

## Review Article

# Ibuprofen, as a Symptomatic over the Counter (OTC) Treatment for Acute Upper Respiratory Tract Infections

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## Keywords

• Ibuprofen; Common cold; Flu; Safety; Efficacy

## Abstract

Ibuprofen is commonly used to treat symptoms of acute upper respiratory tract infections such as colds and flu (URTI) but there is little published work on the efficacy and safety of ibuprofen as an over the counter treatment (OTC) for URTI. This review will look at the efficacy and safety of ibuprofen as a symptomatic treatment for URTI. The review will demonstrate that the symptoms of URTI are caused by an inflammatory response to infection and that ibuprofen by its mechanism of action as an anti-inflammatory agent is an effective symptomatic treatment. The review looks at the safety of ibuprofen in OTC doses and discusses some of the confusion between the safety of OTC doses for URTI versus high dose therapy for chronic inflammatory conditions such as rheumatoid arthritis. The efficacy and safety of ibuprofen as a treatment for URTI is mainly confirmed from acute and chronic pain studies in adults, and fever studies in infants and children. The review concludes that when used as directed, OTC therapy with ibuprofen is a safe and effective symptomatic treatment for URTI.

## ABBREVIATIONS

URTI: Acute Upper Respiratory Tract Infection; OTC: Over the Counter, AOM: Acute Otitis Media; EMA: European Medicines Agency

## INTRODUCTION

The analgesics aspirin, paracetamol and ibuprofen are commonly used to treat the symptoms of common cold and flu such as fever, sore throat pain, headache, sinus pain, ear pain, chilliness, and malaise, as non-prescription or over the counter (OTC) medicines. Ibuprofen is the most recently discovered analgesic, as it was developed by Boots company in the UK in the 1960's as an anti-inflammatory treatment for rheumatoid arthritis, and it is the last of these analgesics to gain OTC status [1]. Although being a latecomer in the analgesic field, OTC ibuprofen has become one of the most common treatments for acute pain and fever in adults, children and infants. Ibuprofen is widely used as an OTC treatment for common cold across the world and it is often combined with other agents such as decongestants and antihistamines to provide multi-symptom relief medicines. Ibuprofen is also widely available as OTC syrup formulations to treat fever and pain in infants associated with URTI. Despite the widespread use of ibuprofen throughout the world there is little published work on the efficacy of ibuprofen as an OTC treatment for URTI, and clinical trials are mainly directed towards treatment of fever, especially comparisons between ibuprofen and paracetamol as antipyretics in infants and children.

The safety of ibuprofen in OTC doses for treatment of URTI and other acute conditions is not in question, and regulatory

authorities throughout the world have licensed ibuprofen for widespread OTC use. However, there have been recent reports in the media that have confused the public about the safety of ibuprofen.

This review will look at the efficacy and safety of ibuprofen as a symptomatic treatment for URTI. The review will demonstrate that the symptoms of URTI are caused by an inflammatory response to infection and that ibuprofen by its mechanism of action as an anti-inflammatory agent is an effective symptomatic treatment. The review will also look at the safety of ibuprofen in OTC doses and try to address some of the confusion between the safety of OTC doses for URTI versus high dose therapy for chronic inflammatory conditions such as rheumatoid arthritis.

## MECHANISM OF SYMPTOMS OF COMMON COLD AND FLU

The symptoms of URTI are triggered in response to viral infection of the upper airways. Rhinoviruses account for 30-50% of all colds and corona viruses are the second most common viruses, accounting for 10-15% of colds [2]. Influenza viruses account for 5-15% of colds and colds viruses such as respiratory syncytial viruses are responsible for much flu-like illness [3], demonstrating that there is much overlap in the aetiology and symptomatology of common cold and flu. The symptoms of URTI are caused by an inflammatory response to viral infection and it is the immune response rather than tissue damage that generates the symptoms [4,5]. Histological surveys of the nasal epithelium in patients with experimental rhinovirus infection have not found any signs of tissue damage but have found substantial increase in leukocytes early in the course of the infection [6]. During the

course of URTI the nasal fluid changes colour from clear to yellow to green due to the huge increase in leukocytes passing through the nasal epithelium [7]. The local inflammatory response to infection consists of the generation of prostaglandins and the release of cytokines from leukocytes and it is these mediators that act on the central nervous system, peripheral sensory nerves, blood vessels and glands to generate the symptoms of URTI [7].

