PACKAGE INSERT

SCHEDULING STATUS

Schedule 6

PROPRIETARY NAME AND DOSAGE FORM

DUROGESIC® 12 µg/h transdermal patch

DUROGESIC® 25 µg/h transdermal patch

DUROGESIC® 50 µg/h transdermal patch

DUROGESIC® 75 µg/h transdermal patch

DUROGESIC® 100 µg/h transdermal patch

COMPOSITION

	DUROGESIC Dose µg/h)	Active Surface Area (cm^2)	Fentanyl Content In Patch (mg)
DUROGESIC	12[1]	5,25	2,1
DUROGESIC	25	10,5	4,2
DUROGESIC	50	21,0	8,4
DUROGESIC	75	31,5	12,6
DUROGESIC	100	42,0	16,8

[1] The lowest dose is designated as 12 µg/h (however, the actual dose is 12,5 µg/h) to distinguish it from 125 µg/h dose that could be prescribed by using multiple patches.

Excipients:

Backing layer: Polyester*/EVA**

Medicine layer: Polyacrylate adhesive

Inks (on backing): Orange/red/green/blue/grey printing ink

Protective liner: Siliconised polyester

* Polyester = Polyethylene terephthalate

**EVA = Ethyl vinyl acetate

PHARMACOLOGICAL CLASSIFICATION

A.2.9 Central nervous system depressants. Other.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Fentanyl is an opioid analgesic, interacting predominantly with the μ-opioid receptor. Its primary actions of therapeutic value are analgesia and sedation. Minimum effective analgesic serum concentrations of fentanyl in opioid-naive patients range from 0,3 - 1,2 ng/mℓ; side effects increase in frequency at serum levels above 2 ng/mℓ. Both the minimum concentration and the concentration at which opioid-related toxicity occurs, rise with increasing patient exposure to the medicine. The rate of development of tolerance varies widely among individuals.

Pharmacokinetic properties

While there is variation in the dose delivered among patients, the normal flux of the individual patch is sufficiently accurate to allow individual titration of dosage for a given patient.
Transdermal fentanyl provides nearly constant systemic delivery of fentanyl during the 72 hours application period. After initial transdermal fentanyl application, serum fentanyl concentrations increase gradually, generally leveling off between 12 and 24 hours and remaining relatively constant for the remainder of the 72 hours application period. Serum fentanyl concentrations attained are proportional to the transdermal fentanyl patch size. After repeated 72 - hour applications, patients reach a steady-state serum concentration that is maintained during subsequent applications of the patch of the same size.

After removal of transdermal fentanyl, serum fentanyl concentrations decline gradually, falling about 50 % in approximately 17 (range: 13 - 22) hours following a 24 - hour application. Following a 72 - hour application, the mean terminal half-life ranges from 20 - 25 hours. Continued absorption of fentanyl

from the skin accounts for a slower disappearance of the medicine from the serum than is seen after an intravenous infusion. Elderly, cachectic or debilitated patients may have reduced clearance of fentanyl and, therefore, the agent may have a greatly prolonged terminal half-life in such patients.

Adjusting for body weight, clearance in paediatric patients was about 20 % higher than that in adults. These findings have been taken into consideration in determining the dosing recommendations for paediatric patients.

Fentanyl is a high clearance medicine and is rapidly and extensively metabolised primarily by CYP3A4 in the liver. Approximately 75 % of fentanyl is excreted in urine mostly as metabolites with less than 10 % representing unchanged medicine. Approximately 9 % of the dose is recovered in the faeces, primarily as metabolites. Mean value for unbound fraction of fentanyl in plasma is estimated to be between 13 and 21 %.

INDICATIONS

DUROGESIC is indicated in the management of chronic intractable pain that requires opioid analgesia, which cannot be managed by lesser means such as paracetamol – opioid combinations, non-steroidal analgesics or as required dosing with short-acting opioids.

CONTRA-INDICATIONS

DUROGESIC is contra-indicated in:

- Pregnancy
- Lactation (See PREGNANCY AND LACTATION)
- Children less than 2 years of age
- Patients with a known hypersensitivity to fentanyl or to the adhesives present in the transdermal patch.
- Concomitant use with CYP3A4 Inhibitors is not recommended unless the patient is closely monitored. Oral ritonavir (one of the most potent CYP3A4 inhibitors) reduced the clearance of IV fentanyl by two thirds (See INTERACTIONS and WARNINGS AND SPECIAL PRECAUTIONS).

