VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Fentanyl is not used to treat a disease. Instead it is used to relieve pain (analgesia) in different types of procedures along with sedatives and/or anaesthetics.

Sedated analgesia (neurolepanalgesia) is a worldwide common practice to allow for pain-free, safe and effective conduct of diagnostic or therapeutic procedures/interventions in a way that minimizes patient awareness, discomfort, and short term memory related to the procedure, while attempting to preserve spontaneous respiration and airway-protective reflexes. Potential adverse effects of the procedure include nausea and vomiting, respiratory depression, hypoxia, and hypotension. If a weak anesthetic is also administered, patient is rendered unconscious and the state converted to neuroleptanaesthesia.

In general anaesthesia, fentanyl is a preffered candidate as analgesic component due to its rapid action in overcoming the discomfort and pain generated by the surgical procedure. It also offers a rapid recovery of patients and minimal unwanted events.

The loss of the ability to feel pain (analgesia) is an essential component of care for many mechanically ventilated patients in ICU. Pain, frequently experienced as a consequence of intubation and mechanical ventilation itself or of other routine clinical care, can be alleviated ensuring patient comfort and potentially reducing accompanying adverse events. Factors such as medical history, increased age, and organ dysfunction must be considered for these patients so that appropriate analgesic medications and dosages can be prescribed.

VI.2.2 Summary of treatment benefits

Many medications are available to facilitate sedated analgesia. Common agents include etomidate, ketamine, fentanyl, and midazolam. These have become the agents of choice because of their ease of use, predictable action, and excellent safety profiles. For analgesia and sedation in the ICU, opioids, benzodiazepines and propofol are the basic medications used to give the patient comfort and facilitate mechanical ventilation.

Fentanyl is a strong medicine used to prevent or relieve pain. It belongs to a group called opioid analgesics. This medicine is used together with other drugs for analgesia or anaesthesia in various types of interventions. It is also used in artificially ventilated patients in the ICU.

Various clinical studies confirm the analgesic efficacy of fentanyl in different surgical and diagnostic manoeuvres. For example, a total of 151 patients intended for endoscopic exploratory procedures (54 patients for upper digestive system and 97 for lower digestive system) obtained a high level of satisfaction during controlled sedation analgesia with concomitant administration of fentanyl and propofol or propofol-midazolam-ketamine proving the efficacy and safety of the maneuver. Safety and efficacy of fentanyl co-administrated with thiopental was also revealed in 66 patients undergoing spinal and general anesthesia for lumbar disc surgery.

VI.2.3 Unknowns relating to treatment benefits

There is no evidence for differences in the efficacy of Fentanyl B. Braun 0.1 mg, 0.25 mg and 0.5 mg solutions for injection in the target population regarding sex, race and ethnicity. There is limited amount of data regarding fentanyl use in pregnant women and impairment of fertility in humans.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Slow or shallow breathing or stop of breathing (Respiratory depression)	Administration of intravenous fentanyl may lead to a temporary fall in blood pressure, especially in patients with decreased blood volume. In doses higher than 200 micrograms, significant difficulty in breathing will occur. Administration in labour may	Fentanyl should only be used under appropriate medical supervision and with individualized dose, according with patient's age and clinical status. Patients should be continuously monitored for vital functions and

Risk	What is known	Preventability
	cause respiratory depression in the new born infant. The most common events associated with administration of Fentanyl are cardiac rhythm disorders, difficulty in breathing and low arterial pressure.	resuscitation equipment and opioid antagonists should be readily available.

Important potential risks

N/A

Missing information

Risk	What is known
Use during pregnancy and lactation	The use and safety of Fentanyl in pregnancy has not been established. Studies in animals have shown reproductive toxicity. For this reason Fentanyl is not recommended during pregnancy. Fentanyl is excreted into breast milk. After the application of Fentanyl breast feeding should be stopped for at least 24 hours.
Use in patients younger than 2 years of age	The safety and effectiveness of Fentanyl when administered to children under two years of age have not been established. Therefore it is not recommended to use this medicine in children under two years of age.

VI.2.5 Summary of risk minimisation measures by safety concern

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

Not applicable

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

Version	Date	Safety Concerns	Comment
1.0	02.12.2015	Identified Risks • Cardio-respiratory depression Potential Risks • Serotonin syndrome Missing information • Use in pregnancy	Risks proposed by MAH; not agreed by the authority

Version	Date	Safety Concerns	Comment
		and lactation • Use in children less than 2 years old • Impairment of fertility	
1.1	13.04.2017	Identified Risks • Respiratory depression Potential Risks NA Missing information • Use during pregnancy and lactation • Use in patients younger than 2 years of age	Changes of risks requested by authority (DE/H/0153/II/011/G)