## EFFICACY OF IBUPROFEN AS A SYMPTOMATIC TREATMENT FOR COLDS AND FLU

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) that acts as a prostaglandin synthesis inhibitor, and its pharmacology is well known, as an inhibitor of the cyclooxygenase enzymes (COX-1 and COX-2), and also as an inhibitor of leukocytes activation at inflamed sites [8]. The efficacy of ibuprofen as a symptomatic treatment for URTI is directly related to its inhibition of prostaglandin synthesis and its inhibitory effects on leukocyte activation and cytokine formation [8]. Prostaglandins and bradykinin have been proposed to account for most of the symptoms of rhinovirus colds [7,9], and therapy with NSAIDs has been shown to inhibit the severity of many URTI symptoms [10,11]. The efficacy of ibuprofen will now be discussed for specific symptoms of URTI.

### Fever

Fever is a common symptom of URTI in infants and children but is less common in the adult [7]. Prostaglandin  $E_2$  generated by the inflammatory response to infection has a major role in fever either by stimulation of peripheral vagal nerve endings or by acting as a final messenger to the temperature control centre in the hypothalamus [12,13]. NSAIDs such as aspirin and ibuprofen reduce fever by inhibiting the synthesis of prostaglandin  $E_2$  [14].

The efficacy of ibuprofen as an inhibitor of fever (antipyretic) is mainly supported by clinical trials on infants and children, especially in comparison studies with paracetamol which was the most common treatment for fever before the introduction of ibuprofen. A meta-analysis of seventeen clinical trials on children less than 18 years of age by Perrott et al. (2004), reported that oral ibuprofen (5-10 mg/kg) was more effective antipyretic than paracetamol (10-15 mg/kg) [15]. Similarly Robertson (2005) reported that ibuprofen more effectively reduces fever than paracetamol [16].

NSAIDs in general act as antipyretics because of their inhibitory effects on prostaglandin synthesis and ibuprofen as an NSAID is recognised as an effective antipyretic medicine.

### Muscle aches and pains

Muscle aches and pains (myalgia) are a common symptom associated with URTI and around 50% of patients with common cold experience these symptoms [17]. Myalgia is caused by the effects of cytokines on joints and muscle with the cytokines causing the synthesis of prostaglandin  $E_2$  that stimulates pain nerve endings in the joints and muscle.

Ibuprofen, 400mg three times a day, has been shown to reduce the symptom scores for myalgia in a placebo controlled study on 80 adults with naturally acquired common cold [11]. The efficacy of ibuprofen for the symptomatic relief of myalgia is supported

by its inhibitory effects on the synthesis of prostaglandins, as prostaglandin  $E_2$  is the pain producing mediator causing myalgia [18]. Ibuprofen has been used to reduce treat the side effect of myalgia associated with treatment with cytokines such as interferons used to treat multiple sclerosis [19].

### Headache

Headache is a common symptom associated with URTI [20]. The mechanism of headache associated with URTI is unknown but is speculated to be caused by cytokines released from leukocytes [21,22]. Ibuprofen, 400mg three times a day, has been shown to reduce the symptom scores for headache in a placebo controlled study on 80 adults with naturally acquired common cold [11]. Ibuprofen (200mg) has been shown to be an effective treatment for mild to moderate headache in a double blind placebo controlled trial on 65 adult patients [23]. Ibuprofen (400mg) has also been shown to be an effective treatment for tension type headache in a double blind placebo controlled trial [24]. Ibuprofen (400 mg) has also been shown to be an effective treatment for other acute headache such as tension type headache and migraine [25,26].

### Sore throat pain

A sensation of throat irritation is often the first sign of URTI [7,27] and throat pain is a common symptom. Intranasal administration of bradykinin causes a sore throat sensation, and sore throat pain is likely caused by the actions of prostaglandins and bradykinin on sensory nerve endings in the airway and mediated by the cranial nerves supplying the nasopharynx and pharynx [7,28].

The analgesic activity of ibuprofen on sore throat pain can be supported from the inhibition of prostaglandin synthesis, which is a general property of NSAIDs. Ibuprofen, 400mg three times a day, has been shown to reduce the symptom scores for sore throat in a placebo controlled study on 80 adults with naturally acquired common cold [11]. Ibuprofen (400mg) was shown to be superior to paracetamol (1000mg) in a double blind placebo controlled trial on 80 patients suffering from sore throat pain associated with tonsillopharyngitis [29].

