

**FENTANYL 50 MICROGRAM/ML INJECTION
PL 01502/0062**

UKPAR

TABLE OF CONTENTS

Lay Summary	Page 2
Scientific discussion	Page 3
Steps taken for assessment	Page 12
Steps taken after authorisation – summary	Page 13
Summary of Product Characteristics	Page 14
Product Information Leaflet	Page 21
Labelling	Page 23

FENTANYL 50 MICROGRAM/ML INJECTION
PL 01502/0062

LAY SUMMARY

The MHRA granted Hameln Pharmaceuticals Ltd a Marketing Authorisation (licence) for the medicinal product Fentanyl 50 microgram/ml Injection (PL 01502/0062) on the 13th of April 2006. This prescription only medicine (POM) is used as an analgesic component in general or local anaesthesia to provide analgesia during short surgical procedures; and as an analgesic/respiratory depressant in patients who need assisted ventilation; and in combination with antipsychotic drugs.

Fentanyl solution for injection contains the active ingredient fentanyl, as fentanyl citrate 78.5 micrograms equivalent to 50 micrograms per ml of fentanyl.

The data presented to the MHRA, pre-licensing, demonstrated that Fentanyl 50 microgram/ml Injection is essentially similar or equivalent to the approved product Sublimaze, Jansen Pharmaceuticals, PL 0242/5001R. Fentanyl 50 microgram/ml Injection can therefore be used interchangeably with Sublimaze™, PL 00242/5001R.

No new or unexpected safety concerns arose from this application and it was, therefore, judged that the benefits of taking Fentanyl 50 microgram/ml Injection outweighs the risks, hence a Marketing Authorisation has been granted.

**FENTANYL 50 MICROGRAM/ML INJECTION
PL 01502/0062**

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction	Page 4
Pharmaceutical assessment	Page 5
Preclinical assessment	Page 8
Clinical assessment	Page 9
Overall conclusions and risk benefit assessment	Page 11

INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted a marketing authorisation to Hameln Pharmaceuticals Ltd a Marketing Authorisation (licence) for the medicinal product Fentanyl 50 microgram/ml Injection (PL 01502/0062) on the 13th of April 2006. This product is a prescription only medicine (POM).

This application was submitted as an abridged application according to article 10.1(a)(iii) of Directive 2001/83/EC, claiming essential similarity to the original product Sublimaze™ PL 00242/5001R.

This product contains the active ingredient fentanyl and is a potent short acting opioid analgesic used as an analgesic component in general or local anaesthesia to provide analgesia during short surgical procedures; and as an analgesic/respiratory depressant in patients who need assisted ventilation; and in combination with neuroleptic drugs as part of the technique of neuroleptanalgesia.

PHARMACEUTICAL ASSESSMENT

1. INTRODUCTION

This is a national standard abridged Marketing Authorisation application for a sterile aqueous solution for intravenous and intramuscular injection containing fentanyl (as the citrate) 50mcg/ml as the active ingredient claiming essential similarity in the UK to Sublimaze™ PL 00242/5001R licensed in February 1980 to Janssen-Cilag. This application was submitted under EC Article 10.1 [formerly Art 10.1(a)(iii)] of Directive 2001/83/EC as amended.

Fentanyl is a short acting opioid analgesic. The proposed indications are

- As an analgesic component in general or local anaesthesia
- To provide analgesia during short surgical procedures
- As an analgesic/respiratory depressant in patients who need assisted ventilation
- In combination with a neuroleptic drug as part of the technique of neuroleptanalgesia.

There are already generic Marketing Authorisations for fentanyl 50mcg/ml injection on the UK market.

