

Part II

Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Fentanyl 100 micrograms in 2 ml Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of solution contains 78.5 micrograms fentanyl citrate equivalent to 50 micrograms Fentanyl base.

Each 2 ml ampoule contains 100 micrograms of fentanyl as Fentanyl Citrate. (50 micrograms of fentanyl per ml).

For a full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection
Clear, colourless, sterile solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

1. As the sole intravenous analgesic agent in surgical procedures.
2. As an adjunct in the maintenance of general anaesthesia and analgesia.
3. In conjunction with a neuroleptic agent in the technique of neuroleptanalgesia.
4. As a respiratory depressant/analgesic in patients requiring prolonged assisted ventilation.

4.2 Posology and method of administration

Route of administration: Intravenous

Recommended Dosage:

As sole IV. analgesic agent in surgical procedures.

Adults: The usual dose is 100 to 800 micrograms (0.1 to 0.8mg) initially, depending on response, with maintenance doses of 50 micrograms (0.05mg) as necessary, in conjunction with controlled ventilation.

Children: The usual dose is 10 micrograms/kg (0.01mg/kg) initially, depending on response, with maintenance doses of 1 microgram/kg (0.001mg/kg) as necessary, in conjunction with controlled ventilation.

2. As an adjunct in the maintenance of general anaesthesia and analgesia.

Adults: 50 micrograms (0.05mg) supplements as necessary.

Children: 1 microgram/kg (0.001mg/kg) supplements as necessary.

3. In conjunction with a neuroleptic agent in the technique of neuroleptanalgesia.

Adults: The usual dose is 100 micrograms (0.1mg) initially, with maintenance doses of 50 micrograms (0.05mg) as necessary.

Children: 10 micrograms/kg (0.01mg/kg) initially, with supplemental doses of 1 microgram/kg (0.001 mg/kg).

4. In patients requiring prolonged assisted ventilation.

Adults: Up to 600 micrograms (0.6mg) initially, with supplemental doses of 50 to 200 micrograms (0.05mg to 0.2mg).

Children: 1 microgram/kg (0.001 mg/kg) supplements as necessary.

Elderly patients: Elderly patients will require reduced doses.

Obese patients: Obese patients should have dosage calculated according to their lean body mass.

4.3 Contraindications

Use in patients with hypersensitivity or idiosyncratic response to the active ingredient.

Use in patients with respiratory depression, cyanosis, excessive bronchial exudation, bronchoconstriction (reversible or irreversible), or chronic pulmonary disease.

Use in patients after operative interventions in the biliary tract.

Use in patients who are receiving, or have within two weeks received, monoamine oxidase inhibitors.

Use in the presence of acute alcoholism, increased intracranial pressure or coma.

4.4 Special warnings and precautions for use

Fentanyl is intended for use in hospitals only by those trained in anaesthesia and familiar with the use of potent opioids when given intravenously. As with all potent opioids, respiratory depression is dose-related and can be reversed by a specific opioid antagonist such as naloxone, but additional doses of the latter may be necessary because the respiratory depression may last longer than the duration of action of the opioid antagonist. Profound analgesia is accompanied by marked respiratory depression, which can persist or recur in the post-operative period. Therefore, patients should remain under appropriate surveillance. Resuscitation equipment and opioid antagonists should be readily available. Hyperventilation during anaesthesia may alter the patient's responses to CO₂, thus affecting respiration post-operatively.

Induction of muscle rigidity, which may also involve the thoracic muscles, can occur, but can be avoided by the following measures: slow iv injection (ordinarily sufficient for lower doses), premedication with benzodiazepines and the use of muscle relaxants.

Non-epileptic (myo) clonic movements can occur.

Bradycardia and possibly asystole can occur if the patient has received an insufficient amount of anticholinergic, or when fentanyl is combined with non-vagolytic muscle relaxants. Bradycardia can be treated with atropine.

Opioids may induce hypotension, especially in hypovolaemic patients. Appropriate measures to maintain a stable arterial pressure should be taken.

Repeated use will result in the development of tolerance requiring increases in dosage to achieve the required effects. Generally it is preferable to vary opioid analgesics at intervals in patients requiring prolonged periods of analgesia.

Dependence on fentanyl, when given as a single dose or finite number of intra-operative

doses has not been reported. However, repeated administration at short term intervals for prolonged periods may result in the development of dependence, with a withdrawal syndrome on cessation of therapy.

The use of rapid bolus injections of opioids should be avoided in patients with compromised intracerebral compliance; in such patients the transient decrease in mean arterial pressure has occasionally been accompanied by a short-lasting reduction of the cerebral perfusion pressure.

This product should only be used with great caution in patients who are dependent on drugs in view of the severe respiratory depression which may ensue. Patients on chronic opioid therapy or with history of opioid abuse may require higher doses.