WARNINGS AND SPECIAL PRECAUTIONS

DUROGESIC SHOULD NOT BE USED IN THE MANAGEMENT OF ACUTE OR POSTOPERATIVE PAIN SINCE SERIOUS OR LIFE THREATENING HYPOVENTILATION COULD RESULT AND THERE IS NO OPPORTUNITY FOR DOSE TITRATION DURING SHORT TERM USE.

PATIENTS WHO HAVE EXPERIENCED OPIOID TOXICITY SHOULD BE MONITORED FOR AT LEAST 12 TO 24 HOURS AFTER DUROGESIC REMOVAL SINCE SERUM FENTANYL CONCENTRATIONS DECLINE GRADUALLY AND ARE REDUCED BY 50 %, 17 (RANGE: 13 - 22) HOURS LATER.

DUROGESIC SHOULD BE PRESCRIBED ONLY BY PERSONS KNOWLEDGEABLE:

- IN THE CONTINUOUS ADMINISTRATION OF POTENT OPIOIDS
- IN THE MANAGEMENT OF PATIENTS RECEIVING POTENT OPIOIDS FOR TREATMENT OF PAIN
- IN THE DETECTION AND MANAGEMENT OF HYPOVENTILATION INCLUDING THE USE OF OPIOD ANTAGONISTS.

DUROGESIC should be kept out of reach of children before and after use. Do not cut DUROGESIC patches.

Opioid-naïve and not opioid-tolerant states

Use of DUROGESIC transdermal system in the opioid-naïve patient has been associated with very rare cases of significant respiratory depression and/or fatality when used as initial opioid therapy. The potential for serious or life threatening hypoventilation exists even if the lowest dose of DUROGESIC transdermal system is used in initiating therapy in opioid-naïve patients. It is recommended that DUROGESIC be used in patients who have demonstrated opioid tolerance. See DOSAGE AND DIRECTIONS FOR USE: Initial dose selection, Adults and Paediatrics

Respiratory Depression

Some patients may experience significant respiratory depression with DUROGESIC; patients must be observed for these effects. Respiratory depression may persist beyond the removal of the DUROGESIC patch. The incidence of respiratory depression increases as the DUROGESIC dose is increased. Central nervous system active agents may increase the respiratory depression. (see INTERACTIONS).

Chronic Pulmonary Disease

DUROGESIC may have more severe adverse effects in patients with chronic obstructive pulmonary disease, or other pulmonary disease. In such patients, opioids may decrease respiratory drive and increase airway resistance.

Drug Dependence

Tolerance, physical dependence, and psychological dependence may develop upon repeated administration of opioids.

DUROGESIC can be abused in a manner similar to other opioid agonists. Abuse or intentional misuse of DUROGESIC may result in overdose and / or death. Patients at increased risk of opioid abuse may still be appropriately treated with DUROGESIC; however, these patients will require monitoring for signs of misuse, abuse or addiction.

Increased Intracranial Pressure

DUROGESIC should not be used in patients who may be particularly susceptible to the intracranial effects of CO_2 retention such as those with evidence of increased intracranial pressure, impaired consciousness, or coma. DUROGESIC should be used with caution in patients with brain tumours. Opioids may obscure the clinical course of patients with head injury.

Cardiac disease

DUROGESIC may produce bradycardia and should therefore be administered with caution to patients with bradyarrhythmias.

Hepatic and Renal Disease

Presently insufficient information exists to make recommendations regarding the use of DUROGESIC in patients with impaired renal or hepatic functions. If the drug is used in these patients, it should be used with caution because of the hepatic metabolism and limited renal excretion of fentanyl.

Fever/external heat application

A pharmacokinetic model suggests that serum fentanyl concentrations may increase by about one third if the skin temperature increases to 40 °C. Therefore, patients with fever should be monitored for opioid side effects and the DUROGESIC dose should be adjusted if necessary.
All patients should be advised to avoid exposing the DUROGESIC application site to direct external heat sources such as heating pads, electric blankets, heated water beds, heat or tanning lamps, intensive sunbathing, hot water bottles, prolonged hot baths, saunas and hot whirlpool spa baths.

