FINAL PRINTED PACKAGE INSERT

SCHEDULING STATUS

Schedule 6

PROPRIETARY NAME (and dosage form)

SUFENTA® 2 ml injection.
SUFENTA® 10 ml injection.

COMPOSITION

Each ml contains sufentanil citrate 0,0075 mg equivalent to 0,005 mg of sufentanil base and 9,0 mg sodium chloride in water for injection.

PHARMACOLOGICAL CLASSIFICATION

A.2.9 Central nervous system depressants. Narcotic analgesics.

PHARMACOLOGICAL ACTION

SUFENTA injection is an opioid analgesic with hypnotic properties. Intravenous SUFENTA produces a dose-related attenuation of catecholamine release, particularly noradrenaline.

The pharmacokinetics of intravenous SUFENTA can be described as a three-compartment model with an average distribution time of 0,72 minutes, a redistribution time of 13,7 minutes and an elimination half-life of 148 minutes. Plasma protein binding is approximately 92,5 %, and 80 % of the administered dose is excreted in 24 hours. The liver and intestine are the major sites of biotransformation.

SUFENTA has an immediate onset of action. A dose dependent attenuation of the sympathetic response to surgical stress has been demonstrated at intravenous doses of 8 - 30 µg/kg.

Peak plasma concentrations of sufentanil administered epidurally are reached within 10 minutes and are 4 - 6 times lower than those after intravenous administration. The addition of adrenaline (50 - 75 µg) further reduces the initial fast absorption by 25 - 50 %.

INDICATIONS

SUFENTA administered intravenously is indicated as an analgesic adjunct in the maintenance of balanced general anaesthesia in surgical procedures requiring endotracheal intubation and ventilation.

SUFENTA administered by epidural route is indicated for:

- The postoperative management of pain following general surgery, thoracic or orthopaedic procedures and caesarean sections.
- As an analgesic adjunct to epidural bupivacaine with or without adrenaline during labour and vaginal deliveries.

CONTRA-INDICATIONS

SUFENTA is contra-indicated in patients with a known intolerance to the medicine or to morphinomimetics in general.

Intravenous use in labour or before clamping of the cord during caesarian section is not recommended due to the possibility of respiratory depression in the newborn infant. This is in contrast to the epidural use in labour, during which sufentanil in doses up to 30 µg does not influence the condition of the mother or the newborn. See Side-effects and Special Precautions and Pregnancy and lactation sections.

Epidural SUFENTA should not be given in the presence of severe haemorrhage or shock, septicaemia, infection at the injection site, disturbances in blood morphology and/or anticoagulant therapy or other concomitant therapy or medical conditions which could contra-indicate the technique of epidural administration.

INTERACTIONS

Barbiturates, benzodiazepines, neuroleptics, halogenic gases and other non-selective central nervous system depressants (e.g. alcohol), may potentiate the respiratory depressive effects of SUFENTA. When patients have received central nervous system depressants, the dose of SUFENTA required will be less than usual. Likewise, following the administration of SUFENTA, the dose of other central nervous system depressants should be reduced.

Sufentanil is metabolised mainly via the human cytochrome P450 3A4 enzyme. However, no *in-vivo* inhibition by erythromycin (a known cytochrome P450 3A4 enzyme inhibitor) has been observed.

Although clinical data are lacking, *in-vitro* data suggest that other potent cytochrome P450 3A4 enzyme inhibitors (eg. fluconazole, ketoconazole, itraconazole, ritonavir, diltiazem and cimetidine) may inhibit the metabolism of sufentanil. This could increase the risk of prolonged or delayed respiratory depression. The concomitant use of such drugs requires special patient care and observation; in particular, it may be necessary to lower the dose of SUFENTA.

Mono-amine oxidase (MOA) inhibitors must be discontinued 2 weeks prior to the administration of SUFENTA.

PREGNANCY AND LACTATION

Safety in pregnancy and lactation has not been established.

SUFENTA added to epidural bupivacaine in total doses up to 30 µg has no detrimental effect on the mother or the newborn, but intravenous use is not recommended in labour.

An antidote for the child should always be at hand, however.

It is not known whether this drug is excreted in human milk. Caution should be exercised when SUFENTA is administered to a nursing woman.

