

OXPZero™ NSAIDs:  
A New Weapon in The Fight Against  
the Opioid Epidemic

# XPZero™ NSAIDs: A New Weapon in The Fight Against the Opioid Epidemic

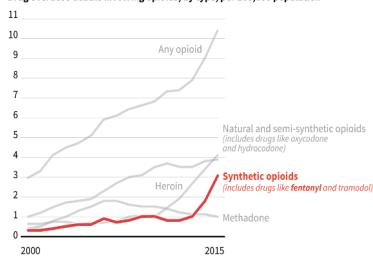


## Opioids: The Problem

According to the US CDC “*The United States is in the midst of an opioid overdose epidemic.*”<sup>1</sup> From 2000 to 2016, over 400,000 people died from opioid overdoses.<sup>2</sup> Many of these overdoses were due to access and exposure to legitimately-prescribed medications.

### Opioid-Related Deaths, Especially From Synthetic Opioids Like Fentanyl, Are On The Rise In The U.S.

Drug overdose deaths involving opioids, by type, per 100,000 population



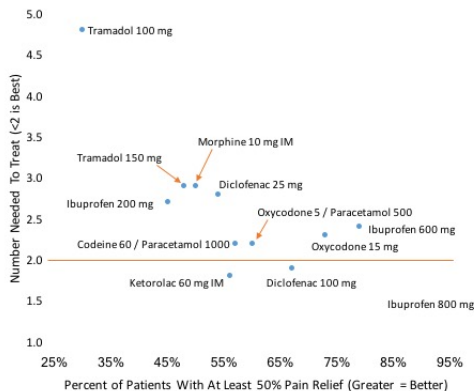
Source: CDC The Huffington Post

Perhaps more troubling are data demonstrating that many common, minor surgical procedures, such as varicose vein removal, are treated with opioids for post-op pain, resulting in major increases in unnecessary opioid exposure, habit forming potential, and overdose,<sup>3</sup> independent of economic conditions.<sup>4</sup> *In other words, expanded access to opioids is driving this epidemic.*

Although many have long believed that opioids are the strongest pain medications and should be used for more severe pain, scientific literature does not support this belief.

The fact is that opioids, while considered “strong pain killers,” are actually mild to moderate pain relievers, and, in many cases, no more effective than over-the-counter ibuprofen.

As a result, prescriptions are being written for these drugs in order to provide pain relief and avoid the gastrointestinal side effects associated with non-steroidal anti-inflammatory drugs, or NSAIDs, such as ibuprofen and diclofenac.<sup>5</sup> Indeed, numerous studies have shown NSAIDs can be more effective than opioids.<sup>6</sup>



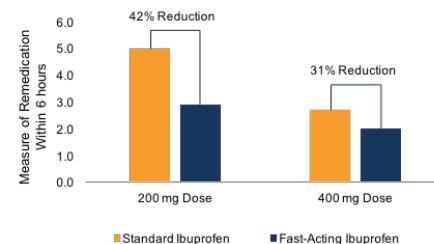
Number Needed to Treat (NNT) is the number of patients who must be treated for one of them to receive the desired effect. So the lower the NNT, the better. NSAIDs have comparable or lower NNT values versus opioids. Thus, NSAIDs can be perfectly suited for many patients who are instead receiving an opioid. Source: Ong, 2007.

Opioids have powerful side effects and addiction potential which harm hundreds of thousands of individuals every year. Even if one disregards the public health problems created by the excessive use of opioid pain killers, these medications are still a poor choice for the treatment of acute pain – regardless of the severity. Why? Because the risk of abuse and habit forming behavior in patients or their families with access is simply too great.

We agree that in some situations, such as cancer pain, limited opioid use is appropriate. But in the majority of situations in which opioid painkillers are used today, they are not.

## NSAIDs: Part of the Solution...

It is widely known that NSAIDs are potent pain relievers in their own right. For example, studies involving very painful molar extraction surgery demonstrate that *fast, early pain reduction in pain intensity* with rapid acting ibuprofen is associated with longer duration of pain relief, as indicated by a lower need for remedication.<sup>7</sup> *Thus, speed of onset is the critical requirement if NSAIDs are to be a viable alternative to opioids for post-surgical pain relief.* In other words, earlier pain relief is associated with better pain relief.



Both OTC and Rx fast-acting ibuprofen are associated with longer duration of pain relief, as indicated by the lower need to remedicate. Source: Moore, 2014, Table 2

## ...With Two Problems

First, NSAID side effects, especially gastric and esophageal irritation, make them an unfeasible option for many patients. In fact, many patients cannot take over-the-counter ibuprofen due to gastric irritation and stomach pain severe enough to discourage use.

Second, physicians perceive opioids as stronger than NSAIDs which is certainly true for the severest forms of pain, like cancer pain. Couple that with fewer stomach side effects for opioids and limited alternatives, we can understand why opioids are widely prescribed for mild-to-moderate pain relief.