2. PART IIA – COMPOSITION AND DEVELOPMENT PHARMACEUTICS

The objective was to produce a solution for injection comparable to the reference product. The composition of Fentanyl 50 microgram/ml Injection is fentanyl citrate, sodium chloride, hydrochloric acid or sodium hydroxide and water for injections. To achieve water solubility, fentanyl citrate is used. Satisfactory justification has been given for the excipients used. The formulation and manufacturing method developed is very simple. The pharmaceutical form and qualitative and quantitative composition of the active ingredient is the same as that of the reference product. Essential similarity in relation to impurities has been demonstrated in comparison to the reference product.

The product may be given by IV, either as a bolus injection or by infusion. The SPC mentions dilution with 5% glucose solution or 0.9% sodium chloride. The maximum dilution allowed is 1:25. Satisfactory physical and chemical stability data have been provided for the product diluted 1:1 and 1:25 with 5% glucose solution or 0.9% sodium chloride and stored for up to 24 hours at 20-25°C.

3. PART IIB – METHOD OF PREPARATION

The manufacturing process is described both in the description and in flow chart form. Comprehensive in-process controls are applied during manufacture.

Essential stages of the manufacturing process have been validated using three batches manufactured at the original manufacturing site. Batch analysis data has been provided.

4. PART IIC - CONTROL OF STARTING MATERIALS

Satisfactory information is provided on the drug substance. The specification proposed complies with Ph.Eur requirements and is supported by batch data. The retest period of 5 years when stored below 25°C is supported by the stability data presented.

All excipients comply with their relevant Ph.Eur monographs. Sodium chloride, hydrochloric acid, sodium hydroxide and nitrogen are obtained from certified suppliers. None of the excipients used contain material of animal or human origin.

The 2ml and 10ml ampoules are made of clear colourless Type I, Ph.Eur glass. Specifications have been submitted and are satisfactory and supported by Certificates of Analysis.

5. PART IIE – CONTROL TESTS ON THE FINISHED PRODUCTS

The finished product specification is satisfactory. The specification proposed complies with BP requirements for Fentanyl Injection and is supported by batch analytical and stability data. Test methods have been described and adequately validated as appropriate.

6. PART IIF – STABILITY

Finished product stability studies have been presented for the 2ml and 10ml ampoules. Based on the results a shelf life of 3 years (36 months) has been set which is satisfactory. The storage precautions 'Keep ampoules in the outer carton' are included in order to protect the product from light.

7. PART IIG – BIOEQUIVALENCE / BIOAVAILABILITY

Bioequivalence studies are not necessary. The product is an aqueous solution for intravenous use and contains the same active and excipients as the reference product.

8. PART I – PRODUCT PARTICULARS

8.1 MAA Forms

The European MAA form is provided and is satisfactory.

8.2 SPC

An SPC is provided and is satisfactory.

8.3 Labelling and Leaflet

Full colour mock-ups for the carton and ampoule labelling and the patient leaflet have been provided and are satisfactory.

8.4 GMP Status

The current manufacturing site was inspected for GMP compliance by German authorities and has been approved for use in the manufacture of granted parenteral products.

A satisfactory manufacturer's licence is provided.

8.5 BSE/TSE Compliance

The applicant has demonstrated that the medicinal product is manufactured in accordance with the Ph.Eur chapter 5.2.8 (2001 supplement) - Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Medicinal Products.

9. PHARMACEUTICAL EXPERT REPORT

The expert report is written by a pharmacist and is a non-critical summary of the data provided.

10. PHARMACEUTICAL CONCLUSION

A product licence should be granted for this product.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with these applications and none are required for an application of this type.

CLINICAL ASSESSMENT

1. INTRODUCTION

This national abridged application claims essential similarity to Sublimaze™ PL 00242/5001R licensed in February 1980 to Janssen-Cilag.

2. BACKGROUND

Fentanyl is a potent short acting opioid analgesic.

3. INDICATIONS

These are satisfactory and consistent with the cross – reference product.

4. DOSE & DOSE SCHEDULE

These are satisfactory and consistent with the cross – reference product.

5. TOXICOLOGY

No new data submitted and none are required for this application.