### Sinus pain

The paranasal sinuses surround the nasal airway and any URTI nearly always involves the sinuses [30]. Sinus pain may be related to pressure changes in the sinuses due to obstruction of the ostium or the effects of inflammatory mediators on pain nerve endings in the sinus [7]. No studies have been found in the literature on the efficacy of ibuprofen as an analgesic for the treatment of pain associated with sinusitis but it is reasonable to assume that because of the efficacy of ibuprofen in other pain conditions such as sore throat pain and post dental surgical pain etc. that ibuprofen will be an effective treatment for pain associated with sinusitis [11,29,31,32].

### Cough

Cough is normally a protective upper airway reflex that prevents aspiration of food and fluid into the airway and which aids expulsion of mucus and foreign bodies from the lower airway [7]. Cough associated with URTI is believed to be caused

by a hypersensitivity of the cough reflex that may be due to the effects of inflammatory mediators on vagus nerve endings in the airway [33,34]. Prostaglandins may have a role in cough as intranasal administration of prostaglandin D<sub>2</sub> and prostaglandin F<sub>2</sub> alpha has been shown to induce cough in adult volunteers with and without allergy [28].

In theory, NSAIDs such as ibuprofen might be expected to work as anti-inflammatory medicines and act as a treatment for cough associated with URTI. However the study by Winther and Mygind (2001) which found beneficial effects of ibuprofen on several common cold symptoms, did not find any effect of ibuprofen on cough [11]. In contrast a study by Sperber et al. (1992), on the effects of the NSAID naproxen on patients with URTI reported that naproxen had a beneficial effect on the symptoms of headache, malaise, myalgia and cough, indicating that NSAIDs may be useful in treating the symptom of cough [10].

### Sneezing

Sneezing associated with URTI is caused by the effects of inflammatory mediators on trigeminal sensory nerves in the nose that cause reflex activation of the sneeze centre in the medulla [7]. No evidence has been found in the literature that prostaglandins cause sneezing and a study by Doyle et al. (1990), on intranasal administration of prostaglandins D<sub>2</sub> and F<sub>2</sub> alpha reported that these prostaglandins caused cough but did not cause sneezing [28].

The only study found in literature searches on the effects of ibuprofen on sneezing is that by Winther et al. (2001), in a placebo controlled study on 80 adults with naturally acquired common cold, which reported that Ibuprofen, 400mg three times a day, reduced the number of sneezes by 40% and the symptom scores for sneezing by 33% [11]. This study by Winther et al. (2001), indicates that prostaglandins generated as inflammatory mediators during URTI may cause sneezing and that the inhibition of prostaglandin synthesis by ibuprofen acts to reduce sneezing, however the authors conclude that the mechanism of action of ibuprofen in reducing sneezing associated with URTI is not well understood [11].

### Nasal congestion

Nasal congestion associated with URTI is caused by the dilation of large veins (venous sinuses) in the nasal mucosa in response to the generation of vasodilator inflammatory mediators [35]. Prostaglandins are in general inflammatory mediators associated with vasodilation and therefore would be expected to cause nasal congestion. However a study by Doyle et al. (1990), reported that intranasal administration of prostaglandin F<sub>2</sub> alpha caused an increase in nasal patency, presumably due to constriction of nasal veins whereas in the same adult volunteers intranasal administration prostaglandin D<sub>2</sub> caused a decrease in nasal patency presumably by dilating nasal veins [28]. In studies on anaesthetised pigs Bedwani and Eccles (1983) reported that administration of prostaglandins via the lingual artery had variable effects; prostaglandin D<sub>2</sub> caused nasal vasoconstriction followed by a prolonged vasodilation whereas prostaglandin I<sub>2</sub> only caused vasodilation, and the effects of prostaglandin E<sub>2</sub> were variable with nasal vasoconstriction in six out of seven pigs and vasodilation in one pig [36].

With such variable effects of different prostaglandins on nasal blood vessels it is difficult to predict the effects of therapy with NSAIDs on the symptom of nasal congestion associated with URTI. The study by Winther and Mygind (2001) on the effects of ibuprofen on symptoms of naturally acquired URTI reported no effect of ibuprofen on the symptom of nasal obstruction [11]. Whereas a study by Sperber et al. (1989), on experimental rhinovirus induced colds reported that ibuprofen (200 mg) in combination with pseudoephedrine (60 mg) significantly reduced the symptom of nasal obstruction whereas pseudoephedrine alone (60 mg) had no effect on the symptom of nasal obstruction [37].

