VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Pain:

In a systematic literature review published by the International Association for the Study of Pain (IASP), 13 chronic (persisting for a long time) pain studies from

various countries around the world were analyzed. (Of the 13 studies, there were three in the United Kingdom, two in Australia, one each in France, the Netherlands, Israel, Canada, Scotland, Spain, and Sweden, and a multinational.) The authors found that the existing cases of chronic pain were very high and that chronic pain consumed a large amount of healthcare resources around the globe. Chronic pain afflicted women at a higher rate than men. They determined that the presence of chronic pain varied from 10.1% to 55.2% of the population. [(4)]

Fever:

Fever is associated with various critically ill conditions. The incidence of mild fever (defined more than 38.0- 38.5 degree) varies from 15 % to 70%, and with an incidence of 8-17% for moderate fever (defined more than 39.0-39.5 degree). Fever may cause discomfort and impose undue metabolic stress on non-neurological critically ill patients. On the other hand, fever is a normal host response to infection and its presence or absence may be used as a means of assessing the activity of infection.

VI.2.2 Summary of treatment benefits

Paracetamol Tablets contains active substance paracetamol which belongs to a group of medicines called analgesics (painkillers). Paracetamol Tablets is used to relieve pain and help reduce fever. The tablets can treat mild to moderate pain and/or fever.

Paracetamol and ibuprofen are widely used for fever in children as monotherapy and as combined therapy. None of the treatments is proven clearly superior to others. Hence, the study was planned to compare the efficacy of paracetamol, ibuprofen and paracetamol-ibuprofen combination for treatment of febrile (Feverish) children. This study was conducted in 99 febrile children, 6 months to 12 years of age, allocated to three groups. First group received paracetamol 15 mg/kg, second group received ibuprofen 10 mg/kg and third group received both paracetamol and ibuprofen, all as a single dose by the oral route. Patients were followed-up at intervals of 1, 2, 3 and 4 h post dose by tympanic thermometry (a device that measures the temperature). Mean tympanic temperature after 4 h of drug administration was significantly lower in the

combination group compared with paracetamol group; however, the difference was not clinically significant. The rate of fall of temperature was highest in the combination group. Number of afebrile (not having fever) children any time post dose until 4 h was highest in the combination group. Difference between combination and paracetamol was significant for the 1st h. Highest fall of temperature was noted in the 1st h of drug administration in all the groups.

Accord has not conducted any studies for paracetamol on expected benefit considering its similarity to the currently marketed product used for the treatment of mild to moderate pain and/or fever.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Severe allergic reactions (Hypersensitivity)	In very rare cases patients may experience severe allergic reactions (hypersensitivity reactions) that may require further treatment. If a patient experiences an allergic reaction they must immediately stop taking Paracetamol effervescent	Yes Patients who are allergic (hypersensitive) to paracetamol or any of the other ingredients within this medicine should not take paracetamol effervescent tablets.

Risk	What is known	Preventability
	tablets.	
Damage caused to the liver due to chemicals (Hepatotoxicity/ abnormal liver function) (Patients with pre-existing liver disease, chronic alcoholism, malnutrition, dehydration, underweight adults)	Take special care with Paracetamol and tell your doctor if you are suffering from liver problems including liver problems due to excessive alcohol consumption or suffering from dehydration and chronic malnutrition. Talk to a doctor at once if you take too much of this medicine even if you feel well. This is because too much paracetamol can cause delayed, serious liver damage. **Possible side effects:** **Rare:** abnormal liver function, liver failure, hepatic necrosis (death of liver cells) **Very rare:** hepatotoxicity (damage caused to the liver due to chemicals)	Yes If any of the side effects gets serious or if you notice any side effects, please tell your doctor or pharmacist.
Overdose (non-intentional and intentional)	Seek Immediate Medical Advice In The Event Of An Overdose, Even If You	Yes Please talk to your doctor while taking paracetamol

