VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Acute pain is a significant problem for inpatients and can occur secondary to acute illness or disease processes, trauma, or operative procedures. In the post-operative period, 80% of individuals suffer from post-operative pain, often related to an inflammatory component, with almost all describing it as moderate to severe. Physiologically, pain serves to alert individuals to tissue damage and to prevent further harm. However, in the acute inpatient setting, it often serves no useful purpose. Pain activates the sympathetic nervous system, increasing blood pressure, cardiac workload and respiratory rate. It impairs recovery by reducing mobility and physical activity and delays hospital discharge. Despite the use of medications to control pain, it often remains undertreated and is a problem in hospitals and long-term care facilities

Fever is the temporary increase in body temperature in response to a disease or condition. Many infants and children develop high fevers with minor viral illnesses or may have a slight fever for a day or two after receiving certain vaccines. Adults with certain inflammatory or autoimmune disorders may feel the fever rises them to the body. When the temperature increases respect to normal corporal temperature (37°C), the symptoms which can appear are from sweat accompanied by flushing, with tachycardia, dyspnea and exhaustion, convulsions, lightheadedness, dizziness, dehydration, weakness, nausea, vomiting, headache to confusion, hallucinations, delusions, drowsiness and coma. In severe cases, in which the temperature exceeds 44°C death may occur.

VI.2.2 Summary of treatment benefits

Ibuprofen is a nonsteroidal anti-inflammatory drug of propionic acid derivative with analgesic activity, antipyretic and anti-inflammatory. It is one of the most world widely used non-steroidal anti-inflammatory (NSAID) analgesics and antipyretics both by prescription and as an over-the-counter medicine for acute, chronic painful conditions and fever. The clinical experience with oral ibuprofen has been acquired during decades of use and its bioequivalence to iv presentation has been stablished

The analgesic efficacy of intravenous ibuprofen has been proved in different painful processes including orthopaedic and abdominal surgery and in fever in controlled, randomised and well-designed clinical trials. Intravenous ibuprofen has also shown to reduce the needs of opiates and their associated risks in the postoperative period.

Regarding safety, intravenous ibuprofen has demonstrated to be safe and well tolerated in clinical trials, without serious adverse events and without differences with respect to placebo.

These products exhibit an excellent benefit/risk ratio provided that it is used in the correct circumstances.

Thus, considering the disability induced by pain and fever and the clinical improvement obtained with this active substance, it should be considered its role as a first line therapy in management of moderate postoperative pain and fever, limited during years due to the lack of an intravenous pharmaceutical form.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concern

Important identified risks

None

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Cardiovascular disorders including thrombotic disturbances	NSAIDs, the family of drugs to which ibuprofen belongs, can affect cardiac function and vessels (arteries) behaviour. Related to this, it has been reported that some patients using high doses and/or long term ibuprofen experienced events of oedema (fluid accumulation), hypertension (high blood pressure), cardiac failure, and arterial thrombotic events (myocardial infarction or stroke). The risk is diminished in case of short-term and low dose treatment.
Hypersensitivity reactions (including skin reactions) particularly in patients with a history of previous hypersensitivity to NSAID and/or allergic disease	Patients may experience allergic reactions ranging from mild to life-threatening in severity. Symptoms include rashes, urticaria, breathing difficulties, swelling of the face and tongue, fever, drowsiness, diarrhoea, sickness, worsening of asthma etc. The treatment should be suspended immediately upon the first sign of skin rash, mucosal lesion or any other sign of hypersensitivity (allergy). Patients with a known hypersensitivity to ibuprofen or any excipients included in the product or patients with a prior history of allergic reactions to aspirin or other NSAIDs should not be administered ibuprofen.

Missing information

Risk	What is known
Use in children	The use of IV ibuprofen has not been studied in children and adolescents. Therefore, the safety and efficacy have not been established. This medicinal product must not be used in children and adolescents.

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

For each safety concern, a reference has been made to the part of the SmPC of all products concerning this report to address the specific safety concerns.

No additional risk minimization measures have been proposed. The MAH believes that the current contraindications, warnings and precautions of the SmPC of all products concerning this report adequately inform prescribers and patients about the rest of safety concerns.

VI.2.6 Planned post authorisation development plan

N/A

VI.2.7 Summary of changes to risk management plan over time

Version	Date	Changes
2.0	February 2015	New RMP format according to Good Pharmacovigilance Practices (GVP) – Module V Risk management systems.
2.1	March 2015	-Adding of a new product: Ibuprofeno Farmalider 5,66 mg/ml solución para perfusión as line extension
3.0	October 2015	-Adding of two new products: Ibuprofen 400 mg Solution for Infusion and Ibuprofen 600 mg Solution for Infusion -Harmonizing of the safety concerns according to RMS Assessment Report included in the procedure DE/H/4085/001-002/DC -Updating of last safety information related with the risk cardiovascular for use of high dose of ibuprofen.
4.0	June 2016	-Adding of one new product: Ibuprofeno Farmalider 400 mg concentrado para solución para perfusion -Elimination of one product Ibuprofeno Farmalider 600 mg concentrado para solución para perfusión - According to RMS Assessment Report included in the procedure ES/H/0390/001/DC and ES/H/0392/001/DC: -Modules SIII, SIV, SV, SVI and SVII of Part II completed -Part VI updated -Harmonization of safety concerns with corresponding changes
4.1	September 2016	-Harmonizing of the SPC and PL of the following products, according to reference medicinal product: Ibuprofen 400 mg solution for infusion and Ibuprofen 600 mg solution for infusion.
4.1	November 2016	-Harmonization of safety concerns according to RMS Assessment Report included in the procedure ES/H/0390/001/DC and ES/H/0392/001/DC. -Other minor changes have been performed
5.0	January 2017	- Change of information on QPPV/PV system due to MAH transfer (from Farmalider to B. Braun) - Concerning products: Ibuprofen 400 mg solution for infusion and Ibuprofen 600 mg solution for infusion - Changes of safety concerns: <u>Identified risks</u> None <u>Potential risks</u> • Cardiovascular disorders including thrombotic disturbances • Hypersensitivity reactions (including skin reactions) particularly in patients with a history of previous hypersensitivity to NSAID and/or allergic disease <u>Missing information</u> • Use in children