APO-go®
Apomorphine hydrochloride

PRESCRIBING INFORMATION

Consult Summary of Product Characteristics before prescribing.

Indications Treatment of motor fluctuations ('ON-OFF' phenomena) in patients with Parkinson's disease which are not sufficiently controlled by oral anti-Parkinson medication.

This prescribing information applies to APO-go® Ampoules 10 mg/ml solution for injection or infusion, APO-go® Pen 10 mg/ml solution for injection, APO-go® 5 ml Solution for Infusion in Pre-filled Syringe.

Dosage and Administration
Apomorphine hydrochloride is administered subcutaneously either as an intermittent bolus injection or by continuous subcutaneous infusion. Apomorphine should be initiated in the controlled environment of a specialist clinic. The patient should be supervised by a physician experienced in the treatment of Parkinson's disease (e.g. neurologist). The patient's treatment with levodopa, with or without dopamine agonists, should be optimised before starting APO-go® treatment. The appropriate dose for each patient is established by incremental dosing schedules. The choice of which minipump and / or syringe-driver to use, and the dosage settings required, will be determined by the physician in accordance with the particular needs of the patient. Alterations in dosage may be made according to the patient's response. The optimal dosage of apomorphine hydrochloride varies between individuals but, once established, remains relatively constant for each patient.

Patients treated with apomorphine will usually need to start domperidone at least two days prior to initiation of therapy. The domperidone dose should be titrated to the lowest effective dose and discontinued as soon as possible. Before the decision to initiate domperidone and apomorphine treatment, risk factors for QT interval prolongation in the individual patient should be carefully assessed to ensure that the benefit outweighs the risk. The optimal dosage of apomorphine HCl has to be determined on an individual patient basis; individual bolus injections should not exceed 10 mg and the total daily dose should not exceed 100 mg.

Do not use if the solution has turned green. The solution should be inspected visually prior to use. Only clear, colourless and particle free solution should be used. Apomorphine must not be used via the intravenous route.

APO-go® Ampoules
1 mg of apomorphine HCl, that is approximately 15–20 micrograms/kg, may be injected subcutaneously during a hypokinetic or 'OFF' period and the patient is observed over 30 minutes for a motor response. If no response, or an inadequate response is obtained, a second dose of 2 mg of apomorphine HCl is injected subcutaneously and the patient observed for an adequate response for a further 30 minutes. The dosage may be increased by incremental injections with at least a 40 minute interval between succeeding injections, until a satisfactory motor response is obtained. Once the appropriate dose is determined a single subcutaneous injection may be given into the lower abdomen or outer thigh at the first signs of an 'OFF' episode. It cannot be excluded that absorption may differ with different injection sites within a single individual. Accordingly, the patient should then be observed for the next hour to assess the quality of their response to treatment. Alterations in dosage may be made according to the patient's response. Patients who have shown a good 'ON' period response during the initiation stage of apomorphine therapy, but whose overall control remains unsatisfactory using intermittent injections, or who require many and frequent injections (more than 10 per day), may be commenced on or transferred to continuous subcutaneous infusion by minipump and/or syringe driver. For continuous infusion the ampoules should be diluted to a concentration of 5 mg/ml using sterile saline. Continuous infusion is started at a rate of 1 mg apomorphine HCl per hour then increased according to the individual response. Increases in the infusion rate should not exceed 0.5 mg per hour at intervals of not less than 4 hours. Hourly infusion rates may range between 1 mg and 4 mg, equivalent to 0.015–0.06 mg/kg/hour. Infusions should run for waking hours only. Unless the patient is experiencing severe night-time problems, 24 hour infusions are not advised. Tolerance to the therapy does not seem to occur as long as there is an overnight period without treatment of at least 4 hours. In any event, the infusion site should be changed every 12 hours. Patients may need to supplement their continuous infusion with intermittent bolus boosts, as necessary, and as directed by their physician. A reduction in dosage of other dopamine agonists may be considered during continuous infusion.