6. CLINICAL PHARMACOLOGY

No new data have been submitted. This is an application for a solution for intravenous use. 100% bioavailability is assumed and there is no requirement for comparative bioavailability studies.

7. EFFICACY

No new data submitted

8. SAFETY

No new data submitted

9. EXPERT REPORTS

A comprehensive clinical expert report by an appropriately qualified physician has been submitted.

10. PATIENT INFORMATION LEAFLET (PIL)

Satisfactory

MHRA UKPAR PL 01502/0062

Fentanyl 50 microgram/ml Injection

11. LABELLING

Satisfactory

12. APPLICATION FORM (MAA)

Satisfactory

13. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

Satisfactory

14. DISCUSSION

The applicant has satisfactorily demonstrated essential similarity to the cross reference product.

15. MEDICAL CONCLUSION

A marketing authorisation is recommended.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Fentanyl 50 microgram/ml Injection are well defined and controlled. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

Bioequivalence studies are not necessary. The product is intended to be administered parenterally as a solution and contains the same active and excipients as the reference product.

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the reference product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product and the innovator product are interchangeable. Clinical experience with fentanyl is considered to have demonstrated the therapeutic value of the compound. The risk benefit is therefore considered to be positive.

**FENTANYL 50 MICROGRAM/ML INJECTION
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STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application on 07/08/2000
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 28/11/2005.
3	Following assessment of the application the MHRA requested further information relating to the dossier on 5/12/2000, 18/12/2000, 15//02/2002, and again on 02/06/2003.
4	The applicant responded to the MHRA's requests, providing further information relating to the quality dossier on 11/06/2001, 28/11/2002, 30/04/2003 and 15/12/2004 and on the 28/11/2005.
5	The application was determined on 13/04/2006.

**FENTANYL 50 MICROGRAM/ML INJECTION
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STEPS TAKEN AFTER ASSESSMENT

Date submitted	Application type	Scope	Outcome

**FENTANYL 50 MICROGRAM/ML INJECTION
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SUMMARY OF PRODUCT CHARACTERISTICS

1. Trade Name of the Medicinal Product

Fentanyl 50 microgram/ml Injection

2. Qualitative and Quantitative Composition

Fentanyl citrate 78.5 micrograms equivalent to 50 micrograms per ml fentanyl.

Each 2ml ampoule contains 100 micrograms of fentanyl as fentanyl citrate.
Each 10ml ampoule contains 500 micrograms of fentanyl as fentanyl citrate.

For excipients, see 6.1.

3. Pharmaceutical Form

Solution for injection

Clear, colourless solution

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Fentanyl is a short acting opioid used

- as an analgesic component in general or local anaesthesia
- to provide analgesia during short surgical procedures
- as an analgesic/respiratory depressant in patients who need assisted ventilation
- in combination with a neuroleptic drug as part of the technique of neuroleptanalgesia

4.2. Posology and Method of Administration

Intravenous and intramuscular routes. Intravenous administration either as a bolus or by infusion. Fentanyl Injection can be administered to both adults and children via the intravenous route according to the following dosage regimen:

	Adults		Children	
	Initial µg	Supplemental µg	Initial µg/kg	Supplemental µg/kg
Spontaneous respiration	50-200	25-100	1-5	1
Assisted ventilation	200-3500	100-200	5-15	1-3

Doses greater than 200 micrograms are solely for use in anaesthesia.

As a premedicament, 1-2 ml may be administered intramuscularly before induction of anaesthesia.

Following intravenous administration in the non-premedicated adult patient, 2 ml fentanyl may be anticipated to provide adequate analgesia for 10 - 20 minutes in surgical procedures involving low pain intensity. A bolus of 10 ml fentanyl can be expected to provide analgesia for about 1 hour. The analgesia produced is generally adequate for surgery involving moderate pain intensity. Administration of 50 µg/kg will provide intense analgesia for some 4 to 6 hours for surgery associated with intense stimulation.