### Earache

Acute otitis media (AOM) is often associated with ear pain or earache and it is usually associated with URTI in children [38]. The ear pain is associated with viral infection of the middle ear causing inflammation, and the inflammatory mediators such as prostaglandins stimulating pain nerve endings. A recent Cochrane review (2016) of clinical trials on the efficacy of analgesics in treating pain associated with AOM in children concludes that there limited information on this topic but that low quality evidence indicates that ibuprofen is superior to placebo in relieving short term ear pain [39]. Ibuprofen, 400mg three times a day, has been shown to reduce the symptom scores for earache in a placebo controlled study on 80 adults with naturally acquired common cold [11].

### SAFETY OF IBUPROFEN IN OTC DOSES

In considering the safety of ibuprofen as a symptomatic treatment for URTI it is important to understand that much of the safety concerns over the use of NSAIDs in general, and ibuprofen in particular, are related to long-term high dose therapy (2,400 mg a day) for chronic conditions such as rheumatoid arthritis. In most countries the OTC dose range for ibuprofen in adults is from 200-400 mg every 4-6 h with a maximum daily dose of 1200mg. The dose range of ibuprofen in infants and children relates to their age [40].

### Gastro intestinal tract (GIT)

All NSAID's because of their inhibitory effects on prostaglandin synthesis in the stomach pose a risk to the GIT, but NSAIDs vary greatly in their adverse event profile and ibuprofen is well tolerated in OTC doses and is ranked lowest among prescription NSAIDs for its effects on the GIT [41]. The literature does not indicate that there is any risk of serious GIT bleeding or damage to the stomach with short courses of OTC doses of ibuprofen [41-43]. A meta-analysis of the safety profile of non-prescription use of ibuprofen looked at eight studies with doses of ibuprofen ranging from 800-1200 mg/day over durations of one to ten days therapy and concluded that the overall adverse event frequency among ibuprofen treated subjects (n = 1094) was numerically less than or equal to the placebo treatment group (n = 1093) [42]. In this study the frequency of digestive system adverse events was comparable for the placebo and ibuprofen treatment groups [42].

### Children

Paracetamol and ibuprofen are the medicines of choice for

use in children and aspirin is not recommended because of the risk of Reye's syndrome [44,45]. Ibuprofen is reported to be safe and well tolerated in children. A meta-analysis of 17 clinical trials concluded that, in children, single doses of ibuprofen (4-10 mg/kg) has similar efficacy in relieving pain and fever and a similar safety profile to paracetamol (7-15 mg/kg) [15]. The safety of paracetamol and ibuprofen in non-prescription doses was comprehensively reviewed by Rainsford in 1997 looking at ten clinical trials involving 544 children aged between 4 and 15 years and the author concluded that there was no difference between the adverse events in any of the major organ systems between paracetamol and ibuprofen taken at recommended OTC doses for less than seven days, and no reports of GIT bleeding in any of the published data for ibuprofen [46]. The review also concluded that all the adverse events reported were minor and reversible on cessation of therapy and that the data attested to the considerable safety for the public for both paracetamol and ibuprofen when taken alone [46]. The safety of ibuprofen has also been demonstrated in a general practitioner based randomized clinical trial involving 27,065 children less than two years old treated for fever with either paracetamol (12 mg/kg), ibuprofen (5 mg/kg) or ibuprofen 10 mg/kg, and the authors concluded that the risk of serious adverse clinical events was small and did not vary by choice of medication [47].

### Elderly

Safety data in the elderly is related to chronic therapy with ibuprofen for the treatment of pain, particularly osteoarthritis and other musculoskeletal disorders. A study on the pharmacokinetics of ibuprofen in an elderly population concluded that an ibuprofen dosage schedule of three or four times daily was unlikely to cause excessive accumulation of ibuprofen regardless of age [48]. Changes in the pharmacokinetics of ibuprofen in the elderly are relatively minor and unlikely to cause toxicity due to accumulation of ibuprofen [49,50]. However, the elderly populations are more likely to have concomitant diseases such as hypertension, impaired renal function, and risk of GIT bleeding which may be complicated by NSAID therapy and therefore in elderly patients the lowest effective dose of ibuprofen should be used for the shortest duration.