Opioid should be titrated with caution in patients with any of the following conditions: uncontrolled hypothyroidism; pulmonary disease, decreased respiratory reserve; alcoholism; impaired hepatic or renal function. Such patients also require prolonged post-operative monitoring.

If fentanyl is administered with a neuroleptic, the user should be familiar with the special properties of each drug, particularly the difference in duration of action. When such a combination is used there is a higher incidence of hypotension. Neuroleptics can induce extrapyramidal symptoms that can be controlled with anti-Parkinson agents.

This medicine contains 3.542mg sodium per ml which should be taken into consideration by patients on a sodium controlled diet and receiving more than 6.5ml.

4.5 Interaction with other medicinal products and other forms of interactions

Concurrent administration or premedication with other central nervous system depressants will induce an increased depressant effect.

Pretreatment with or concurrent administration of cimetidine may increase plasma levels of fentanyl, when repeated doses of both drugs are used.

Bradycardia may be intensified by pretreatment with or concurrent use of drugs such as betablockers, suxamethonium, halothane, vecuronium, which may themselves cause bradycardia.

4.6 Pregnancy and lactation

All narcotic analgesics are able to traverse the placenta and also are excreted in milk. This should be borne in mind when considering their use in patients during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

Where early discharge is envisaged, patients should be advised not to drive or to operate machinery.

4.8 Undesirable effects

Adverse events reported in association with intravenous fentanyl use in clinical trials are listed below:

Central & Peripheral Nervous System Disorders

Common: Muscle rigidity (which may also involve the thoracic muscles), myoclonic movements, dizziness.

Cardiovascular Disorders, General

Common: Hypotension

Heart Rate and Rhythm Disorders

Common: Bradycardia

Respiratory System Disorders

Common: Apnoea, respiratory depression

Uncommon: Laryngospasm

Gastro-Intestinal System Disorders

Very Common: Nausea, vomiting

Body as a Whole-General Disorder

Uncommon: Allergic reactions (such as anaphylaxis, bronchospasm, pruritus, urticaria)

In addition to the adverse reactions reported in clinical trials, the following adverse reactions have been reported in post-marketing and occur rarely: asystole.

Secondary rebound respiratory depression after the operation has been observed in rare instances.

When a neuroleptic is used with fentanyl, the following adverse reactions may be observed: chills and/or shivering, restlessness, post-operative hallucinatory episodes and extrapyramidal symptoms

4.9 Overdose

As with other narcotic analgesics, the possible manifestations of fentanyl overdose include respiratory depression and hypotension, with circulatory failure and deepening coma. Intensive supportive therapy may be required to correct respiratory failure and shock. A patent airway must be maintained and assisted respiration may be required. If depressed respiration is associated with rigidity of respiratory muscles, an intravenous neuromuscular blocking agent may be required to facilitate assisted or controlled respiration. The specific narcotic antagonist naloxone hydrochloride is used to counteract respiratory depression and coma. A dose of 0.4 to 2mg is given intravenously and may be repeated at intervals of 2 to 3 minutes if necessary, up to 10mg. The duration of respiratory depression following overdose with fentanyl may exceed the duration of narcotic antagonist action.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Fentanyl Citrate is a potent narcotic analgesic with a rapid onset of action. The principal actions of therapeutic value are analgesia and sedation. Fentanyl, like other opioid agonists, causes dose-related respiratory depression.

5.2 Pharmacokinetic properties

Metabolism takes place in the liver and excretion is mainly through urine, with a limited amount through faeces. The half-life varies from two to seven hours and may be prolonged to fifteen hours in elderly patients or after repeated administration. Secondary peak plasma levels may occur. Protein binding at physiological pH is approximately 90% and decreases as the pH becomes acidic. Increased plasma levels may occur in patients with hepatic disease, in elderly or obese patients and after repeated doses.

5.3 Preclinical safety data

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

Fentanyl Citrate is incompatible with thiopental and methohexital.

6.3 Shelf life

5 years

If only part of an ampoule is used, discard the remaining solution.

From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the ampoules in the outer carton in order to protect from light.

6.5 Nature and contents of container

2 ml, clear glass one-point-cut (OPC) ampoules, glass type I Ph. Eur. borosilicate glass, packed in cardboard cartons to contain 10 x 2 ml ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

For single use only. Discard any remaining contents.
C.D. (2)

7. MARKETING AUTHORISATION HOLDER

Antigen Pharmaceuticals Limited,
Roscrea,
Tipperary.

8. MARKETING AUTHORISATION NUMBER

PA 73/122/1

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

4th July 1990/4th July 2005

10. DATE OF APPROVAL OF THE TEXT

10th December 2010