It is important when estimating the required dose to assess the likely degree of surgical stimulation, the effect of premedicant drugs, and the duration of the procedure.

Use in elderly: It is important to reduce the dosage in the elderly.

4.3. Contraindications

Fentanyl should not be used in patients with

- known hypersensitivity to fentanyl citrate, other morphinomimetics or muscle relaxants.
- obstructive airways disease or any respiratory depression.
- concurrent administration with monoamine oxidase inhibitors or within 2 weeks of their discontinuation.
- brain trauma.

4.4. Special Warnings and Precautions for Use

In common with other narcotic analgesics, the most common serious adverse reactions with fentanyl are respiratory depression, bradycardia and skeletal muscle rigidity.

As with all narcotic analgesics, care should be observed when administering Fentanyl Injection to patients with myasthenia gravis.

Caution is required when fentanyl is used in patients with increased intracranial pressure.

It is desirable to reduce dosage in the elderly, in hypothyroidism and chronic hepatic disease.

Administration in labour may cause respiratory depression in the new-born infant.

As with all potent opioids, profound analgesia is accompanied by marked respiratory depression, which may persist into or recur in the early post-operative

period. It is imperative to ensure that adequate spontaneous breathing has been established and maintained before discharge from the recovery area whenever large doses of infusions of Fentanyl Injection have been administered. Hyperventilation during anaesthesia may alter the patient's response to CO₂, thus affecting respiration post-operatively. Opioid pre-medication may potentiate or prolong depressant effects of fentanyl citrate.

A transient fall in blood pressure may occur following intravenous administration of fentanyl citrate injection.

Repeated use of fentanyl may result in the development of tolerance and dependence.

After fentanyl an increase of the bile duct pressure can be observed, in isolated cases a spasm of the Sphincter of Oddi: This has to be taken into account during intraoperative diagnostic procedure in bile duct surgery and in pain management of intensive care patients.

As all other opioids, fentanyl can have an inhibitory effect on intestinal motility. This should be considered in the pain management of intensive care patients with inflammatory or obstructive intestinal diseases.

4.5. Interactions with other Medicaments and other forms of Interaction

If other narcotic or CNS-depressant drugs are used concurrently with fentanyl, the effects of the drug may be expected to be additive. The pharmacological effects of fentanyl citrate can be reversed by naloxone.

In patients with preceding medication with MAO inhibitors within the last 14 days before opioid administration life-threatening interactions with pethidine on the central nervous system (i.e. agitation, muscle rigidity, hyperpyrexia, convulsions), and the respiratory and circulatory system (i.e. circulatory depression, hypotension, haemodynamic instability and coma) have been observed and cannot be ruled out with fentanyl.

Prior administration of cimetidine may lead to increased plasma levels of fentanyl.

Co-administration of clonidine may enhance fentanyl effects and especially prolong fentanyl-induced respiratory depression.

Vecuronium can cause haemodynamic depression when combined with fentanyl.

4.6. Pregnancy and Lactation

Placental transfer of fentanyl occurs. There has been little usage in human pregnancy but no evidence of teratogenic effects in animals. Administration in labour may cause respiratory depression in new-born infant. Fentanyl should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. It is not known whether fentanyl is excreted in human milk. Because many

drugs are excreted in human milk, caution should be exercised when administering fentanyl to a nursing mother.

4.7. Effects on Ability to Drive and Use Machines

Where early discharge (*from clinical care*) is envisaged, patients should be advised not to drive or to operate machinery.

4.8. Undesirable Effects

A transient fall in blood pressure may occur following intravenous administration of fentanyl citrate injection.

Significant respiratory depression will occur following administration of fentanyl in doses in excess of 200 µg. This and other pharmacological effects of fentanyl can be reversed by naloxone.

