

ABBREVIATED PRESCRIBING INFORMATION

Consult Summary of Product Characteristics before prescribing. **Uses:** The treatment of disabling motor fluctuations ("on-off" phenomena) in patients with Parkinson's disease which persist despite individually titrated treatment with levodopa (with a peripheral decarboxylase inhibitor) and/or other dopamine agonists. **Dosage and Administration:** Apomorphine hydrochloride is administered subcutaneously either as an intermittent bolus injection or by continuous subcutaneous infusion. Its rapid onset (5-10 mins) and duration of action (about 1 hour) may prevent an "off" episode which is refractory to other treatments. Hospital admission under appropriate specialist supervision is necessary during patient selection and when establishing a patient's therapeutic regime. Please refer to the Summary of Product Characteristics for full details before initiating therapy. Treatment with domperidone (typical dosage 20mg three times a day) before and during apomorphine HCl therapy is essential. The optimal dosage of apomorphine HCl has to be determined on an individual patient bases; individual bolus injections should not exceed 10mg and the total daily dose should not exceed 100mg. **Contraindications:** Children and adolescents (up to 18 years of age). Known sensitivity to apomorphine or any other ingredients of the product. Respiratory depression, dementia, psychotic disease or hepatic insufficiency. Intermittent apomorphine HCl treatment is not suitable for patients who have an "on" response to levodopa which is marred by severe dyskinesia or dystonia. **Pregnancy and lactation:** Caution should be exercised if prescribing apomorphine to pregnant women and women of childbearing age. Breast-feeding should be avoided during apomorphine HCl therapy. **Interactions:** Patients should be monitored for potential interactions during initial stages of apomorphine therapy. Particular caution should be given when apomorphine is used with other medications that have a narrow therapeutic window. It should be noted that there is potential for interaction with neuroleptic and antihypertensive agents. **Precautions:** Use with caution in patients with renal, pulmonary or cardiovascular disease, or who are prone to nausea or vomiting. Extra caution is recommended during initiation of therapy in elderly and/or debilitated patients. Since apomorphine may produce hypotension, care should be exercised in patients with cardiac disease or who are taking vasoactive drugs, particularly when pre-existing postural hypotension is present. Neuropsychiatric disturbances are common in Parkinsonian patients. APO-go should be used with special caution in these patients. Apomorphine has been associated with somnolence and other dopamine agonists can be associated with sudden sleep onset episodes, particularly in patients with Parkinson's disease. Patients must be informed of this and advised to exercise caution whilst driving or operating machines during treatment with apomorphine. Haematology tests should be undertaken at regular intervals as with levodopa with given concomitantly with apomorphine. Pathological gambling, increased libido and hypersexuality have been reported in patients treated with dopamine agonists, including apomorphine. **Side Effects:** Local induration and nodules (usually asymptomatic) often develop at subcutaneous site of injection leading to areas of erythema, tenderness, induration and (rarely) ulceration. Pruritus may occur at the site of injection. Drug-induced dyskinesias during "on" periods can be severe, and in a few patients may result in cessation of therapy. Postural hypotension is seen infrequently and is usually intransient. Transient sedation following each dose of apomorphine may occur at the start of therapy, but this usually resolves after a few weeks of treatment. Nausea and vomiting may occur, particularly when APO-go treatment is initiated, usually as a result of the omission of domperidone. Neuropsychiatric disturbances (including transient mild confusion and visual hallucinations) have occurred during apomorphine therapy and neuropsychiatric disturbances may be exacerbated by apomorphine. Positive Coombs' tests and haemolytic anaemia have been reported in patients receiving apomorphine and levodopa. Local and generalised rashes have been reported. Eosinophilia has occurred in only a few patients during treatment with apomorphine HCl. Patients treated with dopamine agonists, including apomorphine, have been reported as exhibiting signs of pathological gambling, increased libido and hypersexuality (especially at high doses). Apomorphine is associated with somnolence. Breathing difficulties have been reported. Prescribers should consult the Summary of Product Characteristics in relation to other side effects. **Presentation and Basic NHS Cost:** Apo-go ampoules contain apomorphine hydrochloride 10mg/ml, as follows: 20mg in 2ml – basic NHS cost £37.96 per carton of 5 ampoules. 50mg in 5ml – basic NHS cost £73.11 per carton of 5 ampoules. APO-go pens (disposable multiple dosage injector system) contain apomorphine hydrochloride 10mg/ml, as follows: 30mg in 3ml – basic NHS cost £123.91 per carton of 5 pens. APO-go Pre-filled syringes contain apomorphine hydrochloride 5mg/ml, as follows: 50mg in 10ml – basic NHS cost £73.11 per carton of 5 syringes. **Marketing Authorisation Numbers:** APO-go Ampoules: PL04483/0064. APO-go Pens: PL04483/0065. APO-go Pre filled syringes: PL05928/0025. **Legal Category:** POM. **Date of last revision:** November 2008. For further information please contact: Britannia Pharmaceuticals, Park View House, 65 London Road, Newbury, Berkshire, RG14 1JN, UK.

