Doxapram HCl -SLS Solution for IV infusion

Doxapram Hydrochloride 2mg/ml

Solution for IV Infusion

1. QUALITATIVE AND QUANTITATIVE COMPOSITION

Doxapram hydrochloride 2mg/ml Infusion

Each ml solution for infusion contains 2 mg Doxapram Hydrochloride per ml

For the full list of excipients, see section 6.1.

2 PHARMACEUTICAL FORM

Clear colorless solution for intravenous infusion

3 CLINICAL PARTICULARS

3.1 Therapeutic indications

Doxapram HCl -SLS acts as a ventilatory stimulant and is specifically indicated in the following situations:

Acute Respiratory failure:

1. To stimulate ventilation in patients whose blood gas status or clinical condition suggests that severe carbon dioxide retention would occur during controlled oxygen therapy.
2. To stimulate ventilation in patients showing a progressive increase in PCO2 with mental status changes during or after controlled oxygen therapy.

Following anaesthesia

1. To stimulate ventilation in the post-operative period as an aid to the reduction of post-operative pulmonary complications
2. To permit use of effective doses of narcotic analgesics without associated problems of ventilatory depression.

3.2. Posology and Method of Administration

Posology

Dr Yasmin

entral Administration for Pharmaceutical care Approval Date:31 /12/2024 Revisor: Dr.yasmin
eneral Administration of Scientific Reference and Medical Inserts
[edical Inserts Administration According to: mhra

Adults and Elderly:

For the treatment of respiratory failure recommended dosage is 1.5 to 4 mg per minute depending on the condition and response of the patient. Administer concurrently with oxygen. Whenever possible the condition of the patient should be monitored by frequent measurement of blood gas tensions.

The following dosage regimen has been shown to result in the rapid production of a steady state plasma concentration of Doxapram:

0-15 mins 4.0 mg/min

15-30 mins 3.0 mg/min

30-60 mins 2.0 mg/min

60 mins onwards 1.5 mg/min

Following anaesthesia recommended dosage is 2-3 mg per minute, and appropriate adjustments to the administration rate should be made according to the response of the patient.

Paediatric population

Doxapram HCl is not recommended for use in children due to insufficient data on safety and efficacy.

Method of administration

Doxapram HCl infusion is recommended for intravenous use only.

3.3 Contraindications

1. Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
2. Severe hypertension
3. Status asthmaticus
4. Coronary artery disease
5. Epilepsy and other convulsive disorders
6. Cerebral oedema
7. Cerebrovascular accident

8. Hyperthyroidism /Thyrotoxicosis

9. Physical obstruction of the respiratory tract, or conditions resulting in restriction of chest wall, muscles of respiration or alveolar expansion.

10. Head injury

11. Proven/suspected pulmonary embolism

3.4 Special warnings and precautions for use

1. Doxapram HCl should be administered concurrently with oxygen to patients with severe irreversible airways obstruction or severely decreased lung compliance, due to the increased work of breathing in these patients.

2. In patients presenting with bronchoconstriction, Doxapram HCl should always be used in conjunction with β-adrenoceptor bronchodilator drugs in order to reduce the amount of respiratory effort.

3. As Doxapram HCl is metabolised primarily by the liver, use with care in patients with hepatic dysfunction.

4. Doxapram HCl should be administered cautiously to patients receiving sympathomimetic agents since an additive pressor effect may occur.

5. Doxapram HCl should be used with great care in patients who are being treated concurrently with monoamine oxidase inhibiting drugs. Animal studies have shown that the action of doxapram is potentiated after pre-treatment with an MAOI.

6. In patients who have received anaesthetics known to sensitize the myocardium to catecholamines, such as halothane, cyclopropane, and enflurane, initiation of Doxapram HCl therapy should be delayed for at least 10 minutes following discontinuance of anaesthesia, since an increase in adrenaline release has been noted with Doxapram HCl administration.

