VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

A 2011 internet-based, National Health and Wellness Survey of the healthcare attitudes, behaviours and characteristics of the adult population in the United States, Japan, and five European countries including UK, France, Italy, Germany and Spain was conducted.

The European subset of approximately 49.7 million persons, revealed 9.0 million persons in mild pain and 29.4 million persons in moderate pain with approximately 16% and 40% experiencing their mild and moderate pain daily, respectively.

Fever is a common medical sign associated with numerous conditions, the most common of which is viral or bacterial illness. In children, it is one of the most common clinical symptoms and it is estimated that it accounts for one-third of all presenting conditions.

VI.2.2 Summary of treatment benefits

Paracetamol is a medicine that is widely used to treat mild to moderate pain and to reduce fever. Caffeine is added to increase the analgesic effect of paracetamol. The combination is indicated for the treatment of mild to moderate pain including headache, migraine, muscle ache, dysmenorrhoea, sore throat, musculoskeletal pain, fever and pain after vaccination, pain after dental procedures/tooth extraction, toothache, and the pain of osteoarthritis. It is also indicated for the relief of fever.

Ascorbic acid, also known as vitamin C, is a dietary supplement and is particularly valuable in the early stages of acute viral infections, e.g., the common cold, as Vitamin C reserves may be low at this time and the appetite poor. Hence, paracetamol + caffeine + ascorbic acid is used for the symptomatic relief of fever and pain associated with influenza and colds, e.g. headache, muscle aches, sore throat and musculoskeletal pain.

Paracetamol is recommended for the pain of osteoarthritis because of its suitability in the elderly [Am Coll Rheumatology, 2000; Jordan, 2003; Zhang, 2008]. It is recommended by the World Health Organisation (WHO) as an analgesic for cancer pain relief [WHO, 2010]. Paracetamol does not have the gastrointestinal and cardiovascular issues associated with its use, and not as many drug interactions compared to the other over-the- counter analgesics [Hillis, 2002; Hunt, 2007; Matzke1996; Prescott, 2000; Whelton, 2006].

When paracetamol is combined with caffeine, about 5-10% more patients achieve a good level of pain relief compared to paracetamol alone, regardless of the pain condition [Derry, 2012].

VI.2.3 Unknowns relating to treatment benefits

Not applicable for paracetamol + caffeine ± ascorbic acid.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Nausea, sudden weight loss, loss of appetite and yellowing of the eyes and skin. (Hepatic Dysfunction)	Liver dysfunction results in nausea, sudden weight loss, loss of appetite and yellowing of the eyes and skin.	Clear labelling in the Package Leaflet relating to: Informing your doctor if you suffer from serious liver diseases. Do not exceed the recommended doses. Do not take more than one product containing paracetamol at the same time. The minimum time between each dose. Maximum number of doses that can be taken in 24 hours.
Allergic reactions, skin reactions, breathing problems. (Hypersensitivity reactions)	Allergic reactions include skin rash sometimes with breathing problems or swelling of the lips, tongue, throat or face. Skin reactions include skin rash with peeling or mouth ulcers. Bronchospam may occur in patients sensitive to aspirin and other non-steroidal anti-inflammatory drugs.	Clear labelling in the Package Leaflet relating to: Do not use paracetamol if you are hypersensitive (allergic) to paracetamol or any of the other ingredients of this medicine. Stop taking paracetamol and see your doctor if you notice the following side effects, which are very rare but may still occur: • Allergic reactions such as cutaneous eruptions, sometimes accompanied by respiratory problems or swelling of the lips, tongue, throat or face. • Skin rash with peeling or mouth ulcer. • Difficulties breathing in patients allergic to acetylsalicylic acid (aspirin) and to other non-steroidal anti-inflammatory drugs.
Accidentally taking more than recommended dose. (Overdose)	Taking too much paracetamol can lead to liver damage.	Package sizes: A number of countries limit the number of paracetamol tablets per packet. Clear labelling in the Package Leaflet relating to: In case of over dosage seek immediate medical attention; there is the risk of irreversible liver damage. Do not exceed the recommended doses. Do not take more than one product containing

Risk	What is known	Preventability
		paracetamol at the same time. The minimum time between each dose. Maximum number of doses that can be taken in 24 hours.

Drug interaction with warfarin and other coumarins.	The use of warfarin and other anticoagulants with prolonged daily use of paracetamol may increase the risk of bleeding; occasional use of paracetamol has no significant effect.	Clear labelling in the Package Leaflet relating to: Informing your doctor if you use or if you intend to use one of the following medicines: Warfarin and other coumarins (anticoagulants).

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Pregnancy loss (Spontaneous abortion)	There is possibly an increased risk of spontaneous abortion associated with caffeine consumption.

Missing information

Risk	What is known
None	

VI.2.5 Summary of additional risk minimisation measures by safety concern

There are no additional global risk minimisation measures for paracetamol. At the national level some countries have restrictions to access or pack sizes to prevent patients taking a large overdose of paracetamol (see Module SV.1 Action taken by regulatory authorities and/or marketing authorisation holders for safety reasons).

VI.2.6 Planned post authorisation development plan

There are no planned post authorisation development plan for paracetamol + caffeine ± ascorbic acid.

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

This is the first risk management plan for paracetamol + caffeine ± ascorbic acid.