Adverse events should be reported.
Reporting forms and information can be found
at www.yellowcard.gov.uk.
Adverse events should also be reported to
Medical Information on 0870 851 0207 or
drugsafety@britannia-pharm.com

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Neurological Signs: Geophagia (Geophagy) and Pica (Pagophagia)

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29th November [1870]. – *Safura* is the name of the disease of clay or earth eating, at Zanzibar; it often affects slaves, and the clay is said to have a pleasant odour to the eaters, but it is not confined to slaves, nor do slaves eat in order to kill themselves; it is a diseased appetite, and rich men who have plenty to eat are often subject to it. The feet swell, flesh is lost, and the face looks haggard; the patient can scarcely walk for shortness of breath and weakness, and he continues eating until he dies.

This extract from the last journals of Dr David Livingstone^{1,2} describes geophagia (geophagy), earth or clay eating. This may also fall under the rubric of pica, or pagophagia, a morbid craving for unusual or unsuitable food. Another example may be found in the novel *One hundred years of solitude* by Gabriel Garcia Marquez, first published in 1967, concerning an eleven year old girl, Rebeca, who arrives in the town of Macondo carrying a canvas sack which contains her dead parents' bones: "Rebeca only liked to eat the damp earth of the courtyard". The behaviour recurs later in her life when she experiences the passion of unrequited love.³

Although one might possibly dismiss the latter account as nothing more than "magic realism", pica is a recognised symptom in childhood, sometimes associated with brain damage, learning disability, and emotional distress. Other inedible items which are sometimes eaten include paper and paint. Sufferers are obviously at risk of infection from contaminated foods, such as soil.⁴ An association of pica with iron deficiency is well recognised,⁵ as is a link with pregnancy. Livingstone noted that "clay built in walls is preferred, and Manyema women when pregnant often eat it".¹ Reports of geophagia have been found dating back to Hippocrates.⁶

Geophagia may be associated with neurological complications. Cases have been reported of flaccid quadriplegia⁷ and of proximal myopathy⁸ associated with profound hypokalaemia in the context of geophagia. Livingstone mentioned weakness associated with clay eating (see above); he also mentioned "A Banyamwezi carrier, who bore an enormous load of copper, is now by safura scarcely able to walk".¹ A previous review of neurological problems described by Livingstone in his many writings failed to note this particular syndrome of geophagia-associated weakness.⁹ The loss of flesh associated with geophagia which was noted by Livingstone was re-reported almost a century later as "Cachexia Africana".¹⁰ ♦

REFERENCES

1. Waller H (ed.). *The last journals of David Livingstone in Central Africa, from 1865 to his death. Continued by a narrative of his last moments and sufferings obtained from his faithful servants Chuma and Susi.* London, 1874 (2 volumes): 1183-4.
2. Gelfand M. *Livingstone the doctor. His life and travels. A study in medical history.* Oxford: Basil Blackwell, 1957:10;256-7.
3. Garcia Marquez G. *One hundred years of solitude.* London: Picador, 1978 [1967]: 42,59,61,79,81-82.
4. Gelder M, Gath D, Mayou R. *Oxford textbook of psychiatry.* Oxford: Oxford University Press, 1983:645.
5. Von Garnier C, Stunitz H, Decker M, Battegay E, Zeller A. *Pica and refractory iron deficiency anaemia: a case report.* J Med Case Reports 2008;2:324.
6. Woywodt A, Kiss A. *Geophagia: the history of earth-eating.* J R Soc Med 2002;95:143-6.
7. Trivedi TH, Daga GL, Yeolekar ME. *Geophagia leading to hypokalemic quadriplegia in a postpartum patient.* J Assoc Physicians India 2005;53:205-7.
8. McKenna D. *Myopathy, hypokalaemia and pica (geophagia) in pregnancy.* Ulster Med J 2006;75:159-60.
9. Larner AJ. *Dr David Livingstone (1813-1873): some neurological observations.* Scott Med J 2008;53(2):35-7.
10. Mengel CE, Carter WA, Horton ES. *Geophagia with iron deficiency and hypokalemia. Cachexia Africana.* Arch Intern Med 1964;114:470-4.