Unique Protocol ID: LUI-S4

Brief Title: An Efficacy and Safety Trial of Intranasal Ketorolac in Emergency Department Patients for the Treatment of Acute Pain (Sprix)

Official Title: A Prospective, Open-label, Nonrandomized Efficacy and Safety Trial of Intranasal Ketorolac in Emergency Department Patients for the Treatment of Acute Pain

Protocol #: Version 4.0/ September 21, 2011

Principal Investigator: Sharon E. Mace, MD

Sponsor: Luitpold Pharmaceuticals, Inc.

Cleveland Clinic
Consent to Participate in a Research Study

Study Title: A Prospective, Open-label, Nonrandomized Efficacy and Safety Trial of Intranasal Ketorolac in Emergency Department Patients for the Treatment of Acute Pain

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Carefully review this consent document. The purpose of a consent document is to provide you with information to help you decide whether you wish to participate in research. Your decision is completely voluntary and will not affect your medical care if you choose not to participate. It is important for you to ask questions and understand the research risks, benefits and alternatives.

Please note:

- **You are being asked to participate in a research study**
- **Carefully consider the risks, benefits and alternatives of the research**
- **Your decision to participate is completely voluntary**

Your doctor may be an investigator in this research study, and as a research investigator, is interested in both your welfare and in the conduct of the research study. Before entering this study or at any time during this research, you may ask for a second opinion about your care from another doctor who is not involved with the research study. You are not under any obligation to participate in any research project offered by your doctor.

1. INFORMATION ON THE RESEARCH

Why Are You Being Asked To Take Part In This Research?

You are being asked to participate in this research study because you have come to the Emergency Department (ED) due to pain that has come on quickly and is not related to any illness or injury that you have experienced prior to today ("acute").

Pain is a common reason for people to seek healthcare, especially in emergency care. This study will use an intranasal (in the nose) medication called ketorolac (Sprix) to try to decrease the pain you are experiencing now.

Why Is This Study Being Done?

The purpose of this study is to determine the effectiveness, the safety, and the tolerability of intranasal ketorolac (Sprix) in relieving acute pain in adults ages 18-64 who come to the ED seeking care. Considering all ED visits, pain is the most common chief complaint. Giving intranasal ketorolac (Sprix) after stomach and dental surgeries has been shown to be safe and effective, but no studies have investigated the use of intranasal ketorolac (Sprix) for the treatment of acute pain in the ED.

Ketorolac (Sprix) has several advantages over other drugs commonly given for pain, including opioids. Ketorolac (Sprix) is non-addicting and has fewer side effects than opioids. The administration of ketorolac (Sprix) by other methods, such as IV, intramuscular shot, and oral pill form, has been shown to be safe and effective in treating acute pain.
This study is being done to find out if giving ketorolac (Sprix) as a single dose nasal spray will have the same outcome for patients.

How Many People Will Take Part In The Study?

About 25 people will take part in this study at Cleveland Clinic.

What Is Involved In The Study?

If you choose to participate in this study, you will have to sign the consent form and then the following study procedures will take place. Your healthcare provider will examine your nasal passages and record any findings, such as redness or drainage, before you are given the ketorolac (Sprix) nasal spray for pain. Baseline (*before* ketorolac) pain scores will be recorded using the Numeric Rating Scale (NRS) where you will rate your pain on a scale where 0 = no pain to 100 = worst pain imaginable. Vital signs (i.e. heart rate, blood pressure) will also be recorded.

Following this, the healthcare provider will administer the intranasal ketorolac (Sprix) to you and will examine your nasal passages after the spray and record any findings, such as redness or drainage. You will be asked to tell the healthcare provider when you begin to feel some pain relief and when you definitely feel much better. The healthcare provider will record these times.

NRS Pain scores will be collected beginning 20 minutes after you received the nasal spray, 40 minutes after, and 60 minutes after you received the ketorolac (Sprix) nasal spray. Then, pain assessments will be recorded at 1 hour intervals after the nasal spray for up to 6 hours. Other pain assessments will be conducted immediately after any additional pain medications or sedatives are given to you for pain relief besides the ketorolac (Sprix) and immediately before you are discharged from the ED. Vital signs will also be recorded after you take the ketorolac (Sprix) nasal spray.

In addition to the pain assessment ratings, you will be asked to answer a few questions about the intranasal ketorolac (Sprix) and its effectiveness at relieving your pain. You will also be asked about your satisfaction with the ketorolac (Sprix) nasal spray.