Bradycardia may occur due to increased cardiac vagal stimulation; it can be reversed by atropine or glycopyrrolate. Skeletal muscle rigidity (morphine-like effect) may occur and muscle relaxants have been found helpful in such cases. Nausea and vomiting may be troublesome.

The opioid specific effect on smooth muscles may lead to constipation, increased muscle tone of the ureter resulting in urinary retention, especially in patients with prostatic hypertrophy.

Fentanyl may cause miosis and disturbances of vision.

Allergic reactions like anaphylaxis, pruritus and urticaria may occur.

Sweating, singultus and spasm of the sphincter of Oddi are further side-effects which have been observed after the application of fentanyl.

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. The specific narcotic antagonist naloxone hydrochloride is used to counteract respiratory depression and coma. A dose of 0.4 to 2 mg is given intravenously and may be repeated at intervals of 2 to 3 minutes if necessary, up to 10 mg. The duration of respiratory depression following overdose with fentanyl may exceed the duration of narcotic antagonist action.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Phenylpiperidine derivatives, Opioids
ATC code: N02AB

Fentanyl citrate is a potent narcotic analgesic

The principal actions of therapeutic value are analgesia and sedation. When used with a neuroleptic agent it can induce a state of neuroleptanalgesia. As with other narcotic analgesics, fentanyl depresses respiration and this effect increases as the dose is increased.

Following intravenous injection fentanyl has rapid onset of action, although the maximal analgesic and respiratory depressant effect may not occur for several minutes.

Fentanyl Injection is usually given by the intravenous route.

5.2. Pharmacokinetic Properties

After intravenous injection the fentanyl plasma concentrations decrease rapidly. The disposition of fentanyl is triphasic with half-lives of about 1 minute, 15 minutes and 6 hours. Fentanyl has a volume of distribution of the central compartment of about 15 litres and a total volume of distribution of about 400 litres.

Especially in elderly patients or after repeated administration, half-lives may be prolonged. Secondary peak plasma levels may occur.

Fentanyl is 80 – 85 % bound to plasma proteins. Fentanyl is metabolised rapidly, mainly in the liver, mainly by oxidative N-desalkylation. The clearance is about 0.5 l/hour/kg. About 75 % of the administered dose is eliminated within 24 hours. Only 10 % of the dose is excreted as intact substance.

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, Water for Injections, hydrochloric acid or sodium hydroxide for pH adjustment.

6.2. Incompatibilities

Fentanyl citrate is reportedly physically incompatible with pentobarbital sodium, methohexital sodium, thiopental sodium and nafcilline.

6.3. Shelf Life

Shelf-life of the product as package for sale:	3 years (36 months)
Shelf-life after dilution:	24 hours
Shelf-life after first opening:	use immediately.

6.4. Special Precautions for Storage

Keep ampoules in the outer carton.

Chemical and physical in-use stability has been demonstrated for 24 hours at 20-25°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled validated aseptic conditions

6.5. Nature and Contents of Container

2 ml or 10 ml clear glass ampoules, glass type I Ph. Eur., packed in cardboard cartons and containing 5 x 2 ml/10 ml ampoules or 10 x 2 ml/10 ml ampoules.

6.6. Instruction for Use/Handling

Use finger protection when opening an ampoule.

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.

The product can be used either undiluted or diluted. Dilution ranges tested with 0.9 % sodium chloride and 5 % glucose solutions are 1:1 and 1:25. Hence the maximal dilution must not exceed 1 part fentanyl with 25 parts 0.9 % sodium chloride or 5 % glucose solutions.

7. MARKETING AUTHORISATION HOLDER

hameln pharmaceuticals ltd.
Nexus
Gloucester Business Park
Gloucester
GL3 4AG
UK

8. MARKETING AUTHORISATION NUMBER

PL 01502/0062

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

13/04/2006

10 DATE OF REVISION OF THE TEXT

13/04/2006

FENTANYL 50 MICROGRAM/ML INJECTION

PL 01502/0062

PATIENT INFORMATION LEAFLET



Fentanyl 50 micrograms/ml Injection

This leaflet is a summary of the information available for this medication. You should ask your doctor or pharmacist if you are unsure about any aspect of this medication.