DOSAGE AND DIRECTIONS FOR USE

The dosage of SUFENTA should be individualised. Factors to be considered in determining the dose are age, body mass, physical status, underlying pathological condition, use of other medicines, type of anaesthesia to be used and duration of the surgical procedure.

In obese patients, the dosage of SUFENTA should be determined on the basis of standard body mass.

Compatibility:
If desired, SUFENTA may be mixed with sodium chloride or glucose intravenous infusions. Such dilutions are compatible with plastic infusion sets. They should be used within 24 hours of preparation.

ADMINISTRATION AS AN ANALGESIC ADJUNCT TO NITROUS OXIDE/OXYGEN
Droperidol may be given to reduce the incidence of nausea and vomiting.

INTRAVENOUS ADMINISTRATION - ADULTS:
Initial dose: 1 - 8 µg/kg administered with nitrous oxide/oxygen. The duration of action is 1 - 8 hours depending on the dose.

Maintenance dose: 0,1 - 0,5 µg/kg as needed when movement and/or changes in vital signs indicate surgical stress or lightening of analgesia.

Supplemental dosages should be individualised, and adjusted to the remaining operative time anticipated.

EPIDURAL ADMINISTRATION:

Proper placement of a needle or catheter in the epidural space should be verified before SUFENTA is injected to assure that unintentional intravascular or intrathecal administration does not occur. Unintentional intravascular injection of SUFENTA could result in potentially serious overdose including acute truncal muscular rigidity and apnoea. Unintentional intrathecal injection of the full sufentanil, bupivacaine epidural doses and volume could produce effects of high spinal anaesthesia including prolonged paralysis and delayed recovery. If analgesia is inadequate, the placement and integrity of the catheter should be verified prior to administration of any additional epidural medications. SUFENTA should be administered by slow injection.

With epidural administration, caution should be exercised in the presence of respiratory depression and in the presence of foetal distress.

Epidural administration requires that the patient should be in a high care environment with continuous supervision.

The patient should be closely monitored for at least 2 hours after each dose, as early respiratory depression may occur.

Postoperative management of pain - Adults:
An initial dose of 30 - 50 µg may be expected to provide adequate pain relief for up to 4 - 6 hours. Additional boli of 25 µg may be administered if there is evidence of lightening of analgesia. There should be a minimum interval of 1 hour between doses.

Analgesic adjunct during labour and vaginal deliveries:
The recommended dosage is 10 - 15 µg administered with 10 ml bupivacaine 0,125 % with or without adrenaline. SUFENTA and bupivacaine should be mixed together before

administration. Doses can be repeated twice (for a total of three doses) at not less than one hour intervals until delivery.

Epidural use in children:
The safety and efficacy of epidural SUFENTA in paediatric patients has not been established.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS

Clinical Trial Data

The safety of SUFENTA was evaluated in 650 sufentanil-treated subjects who participated in 6 clinical trials. Of these, 78 subjects participated in 2 trials of sufentanil administered intravenously as an anaesthetic agent for induction and maintenance of anaesthesia in subjects undergoing major surgical procedures (coronary artery bypass or open-heart). The remaining 572 subjects participated in 4 trials of epidural sufentanil administered as a postoperative analgesic or as an analgesic adjunct to epidural bupivacaine during labour and vaginal deliveries. These subjects took at least 1 dose of sufentanil and provided safety data. Adverse Drug Reactions (ADRs) that were reported for ≥1% of sufentanil-treated subjects in these trials are shown in Table 1.

Table 1. Adverse Drug Reactions Reported by ≥1% of Sufentanil-treated Subjects in 6 Clinical Trials of Sufentanil

System / Organ Class Adverse Reaction	Sufentanil (n=650) %
Nervous System Disorders	
Sedation	19.5
Tremor neonatal	4.5
Dizziness	1.4
Headache	1.4
Cardiac Disorders	
Tachycardia	1.8
Vascular Disorders	
Hypertension	4.9
Hypotension	3.2
Pallor	1.4
Respiratory, Thoracic and Mediastinal Disorders	
Cyanosis neonatal	2.0
Gastrointestinal Disorders	
Nausea	9.8
Vomiting	5.7
Skin and Subcutaneous Tissue Disorders	
Pruritus	15.2
Skin discolouration	3.1

Table 1. Adverse Drug Reactions Reported by ≥1% of Sufentanil-treated Subjects in 6 Clinical Trials of Sufentanil

Musculoskeletal and Connective Tissue Disorders	
Muscle twitching	2.0
Renal and Urinary Disorders	
Urinary retention	3.2
Urinary incontinence	1.5
General Disorders and Administration Site Conditions	
Pyrexia	1.7

Additional ADRs that occurred in <1% of sufentanil-treated subjects in the 6 clinical trials are listed in Table 2.

