment for major depressive disorder (MDD), that completed enrollment in a Phase 2 proof-of-concept study in the third quarter of 2023, with topline results expected in the fourth quarter of 2023. TNX-4300 (estianeptine) is

a single isomer version of TNX-601, small molecule oral therapeutic in preclinical development to treat MDD, Alzheimer's disease and Parkinson's disease. Relative to tianeptine, estianeptine lacks activity on the  $\mu$ -opioid receptor while maintaining activity in the rat Novel Object Recognition test *in vivo* and the ability to activate PPAR- $\beta/\delta$  and neuroplasticity in tissue culture. TNX-1900 (intranasal potentiated oxytocin), is in development for preventing headaches in chronic migraine, and has completed enrollment in a Phase 2 proof-of-concept study with topline data expected in the fourth quarter of 2023. TNX-1900 is also being studied in binge eating disorder, pediatric obesity and social anxiety disorder by academic collaborators under investigator-initiated INDs. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication and has been granted Breakthrough Therapy designation by the FDA. A Phase 2 study of TNX-1300 is expected to be initiated in the third quarter of 2023. Tonix's rare disease development portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. Tonix's immunology development portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 was initiated in the third quarter of 2023. Tonix's infectious disease pipeline includes TNX-801, a vaccine in development to prevent smallpox and mpox. TNX-801 also serves as the live virus vaccine platform or recombinant pox vaccine platform for other infectious diseases. The infectious disease development portfolio also includes TNX-3900 and TNX-4000, which are classes of broad-spectrum small molecule oral antivirals.

\*Tonix's product development candidates are investigational new drugs or biologics and have not been approved for any indication.

<sup>1</sup>FDA Drug Shortage, accessed Aug 24, 2023 -

[https://www.accessdata.fda.gov/scripts/drugshortages/dsp\\_ActiveIngredientDetails.cfm?AI=Sumatriptan+Nasal+Spray&st=d&tab=tabs-2](https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Sumatriptan+Nasal+Spray&st=d&tab=tabs-2)

<sup>2</sup>CNN, accessed September 1, 2023 - <https://www.cnn.com/2023/08/10/health/drug-shortage-pharmacist-survey/index.html>

<sup>3</sup>Ailani J, et al. *Headache*. 2021. 61: 1021–1039

<sup>4</sup>Newman LC. *Headache*. 2013. 53 Suppl 1:11-6

<sup>5</sup>Tosymra [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, LLC: 2021

<sup>6</sup>Mathew NT, et al. *Arch Neurol*. 1992. 49(12):1271-6

<sup>7</sup>Wendt J, et al. *Clinical Therapeutics*. 2006. 28(4):517-526

<sup>8</sup>Burch RC, et al. *Neurol Clin*. 2019. 37(4):631-649

<sup>9</sup>Steiner TJ, et al. *J Headache Pain*. 2020. 21(1): 137

Zembrace SymTouch and Tosymra are registered trademarks of Tonix Medicines. Intravail is a registered trademark of Aegis Therapeutics, LLC, a wholly owned subsidiary of Neurelis, Inc. All other marks are property of their respective owners.

This press release and further information about Tonix can be found at [www.tonixpharma.com](http://www.tonixpharma.com).

## Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate,” “expect,” and “intend,” among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; risks related to the failure to successfully market any of our products; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2022, as filed with the Securities and Exchange Commission (the “SEC”) on March 13, 2023, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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### **Tosymra® (sumatriptan nasal spray): IMPORTANT SAFETY INFORMATION**

**Tosymra can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop Tosymra and get emergency medical help if you have any signs of heart attack:**

- discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back
- severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw

- pain or discomfort in your arms, back, neck, jaw, or stomach
- shortness of breath with or without chest discomfort
- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded

Tosymra is not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam is done and shows no problem.

Do not use Tosymra if you have:

- history of heart problems
- narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease)
- uncontrolled high blood pressure
- severe liver problems
- hemiplegic or basilar migraines. If you are not sure if you have these, ask your healthcare provider.
- had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation
- taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, or dihydroergotamine. Ask your provider if you are not sure if your medicine is listed above.
- are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure.
- an allergy to sumatriptan or any ingredient in Tosymra

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements.

Tosymra can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.

Tosymra may cause serious side effects including:

- changes in color or sensation in your fingers and toes
- sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever
- cramping and pain in your legs or hips, feeling of heaviness or tightness in your leg muscles, burning or aching pain in your feet or toes while resting, numbness, tingling, or weakness in your legs, cold feeling or color changes in one or both legs or feet
- increased blood pressure including a sudden severe increase even if you have no history of high blood pressure
- medication overuse headaches from using migraine medicine for 10 or more days each month. **If your headaches get worse, call your provider.**
- serotonin syndrome, a rare but serious problem that can happen in people using Tosymra, especially when used with anti-depressant medicines called SSRIs or SNRIs. **Call your provider right away if you have** mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in

- blood pressure; high body temperature; tight muscles; or trouble walking.
- hives (itchy bumps); swelling of your tongue, mouth, or throat
- seizures even in people who have never had seizures before

**The most common side effects of Tosymra include:** tingling, dizziness, feeling warm or hot, burning feeling, feeling of heaviness, feeling of pressure, flushing, feeling of tightness, numbness, application site (nasal) reactions, abnormal taste, and throat irritation.