What you should know about Fentanyl Injection

Fentanyl Injection is a clear, colourless and sterile solution for injection presented in 2 ml or 10 ml clear glass ampoules in packs of 5 or 10 ampoules. Each millilitre of solution contains fentanyl citrate equivalent to 50 micrograms of fentanyl as active ingredient in water for injection. It also contains sodium chloride and hydrochloric acid or sodium hydroxide. Fentanyl is an analgesic drug, often used in anaesthesia or as a pain relief agent.

The licence holder is:
hameln pharmaceuticals ltd
Gloucester, UK

Manufactured by:
hameln pharmaceuticals gmbh
Langes Feld 13, 31789 Hameln, Germany

Uses

Fentanyl citrate is an analgesic. It is used to provide pain relief during short surgical procedures. Where breathing is assisted, it is also used as an anaesthetic and analgesic because fentanyl depresses respiration. Fentanyl may also be given in combination with a tranquilliser to induce both calmness and pain relief. Fentanyl can also be used as a premedication to sedate and prepare a patient for general anaesthesia.

Warnings

Do not take this medicine without consulting your doctor if any of the following apply:

- You are allergic to fentanyl citrate, drugs similar to morphine or muscle relaxants.
- You have any breathing problems or a lung disorder, such as asthma, chronic bronchitis or emphysema.

- You are taking monoamine oxidase inhibitor (MAOI) drugs for depression, or if you have taken them within the previous 2 weeks.
- You are suffering from increased intracranial pressure or brain trauma.
- You are suffering from myasthenia gravis, reduced blood volume or low blood pressure.

Tell your doctor if you have a thyroid gland deficiency or chronic liver disease, as the doctor may wish to reduce the dosage. Tell your doctor if you are taking any other medicines, like cimetidine, vecuronium, clonidine, pain relieving drugs, tranquilliser or antidepressants, that depress the activity of the brain or spinal cord, as fentanyl may increase the effects of these drugs. Also the drug naloxone will reverse the effects of fentanyl. Also taking fentanyl during labour may depress breathing in the new born infant.

Larger doses of fentanyl produce a deep state of pain relief accompanied by a marked depression of breathing, this may last into or recur in the early period after an operation. You may therefore be kept in a recovery area after an operation and monitored until your normal spontaneous breathing has resumed.

Fentanyl may affect your ability to drive or to operate machinery, if you are discharged soon after receiving fentanyl and plan to resume these activities, ask your doctor when it will be safe to resume these activities.

Tell your doctor if you are pregnant, or think you may be pregnant or if you are breast feeding before being given fentanyl.

Dose

Your doctor will inject Fentanyl Injection into a vein or into a muscle.

Adults

Your doctor will calculate the best dosage for you based on the severity of pain and the length of pain relief required. Initially 0.5 to 4 ml (25 - 200 µg) injected into a vein, followed by 0.5 - 2 ml (25 - 100 µg) as required will provide about 10 to 20 minutes relief of mild pain, prior to minor surgery.

Whilst injection of 10 ml (500 µg) into a vein, should provide moderate pain relief for about 1 hour.

When breathing is artificially assisted, the initial dose can be increased up to a maximum of 70 ml (3500 µg), followed by 2 - 4 ml (100 - 200 µg) as required.

Elderly

It is important that the dosage is reduced in the elderly.

Children

The doctor will calculate the best dosage based on the child's weight severity of pain and length of pain relief required. The initial dose being 0.02 - 0.1 ml per kilogram (1 - 5 µg/kg) body weight followed as required by 0.02 ml per kilogram body weight. If breathing is artificially assisted, the initial dose can be increased up to a maximum of 0.3 ml per kilogram body weight, followed as required by 0.02 - 0.06 ml per kilogram (15 µg/kg) body weight.