7. The respiratory stimulant effect of Doxapram HCl may not outlast the residual effects of the depressant drugs. Since respiratory depression may recur after stimulation with Doxapram HCl , the patient should be closely monitored until fully

entral Administration for Pharmaceutical care Approval Date:31 /12/2024 Revisor: Dr.yasmin
eneral Administration of Scientific Reference and Medical Inserts
ledical Inserts Administration According to: mhra

alert for ½ to 1 hour. Doxapram HCl may temporarily mask the residual effects of curare-type muscle relaxant drugs.

8. To reduce the likelihood of local damage to a vein from 5% glucose solution, the site of administration of Doxapram HCl may need to be changed periodically during prolonged therapy.

9. Doxapram HCl should be administered with caution in patients with hypermetabolic states such as phaeochromocytoma.

10. The administration of this agent does not diminish the need for continuous monitoring of all aspects of patient response, including frequent analysis of arterial-blood gases.

11. If sudden and severe hypertension or dyspnoea develops, Doxapram should be stopped.

12. Monitoring of the blood pressure and deep tendon reflexes is recommended to prevent overdosage.

13. To avoid side effects, it is advisable to use the minimum effective dosage.

14. Doxapram should not be used in conjunction with mechanical ventilation.

15. An adequate airway is essential and airway protection should be considered since Doxapram may stimulate vomiting.

16. There are few reports mentioning possible association of the prolonged use of Doxapram with delay in mental development in preterm infants.

17. Doxapram HCl should be used with caution in hypertensive patients (Doxapram HCl is contraindicated in severe hypertension, see section 4.3) and in patients with impaired cardiac reserve.

18. Contains 50mg glucose per ml. This should be taken into account in patients with diabetes mellitus when doses more than 100ml are administered.

3.5 Interaction with other medicinal products and other forms of interaction

Clinical data suggest that concurrent use of aminophylline/theophylline and Doxapram HCl may be associated with increased CNS stimulation, agitation, muscle fasciculation

and hyperactivity. Care should thus be taken when these two drugs are used concomitantly.

Doxapram HCl should also be administered with great care to patients being treated concurrently with monoamine oxidase inhibitors (MAOIs). Animal studies have shown that the action of Doxapram HCl may be potentiated after pre-treatment with a MAOI (see section 4.4)

Doxapram HCl may potentiate the effects of sympathomimetic agents (see section 4.4).

Doxapram may temporarily mask the residual effects of curare-type muscle relaxant drugs (see section 4.4).

4.6. Fertility, pregnancy and lactation

Pregnancy

Although there is no recognised hazard, this product is not recommended for use in pregnancy unless there are compelling clinical reasons to do so. The physician must weigh the benefit to the risk.

Breast-feeding

It is not known whether this drug is excreted in human milk. Therefore, caution should be exercised when Doxapram HCl is administered to a lactating mother. A risk to the newborns/infants cannot be excluded.

Fertility

There is currently no available data.

3.7. Effects on ability to drive and use machines

Not applicable

3.8 Undesirable effects

Adverse reactions are listed as per System Organ Class. The following adverse reactions have been observed at the frequencies defined using the following convention:

Not known: cannot be estimated from the available data.

entral Administration for Pharmaceutical care Approval Date:31 /12/2024 Revisor: Dr.yasmin
eneral Administration of Scientific Reference and Medical Inserts
[edical Inserts Administration According to: mhra

MedDRA System organ Class	**Frequency**	**Undesirable Effects**
Nervous system disorders:	Not known	Pyrexia[1] Sweating[1] Flushing[1] Salivation[1] Headache[1] Dizziness[1] Hyperactivity[1] Confusion[1] Hallucinations[1] Perineal warmth[1] Muscle fasciculation[1]
		Convulsions1 Muscle spasticity, Clonus, Bilateral babinski, Increased deep tendon reflexes Doxapram can induce a significant decrease in maximal cerebral blood flow velocity.
Cardiac disorders:	Not known	Increase in blood pressure (moderate) Arrhythmias, Sinus tachycardia, Bradycardia and Extrasystoles, Chest pain or chest tightness.
Respiratory, thoracic and mediastinal disorders:	Not known	Dyspnoea, Cough, Bronchospasm Laryngospasm.
Gastrointestinal Disorders:	Not known	Nausea Vomiting
Renal and Urinary	Not known	Urinary retention,

disorders:		Stimulation of urinary bladderwith spontaneous voiding.