Serotonin Syndrome

Caution is advised when DUROGESIC is co-administered with medicines that affect the serotonergic neurotransmitter systems.
The development of a potentially life-threatening serotonin syndrome may occur with the concomitant use of serotonergic agents such as Selective Serotonin Re-uptake Inhibitors (SSRIs) and Serotonin Norepinephrine Re-uptake Inhibitors (SNRIs), and with medicines which impair metabolism of serotonin (including Monoamine Oxidase Inhibitors [MAOIs]). This may occur within the recommended dose.
Serotonin syndrome may include mental-status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g., hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea).

If serotonin syndrome is suspected, treatment with DUROGESIC should be discontinued.

Interactions with other Medicines

Interactions with CYP3A4 Inhibitors:

The concomitant use of DUROGESIC with cytochrome P450 3A4 (CYP3A4) inhibitors (e.g. ritonavir, ketoconazole, itraconazole, troleandomycin, clarithromycin, nelfinavir, nefazodone, verapamil, diltiazem, and amiodarone) may result in an increase in fentanyl plasma concentrations, which could increase or prolong both therapeutic and adverse effects, and may cause serious respiratory depression. Therefore, the concomitant use of transdermal fentanyl and CYP3A4 inhibitors is not recommended unless the patient is closely monitored. Patients, especially those who are receiving DUROGESIC and CYP3A4 inhibitors, should be monitored for signs of respiratory depression and dosage adjustments should be made if warranted. (See CONTRA-INDICATIONS)

Use in elderly patients

Data from intravenous studies with fentanyl suggest that elderly patients may have reduced clearance, a prolonged half-life and they may be more sensitive to the medicine than younger patients. In studies of DUROGESIC, elderly patients had fentanyl pharmacokinetics, which did not differ significantly from young patients although serum concentrations tended to be higher. Elderly patients should be observed carefully for signs of fentanyl toxicity and the dose reduced if necessary.

Use in children

DUROGESIC was not studied in children under 2 years of age. DUROGESIC should be administered only to opioid-tolerant children age 2 years or older (see DOSAGE AND DIRECTIONS FOR USE).

To guard against accidental ingestion by children, use caution when choosing the application site for DUROGESIC (see “Instructions for use, handling and disposal” under section DOSAGE AND DIRECTIONS FOR USE) and monitor adhesion of the patch closely.

Effects on the ability to drive and use machines

DUROGESIC may impair the mental and/or physical ability required for the performance of potentially hazardous tasks such as driving a car or operating machinery.

INTERACTIONS

The concomitant use of other central nervous system depressants, including other opioids, sedatives, hypnotics, general anesthetics, phenothiazines, tranquillizers, skeletal muscle relaxants, sedating antihistamines, and alcoholic beverages may produce significant additive depressant effects; hypoventilation, hypotension, and profound sedation or coma or death may occur. Therefore, the use of any of these medicines concomitantly with DUROGESIC requires special patient care and observation. The initial dose of other central nervous system depressants should be reduced by 50 %.

Fentanyl (as contained in DUROGESIC), a high clearance drug, is rapidly and extensively metabolized mainly by CYP3A4.

The concomitant use of CYP3A4 inhibitors with DUROGESIC may result in an increase in fentanyl plasma concentrations, which could increase or prolong both the therapeutic and adverse effects, and may cause serious respiratory depression. In this situation, special patient care and observation are appropriate. The concomitant use of CYP3A4 inhibitors and DUROGESIC is not recommended, unless the patient is closely monitored (see WARNINGS AND SPECIAL PRECAUTIONS).

Oral ritonavir (one of the most potent CYP3A4 inhibitors) reduced the clearance of IV fentanyl by two thirds.

Although clinical data are lacking, *in vitro* data suggest that other potent cytochrome P4503A4 enzyme inhibitors (e.g. fluconazole, ketoconazole, erythromycin, diltiazem and cimetidine) may inhibit the metabolism of fentanyl.

Monoamine Oxidase Inhibitors (MAOI)

DUROGESIC is not recommended for use in patients who require the concomitant administration of an MAOI. Severe and unpredictable interactions with MAOIs, involving the potentiation of opiate effects or the potentiation of serotoninergic effects, have been reported.

Serotonergic Agents

Co-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.

DUROGESIC should be used with caution in patients who have a history of drug or alcohol abuse, especially if they are outside a medically controlled environment.

PREGNANCY AND LACTATION

Safety in pregnancy and lactation has not been established.