Repeated use of fentanyl may lead to drug dependence, with withdrawal symptoms on stopping the drug.

If you think you have been given too much fentanyl or you begin to experience breathing difficulties, dizziness or symptoms of low blood pressure and a slower heartbeat, tell your doctor immediately or seek medical assistance.

Large doses of fentanyl will significantly and quickly reduce your rate of breathing. You may require artificial assistance to help you breathe and prevent you going into shock. Your doctor may administer other drugs such as naloxone hydrochloride to help you breathe and prevent you going into a coma or atropine to help increase your heartrate.

Side effects

In common with other potent analgesic drugs, the commonest serious undesirable effects with fentanyl are slowness of the heart, depressed breathing and muscle stiffness. Side effects which may occur include nausea, vomiting, breathing difficulties, allergic reactions, a slow heartrate and temporarily reduced blood pressure. Sweating, hiccups and spasm of Sphincter of Oddi are further side-effects which have been observed after the application of fentanyl.

Storing

This product has an expiry date on the ampoule label. The doctor or nurse will check that the product has not passed this date. Any product that has passed this date must be returned to a pharmacist or doctor for safe disposal. If only part of the solution is used, the remainder should be discarded. If the solution appears strongly coloured, it should not be used. Keep ampoules in the outer carton, in order to protect from light. Keep out of reach and sight of children. This is a potent drug which should be stored carefully.

Leaflet revised: September 2005

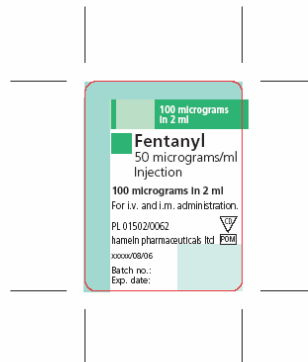
Product licence number: 01502/0062

hameln pharmaceuticals ltd
Gloucester
UK

XXXXXX/41/04

**FENTANYL 50 MICROGRAM/ML INJECTION
PL 01502/0062**

2ml ampoule Label

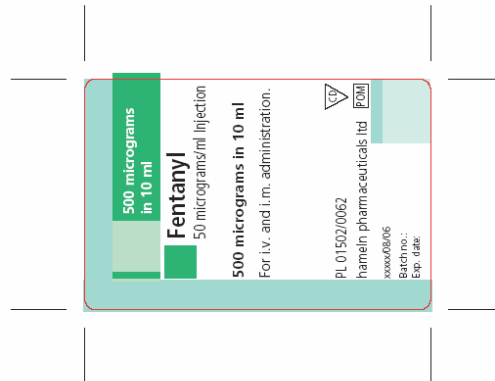



 <p>hameln pharma plus gmbh Langes Feld 13, 31789 Hameln Tel.: 05151/581-0 Fax: 05151/581-501 www.hm-ph.com</p>	
Bearbeitungs-Nr:	2004-353-01
Artikel-Versions-Nr:	xxxxx/08/06
Version vom:	23 / 02 / 2006
Erstellt durch:	Simone Kühl
Unterschrift:	
Geprüft durch / am:	
Unterschrift:	
Kunde:	hameln pharmaceuticals ltd
Land:	England
Sprache PM:	englisch
Wirkstoff:	Fentanyl 50 mcg/ml
Packmittel-Art:	AHETK
Groesse:	36 x 27 mm
Software:	Adobe Illustrator 10
Schriften:	Frutiger light, bold
Farben:	schwarz, P 7482 C
To do:	Kürzel / Datum + Unterschrift
Korrekturen einarbeiten	
PDF-Datei erstellen	
Druckreif	