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Tosymra. For more information, ask your provider.

This is the most important information to know about Tosymra but is not comprehensive. For more information, talk to your provider and read the [Patient Information](#) and [Instructions for Use](#). You can also visit [www.upsher-smith.com](http://www.upsher-smith.com) or call 1-888-650-3789.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.

## **INDICATION AND USAGE**

Tosymra is a prescription medicine used to treat acute migraine headaches with or without aura in adults.

Tosymra is not used to treat other types of headaches such as hemiplegic or basilar migraines or cluster headaches.

Tosymra is not used to prevent migraines. It is not known if Tosymra is safe and effective in children under 18 years of age.

## **Zembrace® SymTouch® (sumatriptan Injection): IMPORTANT SAFETY INFORMATION**

**Zembrace SymTouch (Zembrace) can cause serious side effects, including heart attack and other heart problems, which may lead to death. Stop use and get emergency help if you have any signs of a heart attack:**

- discomfort in the center of your chest that lasts for more than a few minutes or goes away and comes back
- severe tightness, pain, pressure, or heaviness in your chest, throat, neck, or jaw
- pain or discomfort in your arms, back, neck, jaw or stomach
- shortness of breath with or without chest discomfort
- breaking out in a cold sweat
- nausea or vomiting
- feeling lightheaded

Zembrace is not for people with risk factors for heart disease (high blood pressure or cholesterol, smoking, overweight, diabetes, family history of heart disease) unless a heart exam shows no problem.

Do not use Zembrace if you have:

- history of heart problems

- narrowing of blood vessels to your legs, arms, stomach, or kidney (peripheral vascular disease)
- uncontrolled high blood pressure
- hemiplegic or basilar migraines. If you are not sure if you have these, ask your provider.
- had a stroke, transient ischemic attacks (TIAs), or problems with blood circulation
- severe liver problems
- taken any of the following medicines in the last 24 hours: almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, ergotamines, dihydroergotamine.
- are taking certain antidepressants, known as monoamine oxidase (MAO)-A inhibitors or it has been 2 weeks or less since you stopped taking a MAO-A inhibitor. Ask your provider for a list of these medicines if you are not sure.
- an allergy to sumatriptan or any of the components of Zembrace

Tell your provider about all of your medical conditions and medicines you take, including vitamins and supplements.

Zembrace can cause dizziness, weakness, or drowsiness. If so, do not drive a car, use machinery, or do anything where you need to be alert.

Zembrace may cause serious side effects including:

- changes in color or sensation in your fingers and toes
- sudden or severe stomach pain, stomach pain after meals, weight loss, nausea or vomiting, constipation or diarrhea, bloody diarrhea, fever
- cramping and pain in your legs or hips; feeling of heaviness or tightness in your leg muscles; burning or aching pain in your feet or toes while resting; numbness, tingling, or weakness in your legs; cold feeling or color changes in one or both legs or feet
- increased blood pressure including a sudden severe increase even if you have no history of high blood pressure
- medication overuse headaches from using migraine medicine for 10 or more days each month. If your headaches get worse, call your provider.
- serotonin syndrome, a rare but serious problem that can happen in people using Zembrace, especially when used with anti-depressant medicines called SSRIs or SNRIs. Call your provider right away if you have: mental changes such as seeing things that are not there (hallucinations), agitation, or coma; fast heartbeat; changes in blood pressure; high body temperature; tight muscles; or trouble walking.
- hives (itchy bumps); swelling of your tongue, mouth, or throat
- seizures even in people who have never had seizures before

**The most common side effects of Zembrace include:** pain and redness at injection site; tingling or numbness in your fingers or toes; dizziness; warm, hot, burning feeling to your face (flushing); discomfort or stiffness in your neck; feeling weak, drowsy, or tired.

Tell your provider if you have any side effect that bothers you or does not go away. These are not all the possible side effects of Zembrace. For more information, ask your provider.

This is the most important information to know about Zembrace but is not comprehensive. For more information, talk to your provider and read the [Patient Information](#) and [Instructions for Use](#). You can also visit [www.upsher-smith.com](http://www.upsher-smith.com) or call 1-888-650-3789.

You are encouraged to report adverse effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.

## **INDICATION AND USAGE**

Zembrace is a prescription medicine used to treat acute migraine headaches with or without aura in adults who have been diagnosed with migraine.

Zembrace is not used to prevent migraines. It is not known if it is safe and effective in children under 18 years of age.



Source: Tonix Pharmaceuticals Holding Corp.