Neonatal withdrawal syndrome has been reported in newborn infants with chronic maternal use of DUROGESIC during pregnancy.

Use of DUROGESIC during childbirth is not recommended because fentanyl passes through the placenta and may cause respiratory depression in the newborn child.

Fentanyl is excreted in breast milk and may cause sedation/respiratory depression in the newborn/infant. Therefore, women on DUROGESIC should not breastfeed their babies.

DOSAGE AND DIRECTIONS FOR USE

For transdermal use

DUROGESIC doses should be individualised based upon the status of the patients and should be assessed at regular intervals after application. The patches are designed to deliver approximately 12,

25, 50, 75 and 100 µg/h fentanyl to the systemic circulation, which represent about 0,3- 0,6- 1,2- 1,8- and 2,4-mg per day (see COMPOSITION), respectively.

Initial dosage selection

The appropriate initiating dose of DUROGESIC should be based on the patient's current opioid use. Other factors to be considered are the current general condition and medical status of the patient, including body size, age and extent of debilitation as well as degree of opioid tolerance.

Adults

Opioid-tolerant patients

To convert **opioid-tolerant patients** from oral or parenteral opioids to DUROGESIC, refer to Equianalgesic potency conversion (Table 1), and Recommended DUROGESIC dose based upon daily oral morphine dose (Table 2). The dosage may subsequently be titrated upwards or downwards, if required, in increments of either 12 or 25 µg/h to achieve the lowest appropriate dosage of DUROGESIC depending on response and supplementary analgesic requirements.

Opioid-naïve patients

Clinical experience with DUROGESIC is limited in **opioid-naïve patients**. In the circumstance in which therapy with DUROGESIC is considered appropriate in **opioid-naïve patients**, it is recommended that these patients be titrated with low doses of opioids to attain an equianalgesic dose to DUROGESIC 25 µg/h. Patients can then be converted to DUROGESIC 25 µg/h. The dosage may subsequently be titrated upwards or downwards, if required, in increments of either 12 or 25 µg/h to achieve the lowest appropriate dose of DUROGESIC depending on response and supplementary analgesic requirements. (See Tables 1 and 2.) (See also WARNINGS AND SPECIAL PRECAUTIONS: Opioid-naïve and not opioid-tolerant states.)

Paediatrics

DUROGESIC should be administered only to **opioid-tolerant paediatric patients (ages 2 to 16 years)** who are already receiving at least 30 mg oral morphine equivalents per day. To convert paediatric patients from oral or parenteral opioids to DUROGESIC, refer to Equianalgesic potency

conversion (Table 1), and Recommended DUROGESIC dose based upon daily oral morphine dose (Table 2).

Equianalgesic potency conversion

1. Calculate the previous 24-hour analgesic requirement.
2. Convert this amount to the equianalgesic oral morphine dose using Table 1. All intramuscular (IM) and oral doses in this chart are considered equivalent to 10 mg of intramuscular morphine in analgesic effect.
3. Table 2 displays the range of 24-hour oral morphine doses that are recommended for conversion to each DUROGESIC dose. Use this table to derive from the calculated 24-hour morphine dose the corresponding DUROGESIC dose.

TABLE 1: *Equianalgesic potency conversion*

MEDICINE NAME	EQUIANALGESIC DOSE (mg)	
	IM*	Oral
Morphine	10	30 (assuming repeated dosing) ** 60 (assuming single or intermittent dosing)
Methadone	10	20
Pethidine	75	-
Codeine	130	200
Buprenorphine	0,4	0,8 (sublingual)

* Based on single-dose studies in which an intramuscular dose of each medicine listed was compared with morphine to establish the relative potency. Oral doses are those recommended when changing from parenteral to an oral route.

** The oral/IM potency for morphine is based on clinical experience in patients with chronic pain.

TABLE 2: *Recommended DUROGESIC dose based upon daily oral morphine dose*[1]

Oral 24-hour morphine (mg/day)	DUROGESIC Dose (mcg/h)
30 - 44 (for paediatrics)[2]	12
45 - 134 (for paediatrics)[2]	25
< 135 (for adults)	25
135 - 224	50
225 - 314	75
315 - 404	100
405 - 494	125
495 - 584	150
585 - 674	175
675 - 764	200
765 - 854	225
855 - 944	250
945 - 1034	275
1035 - 1124	300

[1] In clinical trials these ranges of daily oral morphine doses were used as a basis for conversion to DUROGESIC.