<sup>1</sup> Centers for Disease Control, *Opioid Overdose*, <https://www.cdc.gov/drugoverdose/index.html>, accessed January 24, 2018.  
<sup>2</sup> Centers for Disease Control, *Understanding the Epidemic*, <https://www.cdc.gov/drugoverdose/epidemic/index.html>, accessed January 24, 2018.  
<sup>3</sup> Brummett, CM et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. *JAMA Surgery* 152(6), 2017.  
<sup>4</sup> The Economist, *America's opioid epidemic is driven by supply*, <https://www.economist.com/blogs/democracyinamerica/2018/01/another-prescription>, accessed February 18, 2018.  
<sup>5</sup> Tealder, D. Evidence for the efficacy of pain medications. National Safety Council, 2014. <http://www.nsc.org/team/about/Pages/Over-the-counter-pain-medications.aspx>  
<sup>6</sup> Ong, CKS. An Evidence-Based Update on NSAIDs. *Clin Med Res* 5(1):19-34, 2007.  
<sup>7</sup> Moore, R.A., et al. Faster, higher stronger? Evidence for formulation and efficacy for ibuprofen in acute pain. *Pain* 155:12-21, 2014.

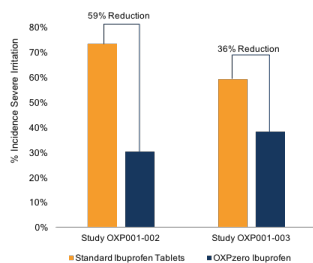
# OXZero™ NSAIDs: A New Weapon in The Fight Against the Opioid Epidemic

## Our Solution: Speed and Safety...Without Opioids

**Oxford Pharmascience** is private company based in the United Kingdom. The company is developing a pipeline of patented, novel derivatives of ibuprofen, naproxen, diclofenac, and other NSAIDs, based on our patented OXZero™ technology. Our products address both of the critical needs of the pain market:

**Speed:** Our clinical studies demonstrate that our patented OXZero™ ibuprofen enters the circulation faster than conventional products...up to 58% faster. Since faster pain relief is associated with better pain relief, our versions of these drugs will achieve better pain relief.

**Safety:** Our clinical studies demonstrate that our patented OXZero™ ibuprofen and naproxen have up to 60% reduction in severe mucosal gastroduodenal damage versus conventional NSAIDs.



Multiple clinical studies demonstrate lower incidence of gastrointestinal lesions from OXZero™ ibuprofen versus conventional ibuprofen. Similar results demonstrated for naproxen. Source: Oxford Pharmascience

In other words, our OXZero™ version of ibuprofen provides faster pain relief, which is associated with better pain relief. But, unlike other fast-acting products, our OXZero™ version of ibuprofen is far safer, making it a truly viable option to opioids for mild-to-moderate pain.

## Our OXZero™ Technology

Using our OXZero™ technology, we have created new and patented salts of these NSAIDs. These salts consist of layers of NSAID molecules and various buffer salts (usually aluminum and magnesium hydroxide). In the stomach, the salt creates a localized buffer, increasing NSAID solubility. **This results in faster absorption and far less esophageal damage.** We have made and studied OXZero™ forms of ibuprofen, naproxen, and diclofenac, with others also in development.

Our OXZero™ versions of common NSAIDs can be prepared as tablets and capsules. and since they are fully taste masked and non-irritating, they can also be prepared as direct-to-mouth granules, liquid suspensions and hot drink powders.

Our technology is described and protected by a series of patents, with coverage in North America, Europe, Asia, and other selected territories.

## Key Advantages

- Well-understood molecules...no need to dramatically change therapeutic practices
- Rapid onset...perfect for post-op and acute pain
- Clinically-demonstrated fewer GI side effects compared to conventional NSAIDs
- No addiction risk
- Easy to synthesize and manufacture at scale into multiple formulations

## Commercial Potential

The market for oral opioids in the US alone is approximately \$5 billion. Lower back, arthritis and cancer pain are the most common uses for these products. Intravenous acetaminophen, a product with many side effect and related issues, is a \$400 million product. This suggests that the market is willing to use a less than ideal product in the post-op setting in order to avoid

opioids...a perfect opportunity for OXZero™ ibuprofen to serve as a better, safer, more viable alternative.

## Partnering Opportunity

Oxford Pharmascience is seeking to license the development and commercial rights to OXZero™ ibuprofen across multiple territories. Upon execution of a confidentiality agreement, access to a well-organized data room can be provided, with full access to all Preclinical, and Clinical data.



For more information about Oxford Pharmascience contact:

Marcelo Bravo, CEO  
marcelo.bravo@pharmascience.co.uk  
+44(0)207 554 5875