Therapeutic Indications:

- Containing either 1mg of alfentanil base in 2ml or 5mg of alfentanil base in 5ml containing 2mg of alfentanil base in 10ml.

**Clinical Considerations**

Therapeutic Indications: As an analgesic supplement for use before and during anaesthesia. It is indicated for:

- Inhalation anaesthesia in a volatile agent. In this case, it may be given at lower concentrations of a volatile agent for brief periods.
- In spontaneous breathing patients, the initial bolus dose should be given slowly over about 30 seconds (dilution may be helpful).

**Additional Information**

- Spontaneous breathing patients: In spontaneously breathing patients, the initial bolus dose should be given slowly over about 30 seconds (dilution may be helpful).
- Anti-convulsants: Alfentanil Injection may be expected to have a peak effect in 90 seconds and may be given slowly over about 30 seconds (dilution may be helpful).

**Administration**

- Following administration of Alfentanil 500 micrograms/ml Solution for Injection, a transient fall in blood pressure may occur. The magnitude of this effect varies from patient to patient, being larger in patients with compromised intracerebral compliance; in such cases, continuous monitoring of blood pressure should therefore be monitored carefully. If hypotension or bradycardia occur, appropriate measures should be instituted.

- Asthma: Asthma has occasionally been accompanied by a transient reduction of the central and peripheral blood pressure.

**Interactions with other medical products and other forms of interaction**

- Alfentanil hydrochloride is metabolised mainly via the human cytochrome P450 3A4 enzyme. Available evidence indicates that the metabolism of alfentanil may be inhibited by Fluconazole, Irinotecan, Diltiazem and Cimetidine (known P450 3A4 enzyme inhibitors).

- In vitro data suggest that other potent cytochrome P450 3A4 enzyme inhibitors (e.g. Ketoconazole, Itraconazole, Reductase) may also inhibit the metabolism of alfentanil. This could increase the risk of prolonged or delayed respiratory depression. In such cases, the concomitant use of such drugs requires special patient care and observation; in particular, it may be necessary to lower the dose of Alfentanil 500 micrograms/ml Solution for Injection in combination with non-vagolytic muscle relaxants.

- The use of opioid premedication, barbiturates, benzodiazepines, benzamines, halothane and other non-selective muscle relaxants may enhance or prolong the respiratory depressant effects of alfentanil.

- If other narcotic or Opioid drugs are used concomitantly with alfentanil, the effects of the drugs can be expected to be additive. When patients have received such drugs the dose of alfentanil required will be less than usual. Likewise, following the administration of Alfentanil 500 micrograms/ml Solution for Injection, a transient fall in blood pressure may occur. The magnitude of this effect varies from patient to patient, being larger in patients with compromised intracerebral compliance; in such cases, continuous monitoring of blood pressure should therefore be monitored carefully. If hypotension or bradycardia occur, appropriate measures should be instituted.

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administration of alfentanil, the dose of other CNS depressant drugs should be reduced.

Pharmacology and Lactation: Although no teratogenic or acute embryotoxic effects have been observed in animal experiments, insufficient data are available to evaluate any potential effects in man.

The drug should only be given to pregnant patients who are believed to derive possible risks and potential advantages before administering this drug to pregnant patients.

Intrauterine administration during childbirth (including caesarean section) is not recommended, because alfentanil crosses the placenta and because the fetal respiratory centre is particularly sensitive to opiates. If, however, alfentanil 500 micrograms/ml (solution for injection), is administered, an antiputty should always be at hand for the child.

Alfentanil may appear in breast milk. It is therefore recommended that breast feeding is not initiated within 24 hours of treatment.

Effects on the Ability to Drive and Use Machines: Where early discharge is envisaged, patients should be advised not to drive or operate machinery for 24 hours following administration.

Other Undesirable Effects: Adverse events reported in association with alfentanil 0.5mg/ml injection are listed below. Decreasing frequency within each body system is indicated by the frequency estimate categories. Very common: >10% (indicates a limited distribution of alfentanil to the tissues). Plaenic clearance, varying from 2 to 3 ml/kg/min, is approximately one third of liver plasma flow indicating that the elimination of alfentanil is not flow dependent. The incidence of the dose is excrated in the urine as unchanged drug, elimination of alfentanil occurs mainly by metabolism.

These main parameters in patients undergoing surgery are similar to those in healthy volunteers. Only when the drug was given as the sole anaesthetic in a continuous high inflation over about 5 minutes, was the clearance of alfentanil reduced resulting in a plasma half-life of about 200 minutes, the distribution volume not being markedly changed.

Plasma protein binding of alfentanil is 92%, mainly due to a strong binding to the alpha-acid glycoprotein. It is not bound to the blood cells.

Pharmacokinetics: After bolus injections ranging from 2.4 to 125 micrograms/kg, plasma levels in 10 minutes were virtually terminal with a half-life of approximately 90 minutes. Total distribution volume varies from 0.4 to 1.2 L/kg, indicating a limited distribution of alfentanil to the tissues. Plaenic clearance, varying from 2 to 3 ml/kg/min, is approximately one third of liver plasma flow indicating that alfentanil is not flow dependent. This metabolism is highly variable and patients. Only when the drug was given as the sole anaesthetic in a continuous high inflation over about 5 minutes, was the clearance of alfentanil reduced resulting in a plasma half-life of about 200 minutes, the distribution volume not being markedly changed.

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