

August 10, 2023



Tonix Pharmaceuticals Reports Second Quarter 2023 Financial Results and Operational Highlights

Topline Results from Four CNS Clinical Trials Expected in the Third and Fourth Quarters of 2023

Fibromyalgia Topline Results Expected in the Fourth Quarter of 2023 for Phase 3 Potentially NDA-Enabling Study of the Centrally-Acting Non-Opioid Analgesic TNX-102 SL

Completed Strategic Acquisition of Two Marketed Acute Migraine Products: Zembrace[®] SymTouch[®] (sumatriptan injection) and Tosymra[®] (sumatriptan nasal spray)

CHATHAM, N.J., Aug. 10, 2023 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a biopharmaceutical company, today announced financial results for the second quarter ended June 30, 2023, and provided an overview of recent operational highlights.

“We have recently completed enrollment in four clinical trials for central nervous system (CNS) indications, representing our continuing progress towards bringing forth new treatments for serious CNS conditions that affect large patient populations,” said Seth Lederman, M.D., Chief Executive Officer of Tonix. “We look forward to data readouts before year-end 2023 for fibromyalgia, fibromyalgia-type Long COVID, chronic migraine, and depression. The topline results from the Phase 3 fibromyalgia trial are of particular importance because we believe the RESILIENT trial, if successful, will be the final efficacy trial required for submitting a New Drug Application (NDA) for approval by the U.S. Food and Drug Administration (FDA).”

On June 30, 2023, Tonix completed the acquisition of two marketed products from Upsher-Smith Laboratories, LLC (Upsher-Smith): Zembrace[®] SymTouch[®] (sumatriptan injection) 3 mg and Tosymra[®] (sumatriptan nasal spray) 10 mg. Zembrace SymTouch and Tosymra are both non-oral proprietary products indicated for the treatment of acute migraine with or without aura in adults. Zembrace SymTouch is the only branded sumatriptan autoinjector professionally promoted in the United States and is designed for ease of use and favorable tolerability with a low 3 mg dose. Tosymra is a novel intranasal sumatriptan product formulated with a permeation enhancer that provides rapid and efficient absorption of sumatriptan. Collectively, these products generated gross factory sales of approximately \$30 million for the twelve months ended March 31, 2023. Zembrace SymTouch and Tosymra each may provide onset of migraine pain relief in as few as 10 minutes for some patients and currently have patent protection to 2036 and 2031, respectively.

Seth Lederman continued, “The acquisition of these two marketed products is transformative for Tonix as we believe that we are on track to become a fully integrated pharmaceutical company and to expand our expertise in CNS disorders by interacting with health care providers and payers. The build out of our commercial capabilities is timely, given the potential 2025 launch of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) for fibromyalgia, if results from the RESILIENT trial are positive. The two marketed acute migraine products also align strongly with our clinical product candidate TNX-1900 (intranasal potentiated oxytocin), in development as a preventive medication in chronic migraineurs.”

“We plan to submit an IND to study TNX-2900 (intranasal potentiated oxytocin) in Prader-Willi syndrome, for which Orphan Drug Designation has already been granted by the FDA,” said Gregory Sullivan, M.D., Chief Medical Officer of Tonix Pharmaceuticals. “Academic collaborators have initiated enrollment in three Phase 2 investigator-initiated trials studying TNX-1900 (intranasal potentiated oxytocin). The trials in adolescent obesity and binge eating disorder at Massachusetts General Hospital (MGH) have the potential to expand the use of TNX-1900 to the treatment of disorders of appetite, eating behaviors and weight. The trial in social anxiety at University of Washington has the potential to expand the use of TNX-1900 to the treatment of disorders of social functioning.”

Dr. Lederman continued, “During the second quarter of 2023, we also announced the prioritization of our clinical stage CNS programs and de-prioritization of our COVID-19 vaccine and related therapeutic programs, as well as certain other preclinical programs in order to reallocate cash and resources. We also streamlined several CNS studies by eliminating interim analyses and reducing enrollment targets to ensure data readouts this year. We incurred a one-time cash outlay related to our acquisition of Zembrace SymTouch and Tosymra in the second quarter.”

Recent Highlights—Marketed Products

On June 30, 2023, Tonix completed the acquisition of two currently marketed products from Upsher-Smith Laboratories, LLC (Upsher-Smith): Zembrace SymTouch (sumatriptan injection) 3 mg and Tosymra (sumatriptan nasal spray) 10 mg. Zembrace SymTouch and Tosymra are both indicated for the treatment of acute migraine with or without aura in adults.

