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Lancet highlights potential dangers with the most commonly prescribed pain killers

The renowned medical journal The Lancet has recently published¹ a study by Oxford University, which confirms the potential dangers in a class of drugs commonly prescribed in patients with chronic diseases such as osteoarthritis. The study analysed the results of 754 clinical trials of Non Steroidal Anti Inflammatory (NSAID) Drugs, including diclofenac, ibuprofen, naproxen and the COX-II inhibitors: celecoxib, rofecoxib, etoricoxib and lumiracoxib. It confirmed that these drugs significantly increased risks of cardiovascular side effects, including death, and gastrointestinal problems including internal bleeding.

This is yet further confirmation of the potentially fatal risks of this commonly prescribed class of painkillers: In 2009 a Danish national cohort study involving millions of people showed that taking ibuprofen, diclofenac, naproxen, rofecoxib and celecoxib significantly raised the risk of death and heart attack, even after a short treatment period².

Prof Dr. Martin Wehling, director of the Institute of Experimental and Clinical Pharmacology and Toxicology, Mannheim, University of Heidelberg, said "The Lancet article clearly demonstrates what has been known for a while, that NSAIDs have significant side effects. Products such as VIOXX[®] (rofecoxib, representing a supposedly safer type of NSAID) which grew to be a \$1bn + seller were removed from the market because of these health concerns. An often quoted US study³ attributes 16,500 unnecessary deaths a year in America to NSAIDs; estimates for lethal bleeding complications range from 1,100 to 2,200 a year here in Germany. Adding cardiovascular deaths as the other main complication, unsafe NSAID use may claim 3,000-4,000 lives a year in Germany which is close to the 4,200 deaths you would derive from the US figure by simple adjustment of population size".

Putting this in context, according to Federal statistics this NSAID death toll is more than all the 3,6574⁴ German deaths caused by road accidents in 2010 (the latest year for which information is readily available).

Thankfully a recent article in Rheumatology⁵, one of the world's leading medical journals on arthritis, provides a potential solution. The article established that Flexiseq[™], an innovative new drug-free way of treating the pain of arthritis is just as effective as one of the drugs that was confirmed in the above report to increase the risk of serious or fatal side effects.

Prof Bolten, Director Klaus Miehke-Klinik, Rheumatologie, Wiesbaden, Germany, said: "For topical Flexiseq, the study showed the same pain and stiffness reducing qualities as oral celecoxib. As it does not contain any NSAID (or other pharmaceutical ingredient), side effects are very rare and it does not interact with other drugs. Therefore the many elderly osteoarthritis patients with cardiovascular problems, in which NSAIDs are contraindicated, can be treated at low risk."

Flexiseq has been awarded the Innovation 2013 Award by the Federation of German Pharmacists. It is currently available in Germany, where Flexiseq was developed and is now manufactured, and two initial export countries, Malaysia and Ireland, but clearly Flexiseq has global potential to be a major and important new product in the treatment of joint pain.

Professor Conaghan, University of Leeds and NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds, lead author of the Rheumatology study said: "Most people with osteoarthritis live with chronic pain that interferes with their daily activities. Many can't take or can't tolerate current oral analgesics because of side effects. There is therefore a huge unmet need for effective and safe analgesics for osteoarthritis. The new study is interesting because it suggests that a novel topical therapy, that doesn't include a topical anti-inflammatory drug, may help osteoarthritis pain".

¹ Coxib and traditional NSAID Trialists' Collaboration. "Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta analyses of individual participant data from randomised trials." The Lancet, May 2013 (published online [http://dx.doi.org/10.1016/50140-6736\(13\)60900-9](http://dx.doi.org/10.1016/50140-6736(13)60900-9))

² EL Fosbøl et al. "Risk of Myocardial Infarction and Death Associated With the Use of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) Among Healthy Individuals: A Nationwide Cohort Study." Nature Clinical Pharmacology & Therapeutics, 2009; **85** (2) 190 - 197

³ Singh G, "Recent considerations in nonsteroidal anti-inflammatory drug gastropathy" American Journal of Medicine 1998. <http://www.ncbi.nlm.nih.gov/pubmed/9715832>

⁴ Road accident data 2010 Federal Statistical Office Germany

⁵ Conaghan P et al; "A multicentre, randomized, placebo- and active-controlled trial comparing the efficacy and safety of topical ketoprofen in Transfersome gel (IDEA-033) with ketoprofen-free vehicle (TDT 064) and oral celecoxib for knee pain associated with osteoarthritis." Rheumatology, 2013 <http://rheumatology.oxfordjournals.org/content/early/2013/03/27/rheumatology.ket133.abstract>

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About Flexiseq™

Flexiseq™ is a topically applied drug-free gel which is clinically proven to safely relieve the pain and improve the joint stiffness associated with osteoarthritis (OA). Flexiseq™ is unique - it lubricates your joints to address joint damage. Pain is relieved and joint function improved because it lubricates away the friction and associated wear and tear on a user's joints.

www.flexiseq.com

About Pro Bono Bio PLC

Pro Bono Bio PLC is the world's leading healthcare nanotechnology company offering health and lifestyle products, headquartered in London with presence in Europe, Africa and Asia and due to launch in North America. Pro Bono Bio's first product, Flexiseq gel, is a medical device that safely targets joint pain by a unique drug-free lubricating action. It was launched in 2012.

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