Table 2. Adverse Drug Reactions Reported by <1% of Sufentanil-treated Subjects in 6 Clinical Trials of Sufentanil

System / Organ Class Adverse Reaction
Infection and Infestation
Rhinitis
Immune System Disorders
Hypersensitivity
Psychiatric Disorders
Apathy
Nervousness
Nervous System Disorders
Ataxia
Dyskinesia neonatal
Dystonia
Hyperreflexia
Hypertonia
Hypokinesia neonatal
Somnolence
Eye Disorders
Visual disturbance

Table 2. Adverse Drug Reactions Reported by <1% of Sufentanil-treated Subjects in 6 Clinical Trials of Sufentanil

Cardiac Disorders
- Arrhythmia*
- Electrocardiogram abnormal
- Atrioventricular block
- Bradycardia
- Cyanosis

Respiratory, Thoracic and Mediastinal Disorders
- Bronchospasm
- Cough
- Dysphonia
- Hiccups
- Hypoventilation
- Respiratory disorder

Skin and Subcutaneous Tissue Disorders
- Dermatitis allergic*
- Dry skin
- Hyperhidrosis
- Rash
- Rash neonatal

Musculoskeletal and Connective Tissue Disorders
- Back pain
- Hypotonia neonatal
- Muscle rigidity*

General Disorders and Administration Site Conditions
- Chills
- Hypothermia
- Body temperature decreased
- Injection site pain*
- Injection site reaction
- Pain

Investigations
- Body temperature increased

*ADRs reported from only the trials of sufentanil administered intravenously as an anaesthetic agent.

Postmarketing Data

Adverse drug reactions first identified during postmarketing experience with sufentanil citrate are included in Table 3.

Table 3. Adverse Drug Reactions Identified During Postmarketing Experience with SUFENTA

Immune System Disorders
Anaphylactic shock
Anaphylactic reaction
Anaphylactoid reaction
Nervous System Disorders
Coma
Convulsion
Muscle contractions involuntary
Eye Disorders
Miosis
Cardiac Disorders
Cardiac arrest (also see Special Precautions)
Vascular Disorders
Shock
Respiratory, Thoracic and Mediastinal Disorders
Respiratory arrest
Apnoea
Respiratory depression
Pulmonary oedema
Laryngospasm
(also see Contraindications and Special Precautions)
Skin and Subcutaneous Tissue Disorders
Erythema
Musculoskeletal and Connective Tissue Disorders
Muscle spasms (also see Special Precautions)

Special Precautions:

Respiratory depression is dose related and can be reversed by the specific narcotic antagonist, naloxone, but a repeated dose of the antagonist may be necessary because the duration of respiratory depression may last longer than the duration of action of the opioid antagonist. Marked respiratory depression accompanies profound analgesia. It can persist in the post-operative period, and if SUFENTA has been given intravenously it can recur. Therefore, patients should remain under appropriate surveillance. Resuscitation equipment and narcotic antagonists should be readily available. Hyperventilation during anaesthesia may alter the patient's response to CO_2 thus affecting respiration post-operatively.

The incidence and severity of early respiratory depression with epidural administration may be less if adrenaline is added.

Vital signs should be monitored routinely.

Induction of muscle rigidity, which may also involve the thoracic respiratory muscles, can occur but the risk may be reduced if intravenous injections are administered slowly. A neuromuscular blocking agent compatible with the patient's condition may be administered prophylactically to prevent muscle rigidity or to induce muscle relaxation after rigidity occurs.

Because of its weak cholinergic activity, SUFENTA should be used with caution in patients with cardiac arrhythmias.

Bradycardia and possibly cardiac arrest can occur if the patient has received an insufficient amount of anticholinergic or when SUFENTA 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.

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

It is recommended to reduce the dosage in elderly and debilitated patients. Opioids 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.

Effects on driving ability and use of machinery:
Patients should only drive or operate a machine if sufficient time has lapsed after administration of SUFENTA.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Signs and Symptoms:
An overdose of SUFENTA manifests itself as an extension of its pharmacological actions. Depending on the individual sensitivity, the clinical picture is determined primarily by the degree of respiratory depression, which varies from bradypnoea to apnoea.

