SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT:

FENT

Fentanyl Citrate Injection USP

Strength:

50 mcg/ml – 2 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Sr. No.	Particulars	Grade	Qty./ml	Function
1.	Fentanyl Citrate equivalent to Fentanyl	USP	50 mcg	Active

For the list of full excipients see section 6.1.

3. PHARMACEUTICAL FORM:

Solution for Injection

A clear colourless solution.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

Fentanyl Citrate is indicated for:

1. For analgesic action of short duration during the anesthetic periods premedication, induction and maintenance and in the immediate post-operative period as the need arises.
2. For use as a narcotic analgesic supplement in general or regional anaesthesia.
3. For use as an anesthetic agent with oxygen in selected high risk patients, such as those undergoing open heart surgery.
4. For administration with a neuroleptic such as Droperidol Injection as an anesthetic premedication and as an adjunct in the maintenance of regional anesthesia.

4.2 Posology and method of administration:

Route of administration: For I.M. / I.V. use

Adults

Adult dose of spontaneous respiration of initials dose is 50-200 micrograms/kg and supplemental 50 micrograms/kg and assisted ventilation of initials dose is 300-3500 micrograms/kg and supplemental 100-200 micrograms/kg.

Doses in excess of 200 micrograms are for use in anaesthesia only. As a premedicant, 1-2 ml fentanyl may be given intramuscularly 45 minutes before induction of anaesthesia. After intravenous administration in unpremedicated adult patients, 2 ml fentanyl may be expected to provide sufficient analgesia for 10-20 minutes in surgical procedures involving low pain intensity. 10 ml fentanyl injected as a bolus gives analgesia lasting about one hour. The analgesia produced is sufficient for surgery involving moderately painful procedures. Giving a dose of 50 micrograms/kg fentanyl will provide intense analgesia for some four to six hours, for intensely stimulating surgery.

Fentanyl may also be given as an infusion. In ventilated patients, a loading dose of fentanyl may be given as a fast infusion of approximately 1 microgram/kg/min for first 10 minutes followed by an infusion of approximately 0.1 micrograms/kg/min. alternatively the loading dose of fentanyl may be given as a bolus. Infusion rates should be titrated to individual patient response; lower infusion rates may be adequate.

Unless it is planned to ventilate post-operatively, the infusion should be terminated at about 40 minutes before the end of surgery.
Lower infusion rates, e.g. 0.05-0.08 micrograms/kg/minute are necessary if spontaneous ventilation is to be maintained. Higher infusion rates (up to 3 micrograms/ kg/minute) have been used in cardiac surgery.
Fentanyl is chemically incompatible with the induction agents' pentobarbital sodium, thiopentone and methohexitone because of wide differences in pH.

Children:

Children aged 12 to 17 years old Follow adult dosage.
The usual dosage regimen in children is as follows:
Children aged 2 to 11 years old: spontaneous respiration and assisted ventilation of initials dose is 1-3 micrograms/kg and supplemental 1-1.25 micrograms/kg. Analgesia during operation, enhancement of anaesthesia with spontaneous respiration Techniques that involve analgesia in a spontaneous breathing child should only be used as part of an anaesthetic technique, or given as part of a sedation/ analgesia technique with experienced personnel in an environment that can manage sudden chest wall rigidity requiring intubation, or apnoea requiring airway support.

Use in elderly and debilitated patients:

As with other opioids, the initial dose should be reduced in the elderly (>65 years of age) and in debilitated patients. The effect of the initial dose should be taken into account in determining supplemental doses.

4.3 Contraindications:

Fentanyl Citrate is contraindicated in patients with known intolerance to the drug.

4.4 Special warnings and precautions for use:

Warnings:

Fentanyl Citrate should be administered only by persons specifically trained in the use of intravenous anaesthetics and management of the respiratory effects of potent opioids. An opioid antagonist, Resuscitative and incubation equipment and oxygen should be readily available.
If Fentanyl Citrate is administered with a tranquilizer such as Droperidol, the user should become familiar with the special properties of each drug. In addition, when such a combination is used fluids and other counter measures to manage hypotension should be available.
Adequate facilities should be available to post-operative monitoring and ventilation of patients administered anaesthetic doses of Fentanyl Citrate. It is essential that these facilities be fully equipped to handle all degrees of respiratory depression.

Precautions:

General: The initial dose of Fentanyl Citrate should be appropriate reduced in elderly and debilitated patients. The effect of initial dose should be considered in determining incremental dose.
Fentanyl Citrate should be used with caution in patients with chronic obstructive pulmonary disease and to the patients with liver and kidney dysfunction. Intravenous Fentanyl may produce bradycardia, which may be treated with atropine. Fentanyl should be administered with caution patients with bradyarrhythemias. As with of opioids, orthrostatic hypotension is possible.

4.5 Interaction with other medicinal products and other forms of interaction:

The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect.
The use of other CNS depressants such as opioid premedication, barbiturates, neuroleptics, general anaesthetics and other non-selective CNS depressants (e.g. alcohol) may enhance or prolong the respiratory depression, profound sedation, coma, and death of fentanyl.
Fentanyl, a high clearance drug, is rapidly and extensively metabolised mainly by CYP3A4. When IV fentanyl is used, the concomitant use of a CYP3A4 inhibitor may result in a decrease in fentanyl clearance. With single-dose IV fentanyl administration, the period of risk for respiratory depression may be prolonged, which may require special patient care and longer observation. Co-administration of fluconazole or voriconazole (moderate CYP3A4 inhibitors) and fentanyl may result in an increased exposure and/or prolonged exposure to fentanyl.
Administration of fentanyl with a serotonergic agent, such as a Selective Serotonin Re-uptake Inhibitor (SSRI) or a Serotonin Norepinephrine Re-uptake Inhibitor (SNRI) or a Monoamine Oxidase Inhibitor (MAOI), may increase the risk of serotonin syndrome, a potentially life-threatening condition.