Risk	What is known	Preventability
	Feel Well, because of the risk of delayed, serious liver damage. Symptoms of paracetamol overdose are nausea, vomiting and reduced apetite. Unconsciousness does not usually occur. **Possible side effects:** Rare: overdose	tablet
Drug interaction with blood thinning medications (Interaction with anticoagulants)	Tell your doctor before you take Paracetamol Tablets if you are taking drugs to thin the blood (anti-coagulant drugs e.g. Warfarin ,other coumarins)	Yes Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including those you have bought without a prescription.
Drug interaction with liver chemical reaction activator (Interaction with enzyme inducers)	Long time use of alcohol or medicinal products which induce liver enzymes can increase the liver damaging as a result of an increased and fast formation of toxic metabolites. Tell your doctor before you take Paracetamol	Yes Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including those you have bought without a prescription.

Risk	What is known	Preventability
	Tablets if you are taking Barbiturates and tricyclic antidepressants (to treat depression)	

Important potential risks

Risk	What is known
Decrease in red blood cells (Anemia)	Patients treated with paracetamol may develop problems with their blood due to a decrease in red blood cells, which is called aneamia. It is important that patients are aware of this potential risk and seek medical advice if they experience symptoms of anaemia such as tiredness, lack of energy (lethargy) or shortness of breath.
Decrease in white blood cells (Leucopenia)	Patients treated with paracetamol may very rarely develop problems with their blood due to a decrease in white blood cells, which is called leucopenia. It is important that patients are aware of this potential risk and seek medical advice if they experience symptoms of leucopenia. Leucopenia decreases your body's ability to fight infection.
Abnormal vision	Patients treated with paracetamol may rarely develop problems with their vision. It is important that patients are aware of this potential risk and seek medical advice if they experience symptoms of any abnormal vision.
Severe allergic reaction (Anaphylactic shock)	Patients treated with paracetamol may develop severe allergic reactions (anaphylactic shock). It is important

Risk	What is known
	that patients are aware of this potential risk.
Depressive disorders	Patients treated with paracetamol may rarely develop depression. It is important that patients are aware of this potential risk and seek medical advice if they experience symptoms of depression.
Confusion	Patients treated with paracetamol may rarely develop confusion. It is important that patients are aware of this potential risk.
Kidney function alteration (Renal alteration)	Patients treated with paracetamol may develop kidney function alteration (severe renal impairment, kidney disorder). It is important that patients are aware of this potential risk and seek immediate medical advice if they experience symptoms of kidney function alteration.
Breathing distress caused by narrowing of the airways (Bronchospasm)	Patients treated with paracetamol may develop difficulty in breathing, wheezing, coughing, and shortness of breath. These events are more likely in asthmatics sensitive to aspirin or other NSAIDs such as ibuprofen. It is important that patients are aware of this potential risk and seek immediate medical advice if they experience breathing difficulty, coughing or wheezing.
A severe life-threatening skin disorder (Stevens Johnson syndrome)	Patients treated with paracetamol may develop a severe life-threatening skin disorder (Stevens Johnson syndrome). It is important that patients are aware of this potential risk and seek immediate medical advice if they experience any symptoms.

Risk	What is known
A severe life-threatening skin disorder (Toxic epidermal necrolysis)	Patients treated with paracetamol may develop a severe life-threatening skin disorder (Toxic epidermal necrolysis). It is important that patients are aware of this potential risk and seek immediate medical advice if they experience any symptoms.
Allergic reaction or infection of skin (Erythema multiforme)	Patients treated with paracetamol may develop allergic reaction or infection of skin (erythema multiforme). It is important that patients are aware of this potential risk and seek immediate medical advice if they experience any symptoms.
Overdose leading to liver failure	Patients who have taken too much paracetamol may develop delayed, serious liver damage. It is important that patients are aware of this potential risk and seek immediate medical advice even if they feel well.
Medication overuse headache	Headaches caused by overuse of analgesics should not be handled by increasing the dose. In those cases, the use of analgesics should be taken after consulting a doctor.

Missing information

Risk	What is known
Use by children under 12years of age	Children below 12 years of age: Do not give to children younger than 12 years.
Medication errors	None proposed

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (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 (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No studies planned.