Treatment:
In the presence of hypoventilation or apnoea, oxygen should be administered and respiration should be assisted or controlled as indicated. A specific narcotic antagonist such as naloxone, should be used as indicated to control respiratory depression. This does not preclude the use of more immediate countermeasures. The respiratory depression may last longer than the effect of the antagonist; additional doses of the latter may therefore be required.

If depressed respiration is associated with muscular rigidity, an intravenous neuromuscular blocking agent might be required to facilitate assisted or controlled respiration.

The patient should be carefully observed, body warmth and adequate fluid intake should be maintained. If hypotension is severe or if it persists, the possibility of hypovolaemia should be considered, and if present, it should be controlled with appropriate parenteral fluid administration.

IDENTIFICATION

A clear colourless solution. Free from visible foreign material.

PRESENTATION

SUFENTA injections are supplied in cartons containing: 5 x 2 ml and 5 x 10 ml ampoules.

STORAGE INSTRUCTIONS

Store below 25 ^{o}C. Protect from light.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

2 ml - T/2.9/240
10 ml - T/2.9/241

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE REGISTRATION CERTIFICATE

Piramal Critical Care South Africa (Pty) Ltd
Office 2, Ground Floor, Kiepersol House,
300 Acacia Road, Darrenwood, 2194

DATE OF PUBLICATION OF THIS PACKAGE INSERT

02 September 2008

SKEDULERINGSTATUS

Skedule 6

EIENDOMSNAAM (en doseervorm)

SUFENTA® 2 ml inspuiting.
SUFENTA® 10 ml inspuiting.

SAMESTELLING

Elke ml bevat sufentanielsitraat 0,0075 mg gelykstaande aan 0,005 mg sufentanielbasis en 9,0 mg natriumchloried in water vir inspuiting.

FARMAKOLOGIESE KLASSIFIKASIE

A.2.9 Depressante van die sentrale senuweestelsel. Narkotiese analgetika.

FARMAKOLOGIESE WERKING

SUFENTA inspuiting is 'n narkotiese analgetikum met hipnotiese eienskappe. Binneaarse SUFENTA veroorsaak 'n dosisverwante vermindering van katesjolamien-vrystelling, veral noradrenalien.

Die farmakokinetika van intraveneuse SUFENTA kan beskryf word as 'n driekompartement model met 'n gemiddelde distribusietyd van 0,72 minute, 'n herdistribusietyd van 13,7 minute en 'n eliminasie halfleeftyd van 148 minute. Plasmaproteïenbinding is ongeveer 92,5 %, en 80 % van die toegediende dosis word binne 24 uur uitgeskei. Die lewer en ingewande is die belangrikste organe vir biotransformasie.

SUFENTA het 'n onmiddellike werking. 'n Dosis afhanklike verandering van die simpatiese effek as gevolg van chirurgiese spanning is aangetoon met binneaarse dosisse van 8 - 30 µg/kg.

Piek plasma konsentrasies van sufentaniel wanneer epiduraal toegedien word bereik binne 10 minute en is 4 - 6 keer laer as dié van binneaarse toediening. Die toediening van adrenalien (50 - 75 µg) verminder verder die aanvanklike absorpsie met 25 - 50 %.

INDIKASIES

Intraveneustoegediende SUFENTA word aangedui as 'n analgetiese toevoeging by die instandhouding van gebalanseerde algemene narkose by chirurgiese prosedures waar endotrageale intubering en meganiese ventilasie nodig is.

Epiduraaltoegediende SUFENTA, word aangedui vir:
- Die postoperatiewe behandeling van pyn as gevolg van algemene chirurgie, toraks of ortopediese prosedures en keisersnee.
- As 'n analgetiese toevoeging tesame met epidurale bupivakaïen met of sonder adrenalien tydens kraam en vaginale verlossings.

KONTRA-INDIKASIES

SUFENTA word teenaangedui by pasiënte met 'n onverdraagsaamheid vir dié middel of vir morfinomimetiese middels in die algemeen.