Recent Highlights—Key Product Candidates*

Upcoming Data Readouts in Central Nervous System (CNS) Pipeline During 2023

Fibromyalgia (4Q): Phase 3 Potentially NDA-Enabling Study of TNX-102 SL

Fibromyalgia-Type Long COVID (3Q): Phase 2 Proof-of-Concept Study of TNX-102 SL

Chronic Migraine (4Q): Phase 2 Proof-of-Concept Study of TNX-1900

Depression (4Q): Phase 2 Proof-of-Concept Study of TNX-601 ER

Central Nervous System (CNS) Pipeline

TNX-102 SL (cyclobenzaprine HCl sublingual tablets): once-daily at bedtime small molecule for the management of fibromyalgia (FM) – centrally-acting, non-opioid analgesic.

- In August 2023, the Company announced that it completed enrollment of its potentially confirmatory Phase 3 RESILIENT trial of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6 mg in fibromyalgia. A total of 457 participants were randomized in the trial, which, if successful, may serve as the final, well-controlled efficacy trial required for submission of an NDA for approval by the FDA. RESILIENT is a registration-quality, double-blind, placebo-controlled study.
- Topline results from the RESILIENT trial are expected in the fourth quarter of 2023

TNX-102 SL for the treatment of Fibromyalgia-Type Long COVID, also known as Post-Acute Sequelae of COVID-19 (PASC)

- In August 2023, the Company announced it completed the clinical phase of the PREVAIL study, a Phase 2 proof-of-concept study of TNX-102 SL for fibromyalgia-type Long COVID, as the last patient completed their final study visit. PREVAIL is a registration-quality, double-blind, placebo-controlled study.
- Topline results from the PREVAIL Phase 2 trial are expected in the third quarter of 2023.

TNX-1900 (intranasal potentiated oxytocin): small peptide for migraine, craniofacial pain, social anxiety disorder, insulin resistance and related disorders, and adolescent obesity and binge eating disorder

- Tonix has developed a formulation of intranasal oxytocin that contains magnesium (Mg²⁺) which is believed to potentiate the effects of oxytocin and may address the “inverted U” dose response of oxytocin. The company believes that if Mg²⁺ reduces the high dose inhibition of oxytocin alone, then the new formulation may improve consistency in clinical trials.
- Enrollment has been completed in the proof-of-concept Phase 2 PREVENTION study of TNX-1900 for the prevention of migraine headache in chronic migraineurs with a total of 88 patients enrolled. PREVENTION is a registration-quality, double-blind, placebo-controlled study.
- Topline results from the PREVENTION Phase 3 trial are expected in the fourth quarter of 2023.
- In July 2023, Tonix announced that the first participant was enrolled in the investigator-initiated Phase 2 STROBE Study of TNX-1900 for the treatment of binge-eating disorder at the Massachusetts General Hospital (MGH) under the direction of Principal Investigator Elizabeth Lawson. Tonix is supporting the STROBE study through a clinical trial agreement with MGH.
- In July 2023, Tonix announced that the first participant was enrolled in a Phase 2 investigator-initiated, proof-of-concept study of TNX-1900 for enhancing social safety learning in social anxiety disorder (SAD) under the direction of Principal Investigator Angela Fang. Tonix entered into an agreement with the University of Washington to examine the potential role of TNX-1900 in enhancing vicarious extinction learning in SAD, compared to healthy controls.

- In July 2023, Tonix announced that the first participant was enrolled in the Phase 2 POWER study of TNX-1900 for the treatment of pediatric obesity with MGH under the direction of Principal Investigator Elizabeth Lawson. MGH is the sponsor of the National Institutes of Health-funded trial, being conducted under an investigator-initiated IND.
- In May 2023, Tonix entered into a research collaboration agreement with the principal investigator of the study, Dr. Antoinette Maassen van den Brink, Professor of Neurovascular Pharmacology, Erasmus University Medical Center, to evaluate the effect of TNX-1900 on capsaicin- or electrical stimulation-induced forehead dermal blood flow in healthy female volunteers.

TNX-601 ER (tianeptine hemioxalate extended-release tablets): a once-daily orally administered small molecule for the treatment of major depressive disorder (MDD), posttraumatic stress disorder (PTSD), neurocognitive dysfunction associated with corticosteroid use, and potentially Alzheimer's disease

- Enrollment has been completed in the proof-of-concept Phase 2 UPLIFT study for the treatment of MDD, with 116 patients enrolled. UPLIFT is a registration-quality, double-blind, placebo-controlled study.
- Topline results for the UPLIFT Phase 2 trial are expected in the fourth quarter of 2023.
- Scientists at Tonix's Research and Development Center (RDC) in Frederick, Md. established the molecular mechanism of action of tianeptine, the active ingredient of TNX-601 ER. The research supports a direct role for restoring neuroplasticity and neurogenesis, and upsets previously held beliefs about the significance of neurotransmitters in treating depression. It also provides clarity on why tianeptine does not cause sexual dysfunction, weight gain or several other treatment-limiting toxicities associated with traditional antidepressants.