APO-go® Pen
1 mg of apomorphine HCl, that is approximately 15–20 micrograms/kg, may be injected subcutaneously during a hypokinetic, or 'OFF' period and the patient is observed over 30 minutes for a motor response. If no response, or an inadequate response is obtained, a second dose of 2 mg of apomorphine HCl is injected subcutaneously and the patient observed for an adequate response for a further 30 minutes. The dosage may be increased by incremental injections with at least a 40 minute interval between succeeding injections, until a satisfactory motor response is obtained. Once the appropriate dose is determined, a single subcutaneous injection may be given into the lower abdomen or outer thigh at the first signs of an 'OFF' episode. It cannot be excluded that absorption may differ with different injection sites within a single individual. Accordingly, the patient should then be observed for the next hour to assess the quality of their response to treatment. Alterations in dosage may be made according to the patient's response.

APO-go® Pre Filled Syringes
APO-go® PFS 5 mg/ml Solution for Infusion in Pre-filled Syringe is a pre-diluted pre-filled syringe intended for use without dilution as a continuous subcutaneous infusion by minipump and / or syringe-driver. It is not intended to be used for intermittent injection. Patients who have shown a good 'ON' period response during the initiation stage of apomorphine therapy, but whose overall control remains unsatisfactory using intermittent injections, or who require many and frequent injections (more than 10 per day), may be commenced on or transferred to continuous subcutaneous infusion by minipump and / or syringe driver. Continuous infusion is started at a rate of 1 mg apomorphine HCl per hour then increased according to the individual response each day. Increases in the infusion rate should not exceed 0.5 mg at intervals of not less than 4 hours. Hourly infusion rates may range between 1 mg and 4 mg, equivalent to 0.014 – 0.06 mg/kg/hour. Infusions should run for waking hours only. Unless the patient is experiencing severe night-time problems, 24 hour infusions are not advised. Tolerance to the therapy does not seem to occur as long as there is an overnight period without treatment of at least 4 hours. In any event, the infusion site should be changed every 12 hours. Patients may need to supplement their continuous infusion with intermittent bolus boosts, as necessary, and as directed by their physician. A reduction in dosage of other dopamine agonists may be considered during continuous infusion.

Contraindications Children and adolescents (up to 18 years of age). Known hypersensitivity to apomorphine or any excipients of the medicinal 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 Apomorphine should not be used in pregnancy unless clearly necessary. Breastfeeding: It is not known whether apomorphine is excreted in breast milk. A decision on whether to continue/discontinue breastfeeding or to continue/discontinue therapy with APO-go® should be made taking into account the benefit of breast-feeding to the child and the benefit of APO-go® to the woman.

Ability to drive and operate machinery Apomorphine has minor or moderate influence on the ability to drive and use machines. Patients being treated with apomorphine and presenting with somnolence and/or sudden sleep episodes must be informed to refrain from driving or engaging in activities (e.g. operating machines) where impaired alertness may put them or others at risk of serious injury or death until such recurrent episodes and somnolence have resolved.

Interactions Patients should be monitored during initiation with apomorphine therapy particularly when used with other medications that have a narrow therapeutic window. There is potential for interaction with neuroleptic and antihypertensive agents and cardiac active medicinal products. It is recommended to avoid the administration of apomorphine with other drugs known to prolong the QT interval.

Precautions
Caution in patients with renal, pulmonary or cardiovascular disease and persons prone to nausea and vomiting. Extra caution recommended during initiation of therapy in elderly and/or debilitated patients. Since apomorphine may produce hypotension, even when given with domperidone pre-treatment, care should be exercised in patients with pre-existing cardiac disease or in patients taking vasoactive medicinal products such as antihypertensives, and especially in patients with pre-existing postural hypotension. Since apomorphine, especially at high dose, may have the potential for QT prolongation, caution should be exercised when treating patients at risk for torsades de pointes arrhythmia. When used in combination with domperidone, risk factors in the individual patient should be carefully assessed. This should be done before treatment initiation, and during treatment. Important risk factors include serious underlying heart conditions such as congestive cardiac failure, severe hepatic impairment or significant electrolyte disturbance. Also, medication possibly affecting electrolyte balance, CYP3A4 metabolism or QT interval should be assessed. Monitoring for an effect on the QTc interval is advisable. An ECG should be performed: prior to treatment with domperidone, during the treatment initiation phase and as clinically indicated thereafter. The patient should be instructed to report possible cardiac symptoms including palpitations, syncope, or near-syncope. They should also report clinical changes that could lead to hypokalaemia, such as gastroenteritis or the initiation of diuretic therapy. At each medical visit, risk factors should be revisited.