Intraveneuse gebruik gedurende kraam of voor afklamping van die naelstring gedurende ŉ keisersnee word weens die moontlikheid van respiratoriese onderdrukking in die pasgebore baba, nie aanbeveel nie. Dit is in kontras met die epidurale gebruik in kraam, waartydens sufentaniel in dosisse van tot 30 µg nie die kondisie van die moeder of die pasgebore baba beïnvloed nie.(Kyk na "Newe-effekte en Spesiale voorsorgmaatreëls" en "Swangerskap en laktasie")

Epidurale SUFENTA behoort nie toegedien te word in die teenwoordigheid van erge bloeding of skok, septisemie, infeksie by die toedieningsarea, versteuring in bloed morfologie en/of antistol terapie of ander gelyktydige behandeling of mediese toestande wat die tegniek van epidurale toediening kontra-indikeer nie.

INTERAKSIES

Barbiturate, bensodiasepiene, neuroleptika, halogeengasse en ander nie-selektiewe sentrale senuweestelsel depressante (bv. alkohol) mag die respiratoriese onderdrukkende effekte van SUFENTA potensieer. Wanneer pasiënte sentrale senuweestelseldepressante ontvang het, sal die dosis van SUFENTA wat benodig word, minder as gewoonlik wees. Insgelyks, na die toediening van SUFENTA, behoort die dosis van die ander sentrale senuweestelseldepressante verminder te word.

Sufentaniel word hoofsaaklik deur die menslike sitochroom P450 3A4 ensiem gemetaboliseer. Geen *in-vivo* inhibisie deur eritromisien ('n bekende sitochroom P450 3A4 ensiem inhibeerder) is egter al waargeneem nie.

Alhoewel daar 'n gebrek is aan kliniese data, dui *in-vitro* data daarop dat ander kragtige sitochroom P450 3A4 ensiem inhibeerders (bv. flukonasool, ketokonasool, itrakonasool, ritonavir, diltiasem en simetidien) die metabolisme van sufentaniel kan inhibeer. Dit kan die risiko van verlengde of vertraagde respiratoriese onderdrukking verhoog. Die gesamentlike gebruik van sulke geneesmiddels vereis spesiale pasiëntsorg en observasie, in besonder mag dit nodig wees om die SUFENTA dosis te verminder.

Mono-amienoksidaseremmers (MAO-remmers) moet 2 weke voor die toediening van SUFENTA gestaak word.

SWANGERSKAP EN LAKTASIE

Veiligheid tydens swangerskap en laktasie is nog nie vasgestel nie.

SUFENTA, bygevoeg tot epidurale bupivakaïen in totale dosisse van tot soveel as 30 µg, het geen nadelige effek op die moeder of die pasgebore baba nie. Die intraveneuse gebruik word egter nie gedurende kraam aanbeveel nie.

ŉ Teenmiddel vir die kind behoort egter altyd byderhand te wees. Dit is nie bekend of hierdie middel in moedersmelk uitgeskei word nie. Sorg behoort aan die dag gelê te word wanneer SUFENTA aan ŉ sogende moeder toegedien word.

DOSIS EN GEBRUIKSAANWYSINGS

Die dosering van SUFENTA behoort geïndividualiseer te word. Faktore wat in ag geneem behoort te word is ouderdom, liggaamsmassa, fisiese toestand, onderliggende patologiese toestand, die gebruik van ander middels, tipe narkose wat gebruik gaan word en die soort en duur van die chirurgiese ingreep.

By vetsugtige pasiënte behoort die dosis van SUFENTA vasgestel te word op grond van die standaard liggaamsmassa.

Verenigbaarheid:
Indien nodig, kan SUFENTA met 'n natriumchloried of glukose intraveneuse infusie gemeng word. Sulke verdunnings is verenigbaar met plastiek infusie toestelle. Dit moet egter binne 24 uur na voorbereiding gebruik word.

TOEDIENING AS ANALGETIESE TOEVOEGING TOT STIKSTOFMONOKSIED/ SUURSTOF
Droperidol mag gegee word om die insidensie van naarheid en braking te verminder.

BINNEAARSE TOEDIENING - VOLWASSENES:
Aanvangsdosis: 1 - 8 µg/kg toegedien met stikstofmonoksied/suurstof. Die effek duur 1 - 8 ure, afhangende van die dosis.

Instandhoudingsdosis: 0,1 - 0,5 µg/kg soos nodig wanneer beweging en/of veranderings in vitale tekens dui op chirurgiese spanning of vermindering van analgesie.

