MARTINDALE PHARMA
Making lives better

Hubert Road
Brentwood
CM14 4JE
United Kingdom

Dear Healthcare Professional,

Important Caffeine Label Change Information

We would like to inform you that from the 1st November 2013 Caffeine products available from Martindale Pharma are changing their name as follows:

- **Caffeine citrate 10 mg/mL solution for injection** (previously called caffeine 5 mg/mL solution for injection)
- **Caffeine citrate 10 mg/mL oral solution** (previously called caffeine 5 mg/mL oral solution)

There is no change to the actual product this is simply a label change to unify packaging. It is not necessary to return any products.

- This change brings the products in line with the naming of other products available on the UK market (i.e. which are already named in the salt form as caffeine citrate).
- All caffeine products should now be prescribed as caffeine citrate
- Always state dose in terms of caffeine citrate when prescribing these medicines because of the risk of confusion and potential for dosing errors (2 mg caffeine citrate is equivalent to 1mg caffeine base).
- Additional care should be taken when prescribing and dispensing because other manufacturers produce caffeine products in different strengths.

If you would like to receive a wall chart or dosage card that reflects these changes then please complete the enclosed reply card and we will be happy to send copies by return.

Yours sincerely,

Roger Dickinson
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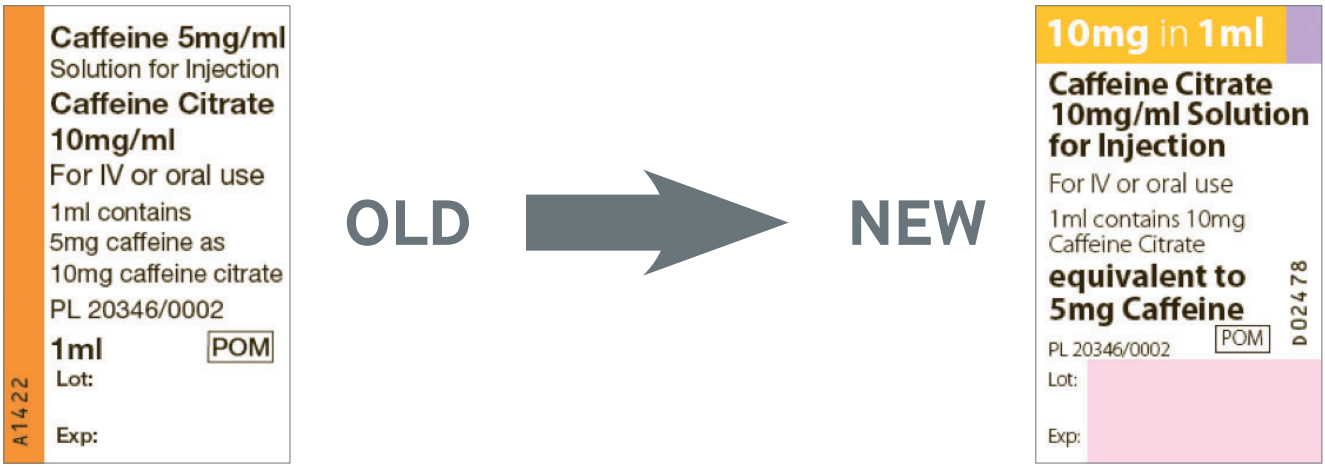
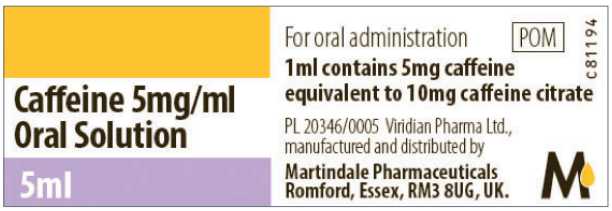
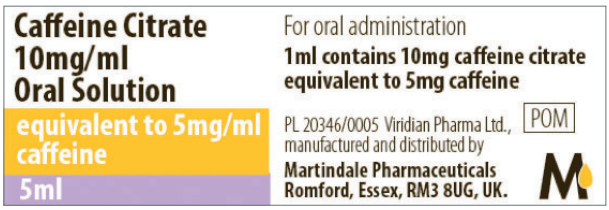
FURTHER INFORMATION:

- http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON155757
- The British National Formulary for Children (BNF-C) has been updated from May 2013 (e-version), and in July 2013 the hard copy version

Labelling is Changing







Caffeine Citrate 10mg/ml Injection and Oral Solution

Prescribing Information

PRESCRIBING INFORMATION for Caffeine Citrate 10mg/ml injection and Oral solution.

Please refer to Summary of Product Characteristics before prescribing.