[2] Conversion to DUROGESIC doses greater than 25 mcg/h is the same for adult and paediatric patients.

Initial evaluation of the maximum analgesic effect of DUROGESIC, cannot be made before the patch is worn for 24 hours. This delay is due to the gradual increase in serum fentanyl concentration in the 24 hours following initial patch application.

Previous analgesic therapy should be gradually phased out after the initial dose application until analgesic efficacy with DUROGESIC is attained.

Dose titration and maintenance therapy

The conversion ratio from oral morphine to DUROGESIC is conservative and 50 % of patients are likely to require a dose increase after the initial application.

A 12 µg/h strength is available for dose titration, which equates to ≈ 45 mg oral morphine/day. The 12 µg/h strength is particularly useful for titration at lower dosages.

The DUROGESIC patch should be replaced every 72 hours. The dose should be titrated individually until analgesic efficacy is attained. If analgesia is insufficient after the initial application, the dose may be increased after 3 days, based on the daily dose of supplementary analgesics required by the patient in the second or third day of initial application. Thereafter, dose adjustment can take place every 3 days. Medical practitioners are advised that it may take up to 6 days after increasing the dose of DUROGESIC for the patient to reach equilibrium on the new dose. Therefore patients should wear a higher dose through two applications before any further increase in dosage is made, on the basis of the average daily use of a supplemental analgesic.

Dosage titration should normally be performed in 12 µg/h or 25 µg/h increments, although the supplementary analgesic requirements (oral morphine 45/90 mg/day ≈ DUROGESIC-12/25 µg/h) and pain status of the patient should be taken into account. More than one DUROGESIC patch may be used for doses greater than 100 µg /h. Patients may require periodic supplementary doses of a short acting analgesic for "breakthrough" pain. Some patients may require additional or alternative methods of opioid administration when the DUROGESIC-dose exceeds 300 µg/h.

Discontinuation of DUROGESIC

If discontinuation of DUROGESIC is necessary, replacement with other opioids should be gradual, starting at low dose and increasing slowly. This is because fentanyl levels fall gradually after DUROGESIC is removed. After system removal, serum fentanyl concentrations decline gradually with mean terminal half-life ranging from 20-25 hours**.** In general, the discontinuation of opioid analgesia should be gradual in order to prevent withdrawal symptoms.

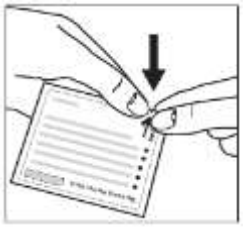
Opioid withdrawal symptoms (see SIDE EFFECTS and WARNINGS AND SPECIAL PRECAUTIONS) are possible in some patients after conversion or dose adjustment.

Instructions for use, handling and disposal

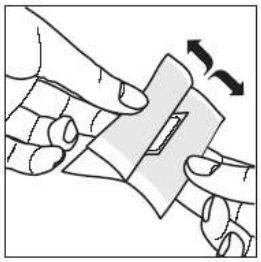
DUROGESIC should be applied to non-irritated and non-irradiated skin on a flat surface of the torso or upper arms. In young children, the upper back is the preferred location to minimize the potential of the child removing the patch. Hair at the application site (a non-hairy area is preferable) should be clipped (not shaved) prior to application. If the site of DUROGESIC application requires cleansing prior to application of the patch, this should be done with clear water. Soap, oils, lotions or any other agent that might irritate the skin or alter its characteristics should not be used. The skin should be completely dry before the patch is applied. Patches should be inspected prior to use. Patches that are cut, divided or damaged in any way should not be used.

When ready to apply the patch, remove it from the sealed protective pouch.

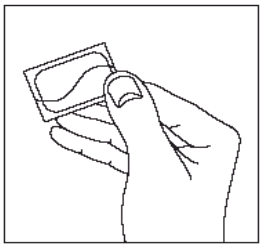
To remove the patch from the protective pouch, locate the pre-cut notch (indicated by an arrow on the back of the pouch label) along the edge of the seal.



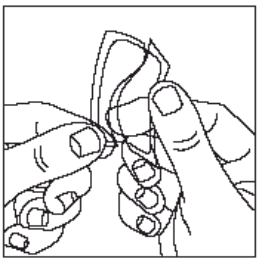
Fold the pouch at the notch, then carefully tear or cut the pouch close to the sealed edge in order not to damage the patch inside. Further open the pouch along both sides, folding the pouch open like a book. Remove the patch from inside.