Supplementêre dosisse behoort geïndividualiseer en aangepas te word na gelang van die verwagte duur van die chirurgiese ingreep.

EPIDURALE TOEDIENING:

Behoorlike plasing van 'n naald of kateter in die epidurale spasie behoort bevestig te word voordat SUFENTA ingespuit word om te verseker dat nie-intensionele intravaskulêre of intratekale toediening nie plaasvind nie. Die nie-intensionele intravaskulêre toediening van SUFENTA kan moontlike ernstige oordosering insluitende akute romp spierrigiditeit en apnee tot gevolg hê. Nie-intensionele intratekale toediening van die algehele sufentaniel, bupivakaïen epidurale dosering en volume, kan die effek van hoë spinale verdowing, insluitende verlengde verlamming en vertraagde herstel tot gevolg hê. Indien die verdowing nie voldoende is nie, moet die korrekte plasing en volledigheid van die kateter bevestig word, voordat enige addisionele middels toegedien word. SUFENTA moet toegedien word deur stadige inspuiting.

Daar behoort met omsigtigheid te werk gegaan te word met epidurale toediening in die teenwoordigheid van respiratoriese onderdrukking en in die teenwoordigheid van fetale krisis.

Epidurale toediening vereis dat die pasiënt in 'n hoë sorg omgewing met aaneenlopende toesig behoort te wees.

Die pasiënt moet behoorlik gemonitor word vir 2 ure na elke dosis omdat vroeë respiratoriese onderdrukking kan plaasvind.

Postoperatiewe behandeling van pyn - Volwassenes:
'n Aanvanklike dosis van 30 - 50 µg behoort genoegsame pynverligting te verskaf vir tot 4 - 6 ure. Verdere boli van 25 µg mag toegedien word indien daar tekens is van vermindering van analgesie. Daar behoort 'n minimum tussenpose van 1 uur tussen dosisse te wees.

Analgetiese toevoeging tydens kraam en vaginale verlossing:

Die aanbevole dosis is 10 - 15 µg toegedien gelyktydig met 10 ml bupivakaïen 0,125 % tesame met of sonder adrenalien. SUFENTA en bupivakaïen moet gemeng word alvorens toediening. Die dosering mag tweekeer herhaal word (vir 'n totaal van drie doserings) met nie minder as een uurlikse tussenposes nie, tot verlossing plaasgevind het .

Epidurale gebruik in kinders:
Die veiligheid en die effektiwiteit van SUFENTA in pediatriese pasiënte is nog nie vasgestel nie.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS

Kliniese Proewe - Data

Die veiligheid van SUFENTA is by 650 behandelde proefpersone wat aan 6 kliniese proewe deelgeneem het, geëvalueer. Van hierdie proefpersone het 78 aan 2 proewe deelgeneem waar sufentaniel intraveneus as anestetikum vir induksie en instandhouding van anestesie aan proefpersone wat ernstige chirurgiese prosedures (hartomleiding of ope hart) ondergaan het, toegedien is. Die oorblywende 572 pasiënte het aan 4 proewe met epidurale sufentaniel deelgeneem, waar dit as post-operatiewe analgetikum, of as analgetiese aanvulling tot epidurale bupivakaïen tydens kraam en vaginale bevallings, toegedien is. Hierdie proefpersone het ten minste 1 dosis sufentaniel ontvang en het die veiligheidsdata voorsien. Ongunstige Geneesmiddelreaksies (OGRs) wat by ≥1 % sufentaniel-behandelde proefpersone met hierdie proewe aangemeld is, word in Tabel 1 weergegee.

Tabel 1. Ongunstige Geneesmiddelreaksies aangemeld deur ≥1 % Sufentaniel-behandelde proefpersone in 6 Kliniese Proewe met Sufentaniel

Sisteem / Orgaanklas Ongunstige Reaksie	Sufentaniel (n=650) %
Senuweestelselsiektes	
Sedasie	19.5
Tremor - neonataal	4.5
Duiseligheid	1.4
Hoofpyn	1.4
Hartsiektes	
Tagikardie	1.8
Vaskulêre siektes	
Hipertensie	4.9
Hipotensie	3.2
Bleekheid	1.4
Respiratoriese, bors- en Mediastinumsiektes	
Sianose – neonatal	2.0
Gastroïntestinale siektes	
Naarheid	9.8
Braking	5.7