MHRA UKPAR PL 01502/0062

Fentanyl 50 microgram/ml Injection

10ml ampoule Label




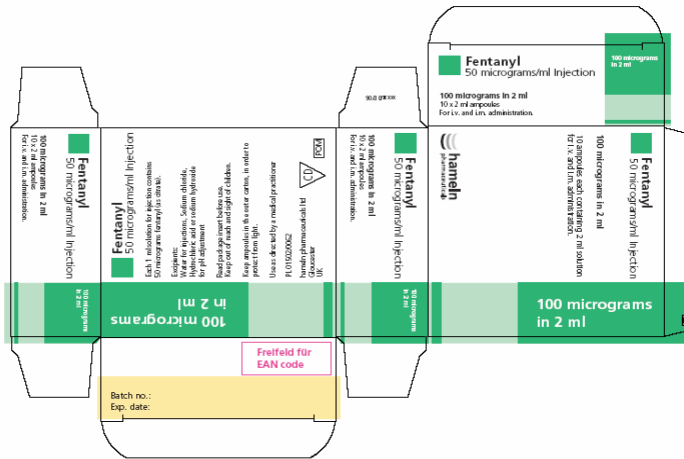
 hameln pharma plus	
hameln pharma plus gmbh Langes Feld 13, 31789 Hameln Tel.: 05151/581-0 Fax: 05151/581-501 www.hm-ph.com	
Bearbeitungs-Nr:	2004-355-01
Artikel-Versions-Nr:	xxxxx/08/06
Version vom:	23 / 02 / 2006
Erstellt durch:	Simone Kühl
Unterschrift:	
Geprüft durch / am:	
Unterschrift:	
Kunde:	hameln pharmaceuticals ltd
Land:	England
Sprache PM:	englisch
Wirkstoff:	Fentanyl 50 mcg/ml
Packmittel-Art:	AHETK
Groesse:	60 x 40 mm
Software:	Adobe Illustrator 10
Schriften:	Frutiger light, bold
Farben:	schwarz, P 7482 C
To do:	Kürzel / Datum + Unterschrift
Korrekturen einarbeiten	
PDF-Datei erstellen	
Druckreif	

MHRA UKPAR PL 01502/0062

Fentanyl 50 microgram/ml Injection

2ml carton label

	
hameln pharma plus gmbh Langes Feld 13, 31789 Hameln Tel.: 0515158110 Fax: 05151581501 www.hm-ph.com	
Bearbeitungs-Nr:	2004-354-02
Artikel-Versions-Nr:	xxxxx/08/06
Version vom:	23 / 02 / 2006
Erstellt durch:	Simone Kühn / A.-C. Suhr
Unterschrift:	
Gepreift durch / am:	
Unterschrift:	
Kunde:	hameln pharmaceuticals ltd
Land:	England
Sprache PM:	englisch
Wirkstoff:	Fentanyl 50 mcg/ml
Packmittel-Art:	FS
Größe:	80 x 31 x 76 mm
Software:	Adobe Illustrator 10
Schriften:	Frutiger light, bold
Farben:	schwarz, P 7482 C
To do:	Kürzel / Datum + Unterschrift
Korrekturen einarbeiten	
PDF-Datei erstellen	
Druckreif	



10ml carton label

	
hameln pharma plus gmbh Langes Feld 13, 31789 Hameln Tel.: 05151581-0 Fax: 05151581-501 www.hmp-ph.com	
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Unterschrift:	
Geprüft durch / am:	
Unterschrift:	
Kunde:	hameln pharmaceuticals ltd
Land:	England
Sprache PM:	englisch
Wirkstoff:	Fentanyl 50 mcg/ml
Packmittel-Art:	FS
Größe:	105 x 25 x 116 mm
Software:	Adobe Illustrator 10
Schriften:	Frutiger light, bold
Farben:	schwarz, P 7482 C
To do:	Kürzel / Datum + Unterschrift
Korrekturen einarbeiten	
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Druckreif	