4.6 Fertility, pregnancy and lactation:

There are no adequate and well-controlled studies in pregnant women, so Fentanyl should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Nursing Mothers

Fentanyl is excreted in human milk; therefore, Fentanyl is not recommended for use in nursing women because of the possibility of effects in their infants.

Paediatric Use

The safety and efficacy of Fentanyl Citrate in children under two years of age has not been established.

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 for at least 24 hours following administration.
This medicine can impair cognitive function and can affect a patient's ability to drive safely.
This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988.
When prescribing this medicine, patients should be told:
· The medicine is likely to affect your ability to drive
· Do not drive until you know how the medicine affects you
· It is an offence to drive while under the influence of this medicine
· However, you would not be committing an offence (called 'statutory defence') if:
· The medicine has been prescribed to treat a medical or dental problem and
· You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and It was not affecting your ability to drive safely.

4.8 Undesirable effects:

As with other narcotic analgesics, the most common serious adverse reactions reported to occur with Fentanyl Citrate are apnea, respiratory depression, rigidity and

bradycardia, if these remain untreated respiratory arrest or cardiac arrest could occur other adverse reactions that have been reported are hypertension, hypotension, dizziness, blurred vision, nausea, emesis and diaphoresia.

When a tranquilizer such as Droperidol is used with Fentanyl, the following adverse reaction may occur chills and/or shivering restlessness and post-operative hallucinatory episodes, extrapyramidal symptoms (dystonia, akathisia and oculogyric crisis) have been observed upto 24 hours Post-operatively when they occur extrapyramidal symptoms can usually be controlled with antiparkinson agents.

Drug Abuse and Dependence

Fentanyl Citrate can produce drug dependence of the morphine type and therefore has the potential for being abused.

4.9 Overdose:

Symptoms and signs:

Acute overdose with Fentanyl Citrate Injection can be manifested by respiratory depression, bradypnoea to apnoea, skeletal muscle rigidity, cold and clammy skin, constricted pupils.

Treatment of overdose:

Hypoventilation or apnoea: O_2 administration assisted or controlled respiration. Respiratory depression: Specific opioid antagonist. This does not preclude the use of immediate countermeasures.

The respiratory depression may last longer than the effect of the antagonist; additional doses of the letter may therefore be required.

Muscular rigidity: Intravenous neuromuscular blocking agent to facilitate assisted or controlled respiration.

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

Fentanyl Citrate is a narcotic analgesic. It is short acting after single doses, but has a relatively long elimination half-life because of rapid redistribution in the body. Fentanyl is usually given intravenously and is used particularly in anaesthesia. A dose of 100 mcg (in 2 ml) is approximately equivalent in analgesic activity to 10 mg of morphine or 75 mg of meperidine. The principal actions of therapeutic value are analgesic and sedation. Large doses may produce apnea.

5.2 Pharmacokinetic properties:

After parenteral administration Fentanyl citrate has a rapid onset and short duration of action. It is metabolised in the liver by N-dealkylation and hydroxylation, Metabolites and some unchanged drug are excreted mainly in the urine. The short duration of action is probably due to rapid redistribution into the tissues rather than metabolism and excretion. An elimination half-life of about 4 hours reflects slower release from tissue depots. About 80% has been reported to be bound to plasma proteins. Fentanyl appears in the cerebrospinal fluid. It crosses the placenta and small amounts have been detected in breast milk.

5.3 Pre-clinical Safety Data:

In vitro fentanyl showed, like other opioid analgesics, mutagenic effects in a mammalian cell culture assay, only at cytotoxic concentrations and along with

metabolic activation. Fentanyl showed no evidence of mutagenicity when tested in in vivo rodent studies and bacterial assays. There are no long-term animal studies to investigate the tumor-forming potential of fentanyl.

Some tests on female rats showed reduced fertility as well as embryo mortality. These findings were related to maternal toxicity and not a direct effect of the drug on the developing embryo. There was no evidence of teratogenic effects.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients:

Water for Injection USP

6.2 Incompatibilities:

Fentanyl citrate is incompatible with alkaline solutions (due to reduced solubility) and some drugs.
Published data show that Fentanyl 50 micrograms/ml Solution for Injection/Infusion is incompatible with alkaline injections including methohexital and thiopental.
Loss of fentanyl citrate due to absorption to PVC containers has been reported when the solution pH was adjusted to the alkaline range.
Compatibility must be checked before administration.

6.3 Shelf – life:

24 Months

6.4 Special precautions for storage:

Store below 30°C., protected from light. Do not freeze.

6.5 Nature and contents of container:

2 ml flint ampoule with red double band snap-off. Such 5 ampoules are packed in a blister, such 2 blisters packed in an inner printed carton along with direction slip.

6.6 Special Precautions for Handling and Disposal:

The injection is for single patient use and should be used immediately after opening. The injection should not be used if particles are present. Any unused portion should be discarded.

7. MARKETING AUTHORIZATION HOLDER:

M/s. NEON LABORATORIES LIMITED
140, Damji Shamji Industrial Complex,
28, Mahal Indl. Estate, Mahakali Caves Road,
Andheri (East), Mumbai - 400 093

8. MARKETING AUTHORIZATION NUMBER:

07065/08224/REN/2021

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORISATION:

Date of first authorization: 01-02-2022

10. DATE OF REVISION OF THE TEXT: JULY 2023

11. REFERENCE

- Fentanyl 50 micrograms/ml Solution for Injection/Infusion - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk)

- Fentanyl 50 micrograms/ml Solution for Injection/Infusion - https://dailymed.nlm.nih.gov/dailymed/