### Pregnancy and lactation

Ibuprofen should not be taken during pregnancy unless advised by a doctor. Ibuprofen is considered safe for breast feeding normal term infants as only very small quantities appear to be excreted in breast milk and ibuprofen is considered to be one of the analgesics of choice in breast feeding mothers. Evidence relating to risk to the child during lactation is scarce but this is offset by the pharmacodynamic and pharmacokinetic properties of ibuprofen and its extensive use both in prescribed and OTC doses since its launch in the UK in 1969 without any reports of adverse effects in breast fed infants [51-54].

### Cardiovascular safety

Concerns over cardiovascular safety of NSAIDs as a therapeutic group of compounds were raised after the results a clinical trial on the NSAID rofecoxib in 2004 suggested an increased risk of thrombotic events [55,56]. The specific safety

concerns for rofecoxib led to the voluntary withdrawal of this product and triggered interest in the cardiovascular safety of all NSAIDs including ibuprofen, when used as treatments for chronic conditions such as osteoarthritis [57,58].

A recent publication by Sondergaard et al. (2017), on cardiovascular risk associated with long term, prescription doses of ibuprofen has reported that the use of NSAIDs such as ibuprofen is associated with an increased risk of cardiac arrest [58] but this study does not provide any information on short term OTC use of ibuprofen. Similarly, a recent study by Wen et al. (2017), on the use of NSAIDs and URTI looked at data from 9,793 patients who were hospitalised for an acute myocardial infarction and used a case cross over design to compare patients using NSAIDs with those not using NSAIDs when suffering from a URTI [59]. This study by Wen et al. (2017), does not provide any evidence that OTC use of ibuprofen for treatment of URTI increases the risk for acute myocardial infarct [59], since according to the authors, ibuprofen was not specifically investigated in this study and the study results should not be interpreted for any specific drug such as ibuprofen [60]. The main finding and conclusion of the study by Wen et al. (2017), was that NSAID use during URTI episodes, especially parenteral NSAIDs was associated with a further increased risk of acute myocardial infarct [59]. The study looked at the use of different NSAIDs all grouped together for analysis and these were administered orally, rectally and parenterally. The study by Wen et al. (2017) does provide some evidence that prescription doses of NSAIDs, especially parenteral NSAID therapy, further increases the risk of adverse cardiovascular events when therapy is associated with a concurrent URTI but it does not provide any information on the risk of OTC therapy with ibuprofen for URTI [59].

The European Medicines Agency (EMA) reviewed the safety of NSAIDs for cardiovascular risk and provided a report on this issue in 2012 [56]. The 2012 EMA report provides an analysis of all the available data from clinical trials and observational studies available at the time. It is important when studying data on the safety of NSAIDs such as the EMA 2012 report to differentiate short term low dose therapy for acute conditions such as acute pain and URTI where the therapy involves a maximum dose of ibuprofen of 1,200 mg over a few days, from therapy for chronic conditions such as rheumatoid arthritis where the therapy involves doses of ibuprofen of 2,400 mg over years. Even with chronic high dose therapy most studies have not found an increased cardiovascular risk associated with ibuprofen [56], and the most recent report from the EMA issued on 23 May 2015 on use of high dose ibuprofen indicates only a small cardiovascular risk in patients taking at or above doses of 2,400 mg ibuprofen a day for chronic inflammatory diseases [61].

The 2015 update on high-dose ibuprofen from the EMA states, "No increase cardiovascular risk is seen with ibuprofen at doses of 1,200 mg per day, which is the highest dose generally used for over-the counter (OTC) preparations taken by mouth in the European Union (EU)" [61]. It is important to note that the reference to the 1,200 mg dose of ibuprofen in the EMA 2015 update relates to chronic use of ibuprofen over years and it can be expected that acute use of this maximum dose of 1,200 mg ibuprofen over a few days for treatment of URTI will similarly have no increased cardiovascular risk [61].

The OTC use of ibuprofen has a typical pattern of only a few days therapy for treatment of acute pain symptoms, and a study in France on OTC use of NSAID's has reported that, "Considering the very short exposure to NSAID's for the vast majority of these low-risk patients, the probability of a significant impact on cardiovascular risk or interaction with cardiovascular drugs appears remote" [62]. The studies published by Wen et al. (2017) [59], and Sondergaard et al. (2017) [58], do not change this conclusion.