TNX-4300 (estianeptine): small molecule oral therapeutic for MDD, bipolar disorder, Alzheimer's disease and Parkinson's disease

- In July 2023, the Company announced that it would focus resources on the development of single isomer TNX-4300 as a first-in-class oral therapy for mood disorders, Alzheimer's disease and other psychiatric and neurodegenerative conditions with memory deficits. The decision follows the Company's announcement in May 2023 of the isolation and characterization of the (S)-isomer of tianeptine, which activates PPAR- β/δ , restores neuroplasticity in neuronal tissue culture and is free of μ -opioid receptor activity.

TNX-1300 (recombinant double mutant cocaine esterase): biologic for life-threatening cocaine intoxication

- Tonix expects to initiate a potentially pivotal Phase 2 clinical study of TNX-1300 for the treatment of cocaine intoxication in the third quarter of 2023. In 2022, Tonix was awarded a Cooperative Agreement grant from the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health (NIH), to support development of TNX-1300.

- TNX-1300 has been granted Breakthrough Therapy designation by the FDA.

Rare Disease Pipeline

TNX-2900 (intranasal potentiated oxytocin): small peptide for the treatment of Prader-Willi syndrome (PWS)

- TNX-2900 has been granted Orphan Drug designation from the FDA for the treatment of PWS and the preparation of the IND is in process.
- TNX-2900 is in development to treat PWS and the planned clinical study will study its effects on hyperphagia, or pathological over-eating, in children and young adult patients with PWS.

Immunology Pipeline

TNX-1500 (anti-CD40L monoclonal antibody): third generation anti-CD40L monoclonal antibody for prophylaxis of organ transplant rejection and treatment of autoimmune disorders.

- In May 2023, the IND for prevention of organ rejection in patients receiving a kidney transplant was cleared by FDA. A first-in-human Phase 1 study is expected to start in the third quarter of 2023. The first indication for TNX-1500 will be prophylaxis of organ rejection in adult patients receiving a kidney transplant, but multiple additional indications are possible, including autoimmune diseases. Two peer reviewed publications described the work at the Massachusetts General Hospital on allogeneic transplants in animals.^{1,2}

**All of Tonix's product candidates are investigational new drugs or biologics and none have been approved for any indication.*

¹Lassiter, G., et al. (2023). TNX-1500, a crystallizable fragment–modified anti-CD154 antibody, prolongs non-human primate renal allograft survival. *American Journal of Transplantation*. <https://doi.org/10.1016/j.ajt.2023.03.022>

²Miura, S., et al. (2023). TNX-1500, a crystallizable fragment–modified anti-CD154 antibody, prolongs non-human primate cardiac allograft survival. *American Journal of Transplantation*. <https://doi.org/10.1016/j.ajt.2023.03.025>

Recent Highlights—Financial

As of June 30, 2023, Tonix had approximately \$25.6 million of cash and cash equivalents, compared to \$120.2 million as of December 31, 2022. Subsequent to the end of the second quarter of 2023, Tonix raised \$7.0 million in gross proceeds through a public offering of its common stock. Cash used in operations was approximately \$56.3 million for the six months ended June 30, 2023, compared to \$52.2 million for the same period in 2022. Cash used by investing activities for the six months ended June 30, 2023 was approximately \$27.8 million, primarily driven by the purchase of certain assets from Upsher-Smith Laboratories, LLC.

The acquisition cost of Zembrace SymTouch and Tosymra was \$15 million, consisting of

\$12 million up front and an additional deferred payment of \$3.0 million. We also purchased inventory for \$10.0 million and expect to pay an additional \$1.3 million related to an inventory adjustment.

On April 8, 2020, the Company entered into a sales agreement with AGP of up to \$320.0 million in at-the-market offerings sales. During the quarter ended June 30, 2023, the Company sold approximately 0.4 million shares of common stock under the sales agreement, for net proceeds of approximately \$1.0 million.

On August 1, 2023, the Company sold in a public offering securities consisting of 2,530,000 shares of common stock, pre-funded warrants to purchase up to 4,470,000 shares of common stock, and accompanying common warrants to purchase 7,000,000 shares of common stock, at \$1.00 per unit of common stock and common warrant, and \$0.99 per pre-funded warrant and common warrant. The Company received net proceeds of approximately \$6.2 million, after deducting underwriting discount and other offering expenses.