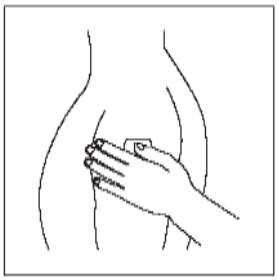
Notice that the surface area of the protective liner is bigger than the patch. Remove the protective liner before applying the patch as described below.



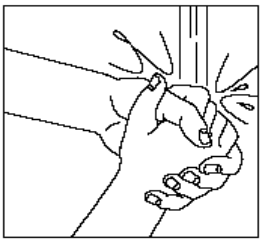
The protective liner for the matrix patch is slit (s shaped cut). Fold the patch in the middle and remove each half of the liner separately. Avoid touching the adhesive side of the patch.



DUROGESIC should be applied immediately upon removal of the protective liner. Apply the patch to the skin by applying light pressure with the palm of the hand for about 30 seconds. Make certain that the edges of the patch are adhering properly.



Then wash hands with clean water.



DUROGESIC may be worn continuously for 72 hours. A new patch should be applied on a different skin site after removal of the previous transdermal patch. Several days should elapse before a new patch is applied to the same area of the skin.

Disposal of the patch

Used patches should be folded firmly in half, adhesive side inwards so that the patch adheres to itself, and then discarded safely and out of the reach of children.

Wash hands, with clean water only, after applying or removing the patch.

SIDE EFFECTS

Adverse events reported from clinical trials in adults are listed below in Table 3. The adverse events are ranked by system organ class and frequency (unless unknown as is the case for spontaneous reports from post marketing experience) using the following convention:

Very common (≥ 1/10); Common (≥ 1/100 and < 1/10); Uncommon (≥ 1/ 1 000 and < 1/100); Rare (≥ 1/10 000 and < 1/1,000); Very Rare (< 1/10 000).

Table 3: Adverse Events from clinical trial reports (regardless of causality, reported by ≥ 1 % of patients)

Body System/Organ Class ***Frequency Category***	**Clinical trials**
Metabolism and nutrition disorders	
Common	Anorexia
Psychiatric Disorders	
Very common	Somnolence, insomnia
Common	Anxiety, depression
Nervous system disorders	
Very common	Dizziness
Common	Muscle contractions involuntary, hypoaesthesia
Eye disorders	
Common	Conjunctivitis
Cardiac disorders	
Common	Palpitations
Respiratory, thoracic, and mediastinal disorders	
Common	Yawning, rhinitis
Gastrointestinal disorders	

Body System/Organ Class ***Frequency Category***	**Clinical trials**
Very common	Nausea, vomiting, constipation
Common	Abdominal pain, dyspepsia, dry mouth
Skin and subcutaneous tissue disorders	
Common	Pruritus, skin disorder, hyperhidrosis
Renal and urinary disorders	
Common	Urinary tract infection
General disorders and administration site conditions	
Common	Feeling of body temperature change, fatigue, malaise, influenza like illness, oedema peripheral, asthenia, drug withdrawal syndrome

Postmarketing data.

Table 4: Postmarketing reports of adverse drug reactions.

Body System/Organ Class	Spontaneous Reports
Immune system disorders	Anaphylactic shock, anaphylactic reaction, anaphylactoid reaction
Metabolism and nutrition disorders	Anorexia
Psychiatric Disorders	Depression, confusional state, hallucination, anxiety, euphoric mood, agitation, insomnia.
Nervous system disorders	Convulsions (including clonic convulsions and grand mal convulsion), amnesia, somnolence, dizziness, headache, tremor, paraesthesia
Cardiac disorders	Tachycardia, bradycardia
Vascular Disorders	Hypotension, hypertension

Body System/Organ Class	Spontaneous Reports
Respiratory, thoracic, and mediastinal disorders	Respiratory depression (including respiratory distress, apnoea, and bradypnoea); (see section "Known Symptoms of Overdose and Particulars of its Treatment"), hypoventilation, dyspnoea
Gastrointestinal disorders	Nausea, vomiting, constipation, diarrhoea, dyspepsia, dry mouth
Hepatobiliary Disorders	Jaundice and increased transaminases.
Skin and subcutaneous tissue disorders	Rash, erythema, pruritus, sweating increased.
Renal and urinary disorders	Urinary retention
Reproductive system and breast disorders	Sexual dysfunction
General disorders and administration site conditions	Drug withdrawal syndrome, asthenia, application site reaction

Adverse events in children and adolescents:

The adverse event profile in children and adolescents treated with DUROGESIC was similar to that observed in adults. No risk was identified in the paediatric population beyond that expected with the use of opioids for the relief of pain associated with serious illness and there does not appear to be any paediatric-specific risk associated with DUROGESIC use in children as young as 2 years old when used as directed.