Tabel 1. Ongunstige Geneesmiddelreaksies aangemeld deur ≥1 % Sufentaniel-behandelde proefpersone in 6 Kliniese Proewe met Sufentaniel

Vel- en subkutane weefselsiektes	
Pruritus	15.2
Vel verkleuring	3.1
Skeletspier- en bindweefselsiektes	
Spierkramp	2.0
Nier- en urienwegsiektes	
Urinêre retensie	3.2
Urinêre inkontinensie	1.5
Algemene siektes en siektes by die gebied van toediening	
Pireksie	1.7

Addisionele OGRs wat by <1 % sufentaniel-behandelde proefpersone in 6 kliniese proewe voorgekom het, word in Tabel 2 weergegee.

Tabel 2. Ongunstige Geneesmiddelreaksies aangemeld deur <1 % Sufentaniel-behandelde proefpersone in 6 Kliniese Proewe met Sufentaniel

Sisteem / Orgaanklas Ongunstige Reaksie
Infeksie en infestasie
Rinitis
Immuunstelselsiekte
Hipersensitiwiteit
Psigiatriese siektes
Apatie
Senuweeagtigheid
Senuweestelselsiektes
Ataksie
Diskinesie - neonataal
Distonie
Hiper refleksie
Hipertonie
Hipokinese - neonataal
Slaapsug
Oogsiektes
Visuele versteurings

Tabel 2. Ongunstige Geneesmiddelreaksies aangemeld deur <1 % Sufentaniel-behandelde proefpersone in 6 Kliniese Proewe met Sufentaniel

Hartsiektes
Artimie*
Elektrokardiogram abnormaal
Atrioventrikulêre blok
Bradikardie
Sianose
Respiratoriese, bors- en mediastinumsiektes
Brongospasma
Hoes
Disfonie
Hik
Hipoventilasie
Respiratoriese siekte
Vel- en onderhuidse weefselsiektes
Dermatitis allergies*
Droë vel
Hiperhidrose
Uitslag
Uitslag – neonatal
Skeletspier- en bindweefselsiektes
Rugpyn
Hipotonie - neonataal
Spierstyfheid *
Algemene siektes en siektes by die gebied van toediening
Koue rillings
Hipotermie
Afname in liggaamstemperatuur
Pyn by plek van inspuiting *
Reaksie by plek van inspuiting
Pyn
Ondersoeke
Verhoogde liggaamstemperatuur

*OGRs slegs by dié proewe waar sufentaniel intraveneus as anestetiese middel toegedien is, aangemeld

Post-bemarkingsdata

Ongunstige geneesmiddelreaksies wat eers na intrede in die mark met sufentanielsitraat ervaar is, word in Tabel 3 weergegee.

Tabel 3. Ongunstige Geneesmiddelreaksies na intrede in die mark met SUFENTA ervaar

Immuunstelselsiektes
Anafilaktiese skok
Anafilaktiese reaksie
Anafilaktoïede reaksie
Senuweestelselsiektes
Koma
Konvulsie
Spierkontraksies – onwillekeurig
Oogsiektes
Miose
Hartsiektes
Hartstilstand (kyk ook Spesiale voorsorgmaatreëls)
Vaskulêre siektes
Skok
Respiratoriese-, bors- en mediastinumsiektes
Respiratoriese stilstand
Apnee
Respiratoriese onderdrukking
Pulmonêre edeem
Laringospasma
(kyk ook Kontra-indikasies en Spesiale voorsorgmaatreëls)
Vel- en subkutane weefselsiektes
Eriteem
Skeletspier- en bindweefselsiektes
Spier spasmas (kyk ook Spesiale voorsorgmaatreëls)

Voorsorgmaatreëls

Respiratoriese onderdrukking is dosisverwant en kan omgekeer word deur die spesifieke narkotiese antagonis, naloksoon, 'n herhaalde dosis van die antagonis mag egter nodig wees aangesien die tydsduur van die respiratoriese onderdrukking langer mag wees as die werkingsduur van die opioïedantagonis. Aansienlike respiratoriese onderdrukking vergesel deur uitgesproke en voldoende analgesie. Dit kan voortduur in die post-operatiewe periode, en indien SUFENTA intraveneus toegedien word, mag dit weer terugkeer. Pasiënte behoort derhalwe onder toepaslike waarneming te bly. Toerusting om asemhaling kunsmatig te ondersteun en narkotiese antagoniste moet geredelik beskikbaar wees. Hiperventilasie gedurende narkose mag die pasiënt se reaksie op CO_2 verander en mag dus asemhaling in die post-operatiewe periode beïnvloed.

