

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Viral upper respiratory tract infections (viral URTIs) including nasopharyngitis (“common cold”) and influenza represent the most common acute illnesses evaluated in the outpatient setting and are one of the most common infectious diseases globally. A person can develop as many as 200 common colds in a lifetime. Adults typically have two to four infections annually, adults older than 60 years have fewer than 1 cold annually. Children may have three to eight URTIs annually and children younger than 5 years have the highest rates of URTIs.

The URTIs may cause acute local and systemic illnesses and considerably worsen the quality of life. Signs and symptoms of URTIs, including upper respiratory tract congestion, swelling, redness, increased upper airway secretion, pain and fever, which result from the inflammatory response of the immune system to invading pathogens (e.g., viruses, bacteria), as well as toxin production from pathogens.

Common early signs and symptoms of URTIs include discomfort associated with headache/sinus headache and muscle ache and pain. In a clinical trial which recruited patients with sore throat associated with URTIs, over 60% of patients experienced headache, 13% of patients experienced sinus headache and 43% experienced muscle aches and pains. Fever was also an associated sign of URIs and was experienced by 32% of patients.

Risk factors for pain and associated with URTIs are the risk factors for contracting URTIs following rhinovirus exposure. These include poor immune function. Lack of sleep and malnutrition are also considered risk factors due to their effects on immune function.

To alleviate the symptoms of fever and pain associated with URTIs, treatments include simple pain killers and fever reducers such as ibuprofen, aspirin and naproxen and paracetamol.

VI.2.2 Summary of treatment benefits

Patients suffering from URTIs have many symptoms such as headache, sore throat, congestion, fever, sneezing etc. which considerably worsen their quality of life. Paracetamol/ascorbic acid is effective in symptomatic treatment of URTIs including the common cold and influenza as well as in bacterial URTI as it has pain killing and fever reducing properties. The ascorbic acid component can reduce the duration of common cold signs and symptoms.

VI.2.3 Unknowns relating to treatment benefits

Paracetamol has been clinically available since the 1950s. It is one of the most commonly used OTC medicinal products for pain relief worldwide. As such the treatment benefits for paracetamol are well established and there are no unknown factors requiring further investigation.

Ascorbic acid is an essential vitamin necessary for the correct functioning of the organism. It has been available as a supplement for many decades therefore treatment benefits for ascorbic acid are well established and there are no unknown factors requiring further investigation.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
<p>Hepatobiliary risk including acute hepatic failure (severe liver failure)</p>	<p>Paracetamol is a widely used OTC medication for fever and pain relief. The recommended safe total daily dose of paracetamol is 4g. It is often found combined with other active ingredients in other medicinal products. Therefore there is a possibility for accidental overdose by taking other paracetamol containing products at the same time and exceeding the 4g recommended limit.</p> <p>Doses higher than the recommended 4g per day can cause liver toxicity. People who are malnourished, heavy alcohol users and the elderly and those who already have liver problems are at greater risk of developing acute liver failure.</p> <p>Patients with severe liver problems should not take this medicine.</p> <p>Medicines such as rifampicine, sleeping tablets and antiepileptic drugs can increase the risk of liver damage.</p>	<p>By following the recommended dosage information.</p> <p>By not taking other paracetamol containing products at the same time.</p> <p>Immediate treatment at hospital is necessary after an overdose even if there are no significant early signs and symptoms to prevent acute liver failure.</p>
<p>Abnormal Liver Function</p>	<p>Paracetamol is a widely used OTC medication for fever and pain relief. The recommended safe total daily dose of paracetamol is 4g. It is often found combined with other active ingredients in other medicinal products. Therefore there is a possibility for accidental overdose by taking other paracetamol containing products at the same time and exceeding the 4g recommended limit.</p>	<p>By following the recommended dosage information.</p> <p>By not taking other paracetamol containing products at the same time.</p> <p>Immediate treatment at hospital is necessary after an overdose even if there are no significant early signs and symptoms to prevent acute liver failure.</p>

Risk	What is known	Preventability
	<p>Doses higher than the recommended 4g per day can cause liver toxicity. People who are malnourished, heavy alcohol users and the elderly and those who already have liver problems are at greater risk of developing acute liver failure.</p> <p>Patients with severe liver problems should not take this medicine.</p> <p>Medicines such as rifampicine, sleeping tablets and antiepileptic drugs can increase the risk of liver damage.</p>	
Interaction with Anticoagulants	<p>Use of paracetamol lasting more than a week intensifies the effect of oral anticoagulants drugs such as warfarin.</p> <p>Such effects are more likely to happen in the elderly, with alcohol use, use of drugs with reported antiplatelet effects such as aspirin and eating of vitamin-K rich foods such as asparagus, cabbage and leafy greens.</p>	By informing your doctor or pharmacist if you are taking anticoagulant medication such as warfarin
Interaction with Enzyme Inducers	<p>Enzyme-inducing substances such as carbamazepine, phenobarbitone, phenytoine, primidone (antiepileptic agents), rifampicine (antibacterial drug) can increase liver metabolism of paracetamol which can increase the risk of liver damage.</p> <p>Patients with intake of isoniazid, alcohol and tobacco users are also at increased risk of liver damage due to formation of a toxic metabolite of paracetamol.</p>	By informing your doctor or pharmacist if you are taking anticoagulant medication such as warfarin

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
None	Not applicable

Missing information

Risk	What is known
Pregnant and lactating women	Epidemiological data from the use of oral therapeutic doses of paracetamol indicate no undesirable effects on the pregnancy or on the health of the foetus/newborn infant. However pregnant women should not use ascorbic acid in doses higher than 1g as the effect on the foetus is not known. Prospective data on pregnancies exposed to overdoses of paracetamol did not show an increase in malformation.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a SmPC which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PIL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for paracetamol/ascorbic acid can be found in the paracetamol/ascorbic acid's EPAR page.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Paracetamol and ascorbic acid have been on the market for many decades therefore their efficacy and safety profile is well established. There is no planned post authorisation development program.

VI.2.7 Summary of changes to the Risk Management Plan over time

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
This is the first RMP for this product.	Not applicable	Not applicable	Not applicable