The most common adverse events reported in paediatric clinical trials were fever, vomiting and nausea. In addition to the adverse reactions listed in Table 3, the following treatment-related adverse reactions were reported in paediatric patients at a rate ≥ 1 %: pain, syncope, allergic reaction, flushing, nervousness, speech disorder, stupor, paranoid reaction, coughing, rash erythematous and skin reaction localised.

Opioid withdrawal symptoms (such as nausea, vomiting, diarrhoea, anxiety and shivering) are possible in some patients after conversion from their previous opioid analgesic to DUROGESIC or if therapy is stopped suddenly. See DOSAGE AND DIRECTIONS FOR USE.

There have been reports of newborn infants experiencing neonatal withdrawal syndrome when mothers chronically use DUROGESIC during pregnancy.

KNOWN SYMPTOMS OF OVERDOSE AND PARTICULARS OF ITS TREATMENT

Symptoms and signs

The manifestations of fentanyl overdosage are an extension of its pharmacological action, the most serious effect being respiratory depression.

Treatment

For the management of respiratory depression, immediate countermeasures include removing the DUROGESIC patch and physically or verbally stimulating the patient. These actions can be followed by administration of the specific narcotic antagonist, naloxone. Respiratory depression following an overdose may outlast the duration of action of the opioid antagonist. The interval between intravenous antagonist doses should be carefully chosen because of the possibility of re-narcotisation after the patch is removed; repeated administration of naloxone may be necessary. Reversal of the narcotic effect may result in acute onset of pain and release of catecholamines.

If the clinical situation warrants, a patent airway should be established and maintained, possibly with an oropharyngeal airway or endotracheal tube, and oxygen should be administered and respiration assisted or controlled, as appropriate. Adequate body temperature and fluid intake should be maintained. If severe or persistent hypotension occurs, the possibility of hypovolemia should be considered and the condition should be managed with appropriate parenteral fluid therapy.

IDENTIFICATION

DUROGESIC patches are rectangular with rounded corners, translucent units comprising a protective

liner and two functional layers.

DUROGESIC patches are available in 5 strengths and each patch has a border with its name and strength printed on it in its respective colour:

- DUROGESIC 12 µg/h: orange coloured printing
- DUROGESIC 25 µg/h: red coloured printing
- DUROGESIC 50 µg/h: green coloured printing
- DUROGESIC 75 µg/h: blue coloured printing
- DUROGESIC 100 µg/h: grey coloured printing

PRESENTATION

Each DUROGESIC patch is packed in a flat colour-coded (refer IDENTIFICATION) heat-sealed pouch. 5 Pouches are packed into an outer cardboard carton together with a PACKAGE INSERT insert / patient information leaflet.

STORAGE INSTRUCTIONS

Store in sealed pouch at or below 25 °C.

Keep sealed pouch in carton until use.

KEEP OUT OF REACH OF CHILDREN BEFORE AND AFTER USE.

REGISTRATION NUMBER

12 µg/h - A40/2.9/0203

25 µg/h - 28/2.9/0288

50 µg/h - 28/2.9/0289

75 µg/h - 28/2.9/0290

100 µg/h - 28/2.9/0291

NAME AND ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

JANSSEN PHARMACEUTICA (Pty.) Ltd.

(Reg No.: 1980/011122/07)

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DATE OF PUBLICATION OF THE PACKAGE INSERT INSERT

- **Date of registration of DUROGESIC range**:

  12 µg/h – 15 August 2008

  25 µg/h – 09 March 1994

  50 µg/h - 06 June 1994

  75 µg/h – 30 March 1994

  100 µg/h - 30 March 1994

- **Date of most recently revised PACKAGE INSERT insert as approved by Council**:

  28 May 2018.