### Renal safety

All NSAIDs because of their inhibitory effects on prostaglandin synthesis have the potential to have renal side effects and cause renal injury, especially in the elderly who have diminished renal function [63]. However, the renal side effects of ibuprofen appear to be dose dependent and are not reported at the recommended OTC doses and even at higher doses (>1.6g/d) [64]. Renal side effects are almost exclusively encountered in patients with low intravascular volume and low cardiac output, particularly in old age and other analgesic and antipyretic medicines have no less risk for renal injury than ibuprofen [64].

### Hepatic safety

Ibuprofen like other NSAID's can affect liver function, especially when used in high doses for chronic conditions, but no evidence has been found to indicate that short courses of ibuprofen in OTC doses cause any hepatotoxicity or liver damage [65].

## EFFECTS ON THE IMMUNE SYSTEM AND COURSE OF URTI

NSAIDs in high doses have a depressant action on the immune response, and this is beneficial when used to treat inflammatory conditions such as rheumatoid arthritis where the autoimmune response causes damage to joints. However, a depressant effect on the immune system would in theory not be beneficial for the treatment of URTI where the immune response rids the body of the infecting agent. There is little research in this area relating to ibuprofen but a study the effects of OTC doses of aspirin, paracetamol and ibuprofen on immune function, viral shedding, and clinical status in sixty rhinovirus infected volunteers reported significant effects of paracetamol and aspirin on immune function but no effect of ibuprofen [66]. The authors concluded that the clinical consequences of the level of immunosuppression seen in the study with treatment with paracetamol and aspirin are unlikely to have any significance in healthy adults [66]. Short OTC courses of ibuprofen are therefore unlikely to have any significant effect on the course of a URTI by any depressant effects on the immune response.

## DISCUSSION & CONCLUSION

Ibuprofen is a first line treatment for pain and fever associated with URTI as well as other acute pain conditions. However, there is relatively little clinical data on the use of ibuprofen in the treatment of URTI in OTC doses. The efficacy and safety of ibuprofen as a treatment for URTI is mainly confirmed from acute and chronic pain studies in adults, and fever studies in infants and children. The efficacy of ibuprofen as an analgesic has been shown

in a range of pain models such as post-surgical dental pain where there is a clear dose response relationship between 200 and 400 mg doses [31,43]. The analgesic efficacy can be transferred from one pain model to another because ibuprofen has a common mode of action on pain, via inhibition of prostaglandin synthesis. Similarly, the antipyretic efficacy of ibuprofen can be applied to all types of fever [8,40]. One of the few studies that are available on the treatment of symptoms of URTI with ibuprofen confirms its efficacy as a treatment for sore throat pain, myalgia, ear ache, sneezing, and headache [11].

When considering the safety of ibuprofen as an OTC treatment for URTI it is important to consider three fundamental points of basic pharmacology and toxicology: dose of medication, duration of therapy and population treated. It is important not to confuse safety issues relating to long-term high dose therapy of chronic inflammatory conditions with short-term low dose therapy of URTI. When ibuprofen is used as an OTC treatment for symptomatic relief of pain and fever related symptoms associated with URTI the dose is usually restricted to a maximum of 1,200 mg a day, the duration of therapy is four or five days, and the population is the mass of the general public who are generally otherwise healthy but will include some with concomitant disease. When ibuprofen is used as a prescription treatment of chronic inflammatory diseases such as rheumatoid arthritis and osteoarthritis the dose is usually a prescription dose of 2,400 mg a day over long periods and the population is usually an older sample of the general population with more concomitant disease such as hypertension, heart failure, diabetes etc.

A search of the literature has not found any publications on the cardiovascular safety of ibuprofen when used in OTC doses for short duration therapy of acute pain in conditions such as URTI. After an extensive review of the safety of ibuprofen in 2012 and an update in 2015 the EMA concludes that there is no increased cardiovascular risk for the highest OTC oral dose of ibuprofen (1,200 mg) [56, 61]. This is based on the research on long-term therapy with ibuprofen and provides reassuring safety data for short-term therapy with ibuprofen for acute pain conditions such as URTI.

As with all medicines the safety of OTC therapy with ibuprofen comes with certain caveats and there will be some increased risk of GIT disturbance and possible bleeding, and the medicine should be used with caution in the elderly and those with concomitant disease as indicated on the summary of product characteristics and patient information leaflet provided with the medicine. In general, the benefit associated with the URTI symptom relief will outweigh any small risks associated with therapy for the vast majority of users of ibuprofen.

## CONFLICT OF INTEREST

The author regularly works as a consultant for the pharmaceutical industry but has no financial interest in any pharmaceutical company or any medicine.

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