Second Quarter 2023 Financial Results

R&D expenses for the second quarter 2023 were approximately \$22.0 million, compared to \$16.6 million for the same period in 2022. As expected, R&D expenses have increased during 2023 due to progressing clinical development programs forward and investing in our preclinical development pipeline.

G&A expenses for the second quarter 2023 were \$7.0 million, compared to \$6.8 million for the same period in 2022.

Net loss available to common stockholders was \$28.4 million, or \$2.68 per share, basic and diluted, for the second quarter 2023, compared to net loss available to common stockholders of \$27.4 million, or \$7.64 per share, basic and diluted, for the same period in 2022. The basic and diluted weighted average common shares outstanding for the second quarter 2023 was 10,587,096 compared to 3,584,699 shares for the same period in 2022.

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 markets Zembrace[®] SymTouch[®] (sumatriptan injection) 3 mg and Tosymra[®] (sumatriptan nasal spray) 10 mg. 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 CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia, having completed enrollment in a potentially registration-enabling study, and with topline data expected in the fourth quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Enrollment in a Phase 2 study has been completed, and topline results are expected in the third quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets), is a once-daily formulation being developed as a treatment for major depressive disorder (MDD). Enrollment is now complete in the UPLIFT trial of TNX-601 ER in MDD and topline results

are expected in the fourth quarter of 2023. TNX-4300 (estianeptine) is a small molecule oral therapeutic in preclinical development to treat MDD, Alzheimer's disease and Parkinson's disease. TNX-1900 (intranasal potentiated oxytocin), is in development for chronic migraine, and the PREVENTION study has completed enrollment with topline data expected in the fourth quarter of 2023. 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 is expected to be 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, classes of broad-spectrum small molecule antivirals.

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

Tonix Medicines has contracted to acquire the Zembrace SymTouch and Tosymra registered trademarks. Intravail is a registered trademark of Aegis Therapeutics, LLC, a wholly owned subsidiary of Neurelis, Inc.

This press release and further information about Tonix can be found at 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.

TONIX PHARMACEUTICALS HOLDING CORP.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(In Thousands, Except Share and Per Share Amounts)
(unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2023	2022	2023	2022
COSTS AND EXPENSES:				
Research and development	\$ 21,976	\$ 16,579	\$ 48,487	\$ 35,001
General and administrative	7,026	6,757	14,417	14,771
	<u>29,002</u>	<u>23,336</u>	<u>62,904</u>	<u>49,772</u>
Operating loss	(29,002)	(23,336)	(62,904)	(49,772)
Interest and other income, net	<u>646</u>	<u>196</u>	<u>1,543</u>	<u>215</u>
Net loss	(28,356)	(23,140)	(61,361)	(49,557)
Preferred stock deemed dividend	<u>—</u>	<u>4,255</u>	<u>—</u>	<u>4,255</u>
Net loss available to common stockholders	\$ (28,356)	\$ (27,395)	\$ (61,361)	\$ (53,812)
Net loss per common share, basic and diluted	\$ (2.68)	\$ (7.64)	\$ (5.88)	\$ (17.28)
Weighted average common shares outstanding, basic and diluted	10,587,096	3,584,699	10,428,678	3,113,965

See the accompanying notes to the condensed consolidated financial statements

TONIX PHARMACEUTICALS HOLDING CORP.
CONDENSED CONSOLIDATED BALANCE SHEETS
(In Thousands)
(Unaudited)

	June 30, 2023	December 31, 2022 ¹
Assets		
Cash and cash equivalents	\$ 25,617	\$ 120,229
Inventory	13,700	-
Prepaid expenses and other	12,012	10,548
Total current assets	51,329	130,777
Other non-current assets	108,407	94,913
Total assets	\$ 159,736	\$ 225,690
Liabilities and stockholders' equity		
Total liabilities	\$ 19,273	\$ 18,508
Stockholders' equity	140,463	207,182
Total liabilities and stockholders' equity	\$ 159,736	\$ 225,690

¹The condensed consolidated balance sheet for the year ended December 31, 2022 has been derived from the audited financial statements but do not include all of the information and footnotes required by accounting principles generally accepted in the United States for complete financial statements.

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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 or call 1-888-650-3789.

You are encouraged to report adverse effects of prescription drugs to the FDA. Visit 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.

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 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, 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.



Source: Tonix Pharmaceuticals Holding Corp.