Die voorkoms en hewigheid van vroeë respiratoriese onderdrukking met epidurale toediening mag minder wees indien adrenalien bygevoeg word.

Vitale tekens moet as roetine gemonitor word.

Induksie van spierrigiditeit wat ook die toraksspiere mag insluit, kan voorkom, maar die risiko kan verminder word indien die intraveneuse inspuitings stadig toegedien word. 'n Neuromuskulêre blokkeermiddel wat verenigbaar is met die pasiënt se toestand mag profilakties toegedien word om spierrigiditeit te voorkom of om spierverslapping te induseer nadat rigiditeit voorgekom het.

As gevolg van die swak cholinergiese werking, behoort SUFENTA met versigtigheid gebruik te word by pasiënte met hartaritmieë.

Bradikardie en moontlike hartstilstand mag voorkom indien die pasiënt 'n onvoldoende hoeveelheid anticholinergikum ontvang het, of wanneer SUFENTA gekombineer is met nie-vagolitiese spierverslappers. Bradikardie kan met atropien behandel word.

Opioïede mag hipertensie induseer, veral in hipovolemiese pasiënte. Toepaslike maatreëls moet geneem word om 'n stabiele arteriële druk te handhaaf.

Die gebruik van spoedige bolus inspuitings van opioïede behoort vermy te word in pasiënte met ontoereikende intraserebrale funksionering; in sulke pasiënte het die verbygaande verlaging in die gemiddelde arteriële druk somtyds gepaard gegaan met 'n kortstondige afname van die serebrale perfusie druk.

Dit word aanbeveel dat die dosering in bejaardes en verswakte pasiënte verlaag word. Opioïede behoort met omsigtigheid getitreer te word in pasiënte met enige van die volgende siektetoestande: onbeheerde hipotiroïedisme, pulmonêre siekte, verminderde respiratoriese reserwe, alkoholisme, verswakte hepatiese of renale funksionering. Sulke pasiënte het ook verlengde post-operatiewe monitering nodig.

Effekte op bestuursvermoë en gebruik van masjinerie
Pasiënte behoort slegs te bestuur of masjinerie te hanteer indien voldoende tyd verstryk het na die toediening van SUFENTA.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN

Tekens en Simptome:
Die manifestasies van oordosering met SUFENTA is 'n uitbreiding van sy farmakologiese effekte. Afhangend van die individuele sensitiwiteit, word die kliniese beeld primêr bepaal deur die graad van respiratoriese onderdrukking, wat wissel van bradipnee tot apnee.

Behandeling:
Indien hipoventilasie of apnee voorkom, behoort suurstof toegedien te word en asemhaling ondersteun of gekontroleer te word soos aangedui. 'n Spesifieke narkotiese antagonis, soos naloksoon, behoort gebruik te word soos aangedui om respiratoriese onderdrukking te behandel. Dit sluit nie die gebruik van ander meer onmiddellike teenmaatreëls uit nie. Die respiratoriese onderdrukking mag langer duur as die werking van die antagonis; bykomende dosisse van laasgenoemde mag derhalwe nodig wees.

Indien onderdrukte asemhaling geassosieer word met spierrigiditeit, mag 'n intraveneuse neuromuskulêre middel nodig wees om ondersteunde of gekontroleerde asemhaling te vergemaklik.

Die pasiënt moet sorgvuldig bewaak word; liggaamstemperatuur en voldoende vloeistofinname moet gehandhaaf word. Indien hipotensie voorkom en hewig is of voortduur, behoort die moontlikheid van hipovolemie oorweeg te word, en indien teenwoordig, moet dit met toepaslike parenterale vloeistofterapie behandel word.

IDENTIFIKASIE

'n Helder kleurlose oplossing sonder enige sigbare, vreemde materiaal.

AANBIEDING

SUFENTA inspuitings is beskikbaar in kartonhouers bevattende: 5 x 2 ml and 5 x 10 ml ampulle.

BERGINGSAANWYSINGS

Bewaar benede 25 ºC. Beskerm teen lig.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER

2 ml - T/2.9/240
10 ml - T/2.9/241

NAAM EN BESIGHEIDADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT

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