Below is a table to help explain the parts of the study:

	Screen	Pre-spray	Sprix Spray	Post-spray	Rescue meds	Post spray Pain scores
Informed Consent	X					
Nasal inspection		X		X		
Pain scores		X			After rescue meds	20 & 40min Hour 1,2,3,4,5, up to 6 hours
Rescue Meds			X		As needed	
Vitals		X		X		
Questionnaires				X		
Adverse events			X	X	X	X

How Long Will You Be In The Study?

Your participation in this study will last up until the time you are discharged from the ED.

2. RISKS AND DISCOMFORTS

What Are The Risks Of The Study?

.Ketorolac has been proven effective for pain relief, especially for certain types of pain; such as musculoskeletal pain, headaches and the pain from renal colic. In appropriate patients; ketorolac is a relatively safe drug for the treatment of pain. Side effects and complications, such as gastrointestinal complaints (e.g. abdominal pain, dyspepsia, GI bleeding) and renal dysfunction (elevation of the BUN and creatinine) have been reported but with appropriate patient selection are uncommon or rare. The use of NSAIDS including ketorolac is not recommended in patients with active peptic ulcer disease, renal disease or at risk for renal failure due to volume depletion, cerebrovascular bleeding, hemorrhagic disorders, or those with a high risk of bleeding. With appropriate patient selection, ketorolac can be a safe and effective medication for the relief of pain.

Potential Risks or Unwanted Reactions:

	Mild	Moderate	Severe
Likely **_____%**			
Less Likely **5-15 %**	-Nasal discomfort or pain -Increased tearing		
Rare **2-3%**	-Nasal Inflammation	-Rash -Heart rate below 60 -High blood pressure -Elevated liver function tests	-Worsening kidney function -Fluid retention -Bleeding in the gastrointestinal tract

Unforeseeable risks:

There may be risks or side effects related to the study drug/device that are unknown at this time. You will be notified of any significant new findings that become known that may affect your willingness to continue in the study.

Pregnant women, fertile females/males:

There may be unforeseen risks to an unborn child associated with your taking intranasal ketorolac (Sprix) Therefore, if you are capable of giving birth to or fathering a child, you and your sexual partner should use adequate birth control measures while you are in the study. These measures may include abstinence, oral contraceptives (birth control pills), IUD, diaphragm, approved hormone injections, condoms, or documentation of medical sterilization. If you are unwilling to do this, we ask that you not participate in this study.

Pregnancy tests will be performed on all women of child-bearing potential before beginning the study and during the study every. If you or your spouse become pregnant while taking part in this study you must notify the study doctor immediately. If birth control methods must continue after the study drug is discontinued, this time period should be provided to subjects.

Questionnaire/Survey Research:

There is, however, the potential risk of loss of confidentiality. Every effort will be made to keep your information confidential, however, this cannot be guaranteed. Some of the questions we will ask you

as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions and you may take a break at any time during the study.

3. BENEFITS

Are There Benefits To Taking Part In The Study?

It is possible that you may benefit by participating in this study because ketorolac (Sprix) should help to alleviate the pain that you are experiencing. It is expected that your pain will decrease with the study treatment of intranasal ketorolac (Sprix). Even if your pain improves with the study drug, you may still require the use of additional "rescue" pain medications or sedatives to feel completely pain-free. This study will also help doctors decide if intranasal ketorolac (Sprix) is an effective and safe medication to give to people who come to the ED with acute pain due to sudden illness or injury.

4. ALTERNATIVES

What Other Options Are There?

You may choose not to participate in this study. Your decision to participate (or not) is completely voluntary. If you choose not to participate in this study and receive the intranasal ketorolac (Sprix), there are a number of other pain relief options available for you, including opioids and sedatives. Your doctor will discuss these other options with you and provide you with one (or more) of these medications for pain.

5. PRIVACY AND CONFIDENTIALITY

The medical and research information recorded about you for this research will be used within the Cleveland Clinic and/or disclosed outside the Cleveland Clinic. Tests and procedures done solely for this research study may be placed in your medical record to indicate your participation in this study. The information recorded about you as part of this research will be maintained in a confidential manner.

Upon completion of the study, you may have access to the research information if contained in the medical record. During the study, your access to research information about you will be limited. Preventing this access during the study keeps the knowledge of study results from affecting the reliability of the study. This information will be available should an emergency arise that would require your treating physician to know this information to assist in treating you.