PRESENTATION: A clear colourless solution, each 1 ml of solution contains 10mg of Caffeine Citrate, equivalent to 5mg of Caffeine base.

INDICATIONS: The treatment of apnoea of prematurity.

DOSAGE AND ADMINISTRATION: For use in premature infants. Infants must be of sufficient respiratory maturity not to require positive pressure ventilation.

ORAL SOLUTION:
For oral use only. **Loading dose:** 20mg/kg of caffeine citrate (10mg/kg of caffeine base). If the patient fails to respond within 4 hours, a second loading dose may be given. If no clinical response after second dose, measure caffeine blood levels; consider other possible aetiologies for apnoea.

Maintenance dose: 5-10mg/kg/24 hrs of caffeine citrate (2.5-5 mg/kg/24 hrs of caffeine base), starting 24 hours after the loading dose. In some cases, maintenance doses higher than 10mg/kg/day (as caffeine citrate) may be required to achieve maximum efficacy (e.g. in continuing apnoeic episodes where plasma levels indicate the dose may be safely increased).

INJECTION:
Oral or slow IV only. Do not give IM. **Loading dose:** 20mg/kg of caffeine citrate (10mg/kg of caffeine base) orally or by IV infusion over 30mins, repeated after 4 hours if necessary. If no clinical response after second dose, measure caffeine blood levels; consider other possible aetiologies for apnoea.

Maintenance dose: 5-10mg/kg/24 hrs of caffeine citrate (2.5-5 mg/kg/24 hrs of caffeine base) orally or by IV infusion over 30 mins, starting 24 hours after the loading dose. In some cases, maintenance doses higher than 10mg/kg/day (as caffeine citrate) may be required to achieve maximum efficacy (e.g. in continuing apnoeic episodes where plasma levels indicate the dose may be safely increased).

Duration of treatment should be based on clinical judgement. Usually treatment should be continued until the infant has reached a gestational age of 37 weeks, by which time apnoea of prematurity should have resolved. Adjust dose according to plasma levels in cases of hepatic or renal impairment.

Adults, children and the elderly: Not applicable.

CONTRA-INDICATIONS: Known hypersensitivity to caffeine or any of the excipients.

WARNINGS AND PRECAUTIONS: Exclude other causes of apnoea before starting treatment. In premature neonates, caffeine has a prolonged half-life. Monitor plasma caffeine levels periodically. Plasma levels should not normally exceed 50 micrograms/ml (10-30 micrograms/ml optimally). If higher maintenance dosages are used, there is the potential for accumulation. Caution in neonates born to mothers who have ingested large quantities of caffeine prior to delivery and neonates previously treated with theophylline as they may have pre-existing caffeine in their blood. Caution if there have been any unusual rhythm disturbances on a CTG trace before the baby is born, in neonates suffering gastro-oesophageal reflux and those with cardiac disease. Caffeine causes an increase in metabolism, diuresis and electrolyte loss.

INTERACTIONS: Other xanthines such as theophylline: concurrent use should be avoided. Theoretical potential for interaction with phenytoin or phenobarbitone if used during pregnancy.

PREGNANCY AND LACTATION: Not applicable.

UNDESIRABLE EFFECTS: May cause irritability, restlessness and jitteriness. Tachycardia, hypertension and increased stroke volume which may be dose related. May increase gastro-oesophageal reflux, enteral secretions and gastric aspirations. It may also reduce splanchnic blood flow and induce intestinal stasis. There is a theoretical increased risk of necrotising enterocolitis, but this has not been reported in clinical trials. Caffeine may suppress erythropoietin synthesis and reduce haemoglobin concentration with prolonged treatment. May also cause hypoglycaemia, hyperglycaemia, increased urine flow rate and increased sodium and calcium excretion. May possibly aggravate cerebral hypoxia. Available evidence does not indicate any adverse long-term effects of neonatal caffeine therapy, but the possibility cannot be ruled out.

PRODUCT LICENCE NUMBER: Injection – PL 20346/0002
Oral solution – PL 20346/0005

PRODUCT LICENCE HOLDER: Viridian Pharma Ltd
Yew Tree House
Hendrew Lane, Llandevaud
Newport, Gwent NP18 2AB

Distributed in the UK by: Macarthys Laboratories Ltd t/a Martindale Pharma
Bampton Road
Romford
RM3 8UG

BASIC NHS PRICE: Injection - £48.82 for a pack of 10 x 1ml ampoules
Oral solution - £24.41 for a 5ml bottle

LEGAL CATEGORY: POM

DATE OF PREPARATION: September 2013

Adverse events should be reported. Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard**. Adverse events should also be reported to Martindale Pharma Tel. 01277 266600 Fax 01708 382739 e-mail **drugsafety@martindalepharma.co.uk .**

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