Apomorphine is associated with local subcutaneous effects. These can sometimes be reduced by the rotation of injection sites or possibly by the use of ultrasound (if available) in order to avoid areas of nodularity and induration. Haemolytic anaemia and thrombocytopenia have been reported in patients treated with apomorphine. Haematology tests should be undertaken at regular intervals as with levodopa, when given concomitantly with apomorphine.

Caution advised when combining apomorphine with other medicinal products, especially those with a narrow therapeutic range.

Neuropsychiatric problems co-exist in many patients with advanced Parkinson's disease. There is evidence that for some patients neuropsychiatric disturbances may be exacerbated by apomorphine. Special care should be exercised when apomorphine is used in these patients.

Apomorphine has been associated with somnolence and episodes of sudden sleep onset, 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. Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines. Furthermore, a reduction of dosage may be considered.

Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including apomorphine. Dose reduction/tapered discontinuation should be considered if such symptoms develop. Dopamine dysregulation Syndrome (DDS) is an addictive disorder resulting in excessive use of the product seen in some patients treated with apomorphine. Before initiation of treatment, patients and caregivers should be warned of the potential risk of developing DDS.

APO-go® Ampoules, Pen and Pre-filled Syringe contain sodium metabisulphite which may rarely cause severe allergic reactions and bronchospasm. These medicinal products contain less than 1 mmol sodium (23 mg) per 10 ml, i.e. essentially "sodium-free".

Side Effects: Very common: Hallucinations. Injection site reactions (particular with continuous use) - these may include subcutaneous nodules, induration, erythema, tenderness and panniculitis. Various other local reactions (such as irritation, itching, bruising and pain) may also occur.

Common: Neuropsychiatric disturbances (including transient mild confusion and visual hallucinations) have occurred during apomorphine HCl therapy, somnolence, transient sedation, dizziness, yawning, nausea and vomiting.

Serious: Uncommonly – Injection site necrosis and ulceration have been reported. Severe drug-induced dyskinesias during 'ON' periods may require discontinuation. Postural hypotension is usually transient and infrequent. Positive Coombs' tests, haemolytic anaemia and thrombocytopenia have been reported. Eosinophilia occurs rarely. Rarely – Allergic reactions (including anaphylaxis and bronchospasm) due to sodium metabisulphite. Symptoms of overdose like excessive emesis, respiratory depression, hypotension and bradycardia may be treated empirically. Breathing difficulties have been reported. Local and generalised rashes have been reported. Apomorphine has been associated with sudden sleep onset episodes.

Prescribers should consult the Summary of Product Characteristics in relation to other adverse reactions.

Presentation and Basic NHS Cost APO-go® Pens (disposable multiple dosage injector system) contain apomorphine hydrochloride 10 mg/ml, as follows: 30 mg in 3 ml – basic NHS cost £123.91 per carton of 5 pens. APO-go® Pre-filled Syringes contain apomorphine hydrochloride 5 mg/ml, as follows: 50 mg in 10 ml – basic NHS cost £73.11 per carton of 5 syringes. APO-go® ampoules contain apomorphine hydrochloride 10 mg/ml as follows: 50 mg in 5 ml – basic NHS cost £73.11 per carton of 5 ampoules.

Marketing Authorisation Numbers:
APO-go® Ampoules: PL 04483/0072
APO-go® Pen: PL 04483/0073
APO-go® Pre-filled Syringes: PL 04483/0074

Legal Category POM

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Marketing Authorisation Holder in the UK Britannia Pharmaceuticals Limited, 200 Longwater Avenue, Green Park, Reading, Berkshire, RG2 6GP

Full prescribing information and further information is available from Britannia Pharmaceuticals Limited at medinfo@britannia-pharm.com or 0808 196 8585.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Britannia Pharmaceuticals Ltd at dso@britannia-pharm.com or 0808 196 8585.

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