Federal regulations require that you authorize the release of any health information that may reveal your identity. The persons and entities that you are authorizing to use or disclose your individually identifiable health information may include the study doctor, the study staff, Cleveland Clinic monitors/auditors and IRB, the study Sponsor, Luitpold Pharmaceuticals, Inc, and its agents, the U.S. Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS), and other governmental agencies from foreign countries. Because of the need to release information to these parties absolute confidentiality cannot be guaranteed. The Cleveland Clinic also may use and

disclose this information for treatment and payment reasons. The Cleveland Clinic must comply with legal requirements that mandate disclosure in unusual situations. Once your personal health information is released it may be re-disclosed and no longer protected by federal privacy laws. The results of this research may be presented at meetings or in publications; however, your identity will not be disclosed in those presentation.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to Dr. Sharon E. Mace at The Cleveland Clinic, 9500 Euclid Avenue, Cleveland, Ohio 44195. If you do so, your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of the research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. Even if you ask us to stop outside disclosures, information collected about you will be disclosed as required by state and federal law.

The Cleveland Clinic will not use or disclose the information collected in this study for another research purpose without your written permission, unless the Cleveland Clinic Institutional Review Board gives permission after ensuring that appropriate privacy safeguards are in place. The Institutional Review Board is a committee whose job is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your medical records. If you choose not to sign this consent form, you will not be permitted to participate in this research study.

6. RESEARCH RELATED INJURIES
What Happens If An Injury Occurs?

Standard language: ***refer to the research contract to determine if the sponsor will cover***

In the event you are injured as a result of participation in this research, medical care is available to you and will be billed to your insurance company. The cost of such medical care that is not covered by your medical insurance shall be paid by the study sponsor, ***(insert sponsor name and terms from the study agreement/contract),*** There are no plans to provide compensation for lost wages, direct or indirect losses. You are not waiving any legal rights by signing this form. Further information about research related injury is available by contacting the Institutional Review Board at 216-444-2924.

OR

In the event you are injured as a result of participation in this research, medical care is available to you. The costs of such medical care will be billed to you or your insurance company. There are no plans to provide compensation for lost wages, direct or indirect losses. The Cleveland Clinic will not voluntarily provide compensation for research related injury. You are not waiving any legal rights by signing this form. Further information about research related injury is available by contacting the Institutional Review Board at 216-444-2924.

7. COSTS

What Are The Costs?

There are no additional costs to you for participation in this research study. The study drug will be provided at no cost to you. The cost for routine tests and services that would normally be performed even if you don't participate in the study will be billed to you or your insurance provider. You will not be paid to participate in this research study.

8. VOLUNTARY PARTICIPATION

What Are Your Rights As A Participant?

Taking part in this study is voluntary. You will be told of any new, relevant information from the research that may affect your health, welfare, or willingness to continue in this study. You may choose not to take part or may leave the study at any time. Withdrawing from the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to withdraw from the study you should discuss with your study doctor your decision to ensure a safe withdrawal.

You may be withdrawn from the study if: you do not fulfill inclusion or exclusion criteria, if you experience a significant complication from the intranasal ketorolac (Sprix), or if you develop another illness or condition that would interfere with your participation. You may also be withdrawn from the study if you violate the protocol or if your healthcare provider believes that it is in your best medical interest to stop your participation in the study.

9. QUESTIONS

Whom Do You Call With Questions Or Problems?

If you have any questions, concerns or complaints about the research, or develop a research-related problem, contact Dr. Sharon E. Mace, Principal Investigator of the study, at (216) 445-4598 during business hours. During non-business hours, you should contact the Cleveland Clinic Emergency Department attending physician at (216) 445-4500. If you have questions about your rights as a research subject, you should contact the Institutional Review Board at (216) 444-2924.

10. SIGNATURE

Statement of Participant

I have read and have had verbally explained to me the above information and have had all my questions answered to my satisfaction. I understand that my participation is voluntary and that I may stop my participation in the study at any time. Signing this form does not waive any of my legal rights. I understand that a copy of this consent will be provided to me. By signing below, I agree to take part in this research study.

_____
Printed name of Participant

_____ _____
Participant Signature Date

Statement of Person Conducting Informed Consent Discussion

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____
Printed name of person obtaining consent

_____ _____
Signature of person obtaining consent Date