[1]Doxapram HCl may produce adverse effects due to general stimulation of the central, peripheral and autonomic nervous systems:

Paediatric population

Doxapram HCl is not recommended in children (see section 4.2). The following adverse reactions have been reported in off-licence use of doxapram in preterm neonates and infants:

• neurodevelopmental delay

• significant prolongation of QT interval, in some cases associated with atrioventricular block.

•bleeding in stools, abdominal distension and necrotizing enterocolitis and multiple gastric perforations

• early teeth eruption involving lower central incisors

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via The Egyptian Pharmaceutical Vigilance Center directly on hotline 15301 or by sending an e-mail to: pv.followup@edaegypt.gov.eg.

3.9. Overdose

Symptoms

Overdosage may result in hypertension, tachycardia and other arrhythmias; skeletal muscle hyperactivity including enhanced deep tendon reflexes, and

entral Administration for Pharmaceutical care Approval Date:31 /12/2024 Revisor: Dr.yasmin
eneral Administration of Scientific Reference and Medical Inserts
ledical Inserts Administration According to: mhra

dyspnoea. Serious symptoms of overdosage may include clonic and generalized seizures.

Management

Intravenous diazepam, phenytoin, and short-acting barbiturates, oxygen and resuscitative equipment should be readily available to manage overdoses

4.1 Pharmacodynamic properties

Pharmacotherapeutic group: Respiratory stimulants,

Mechanism of action

The principal pharmacological action of Doxapram HCl is an increase in minute volume produced primarily by an increase in tidal volume and to a lesser extent by changes in respiratory rate.

Pharmacodynamic effects

Neuropharmacological studies have shown that the primary sites of action of Doxapram HCl are the peripheral carotid chemoreceptors. It is considered that this site of action of Doxapram HCl is responsible for its relative specificity of action; it is only following large doses of doxapram hydrochloride that non-specific central nervous system stimulation occurs.

4.2 Pharmacokinetic properties

Following an I.V. bolus injection of 1.5mg/kg doxapram, the plasma concentration of doxapram declined in a multi-exponential manner. The mean half-life from 4 – 12 hours was 3.4 hours (range 2.4 – 4.1 hours). The mean apparent volume of distribution was 1.5 litres/kg and the whole body clearance was 370ml/min. Renal clearance was not related to urine flow or pH, but increased progressively with time over the first 12 hours. The mean 0 - 24 hour renal clearance values for individual volunteers ranged from 1.1 to 14.1ml/min. The rate of decline of plasma concentration appeared to decrease after 12 hours. Doxapram was extensively metabolised, and less than 5% of an I.V. dose was excreted unchanged in the urine in 24 hours.

5 PHARMACEUTICAL PARTICULARS

5.1 List of excipients

Each 500 ml plastic propylene bag contains :

Dextrose Monohydrate

Sodium hydroxide

Hydrochloride acid

Water for injection

5.2 Incompatibilities

Doxapram HCl is incompatible with alkaline solutions such as aminophylline,

frusemide and thiopentone sodium

5.3. Shelf life

See outer pack

5.4. Special precautions for storage

Store at temperature not exceeding 30°C.

Use after opening immediately.

5.5. Nature and content of container

Carton box contains single use Transparent plastic polypropylene bag with SFC system (2 SFC port and 2 SFC cap which is made of polypropylene (pp) assembled with rubber disc type 1 which made of polyisoprene type 1 free of natural rubber and free of 2 MBT and nitrosamine) of 500 ml solution containing doxapram hydrochloride 2mg/ml + glucose 5% with outer label.

Presentation: each Doxapram bag contains 500 ml.

6. Manafacture & license HOLDER

Stio Life Science –SLS **FOR** El-Nasr for Pharmaceutical Chemicals

Eda revision date :12-2024