Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

APO-go POD 5 mg/ml solution for infusion in cartridge

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution contains 5 mg apomorphine hydrochloride hemihydrate
Each 20 ml cartridge contains 100 mg apomorphine hydrochloride hemihydrate

Excipients with known effect:
Sodium metabisulfite (E223), 0.5 mg per ml

For the full list of excipients, see Section 6.1

3 PHARMACEUTICAL FORM

Solution for infusion in cartridge.

Clear solution, colourless and practically free from visible particles
pH 3.0-4.0

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

APO-go POD is indicated in adults.

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

4.2 Posology and method of administration

Selection of Patients Suitable for APO-go POD:

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, may be transferred to continuous subcutaneous infusion by minipump. Patients who have frequent 'off' periods not controlled by oral/transdermal medication may also be commenced on continuous subcutaneous infusion by minipump without prior use of intermittent injections.

Patients selected for treatment with APO-go POD should be capable of setting up an infusion system themselves or else have a responsible carer able to set up an infusion system for them when required.

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 whenever 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 (see Section 4.4).

Apomorphine should be initiated in the controlled environment of a clinic. During the titration phase of apomorphine the patient should be supervised by a trained healthcare professional 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 POD treatment.

Posology

Determination of Threshold Dose

The threshold dose for continuous infusion should be determined as follows: Continuous infusion is started at a rate of 1 mg apomorphine (0.2 ml) per hour then increased according to the individual response each day. Increases in the infusion rate should not exceed 0.5 mg - 1.0 mg/hr per day. Once there is adequate control of motor symptoms, the infusion rate can remain stable and will usually range between 2 mg/hr and 8 mg/hr (0.4 ml and 1.6 ml). Infusions should run for waking hours only). 24 hour infusions are not advised, unless the patient is experiencing severe night-time problems (as directed by their physician). Please note that the recommended total daily dose should not exceed 100 mg.

Patients may use a cartridge for up to 48 hours as long as a new infusion line and a different site for infusion is used every 24 hours.

Patients may need to supplement their continuous infusion with intermittent bolus boosts, as necessary, and as directed by their physician (but not exceeding the 100 mg maximum daily dose).

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 24 hours.

Establishment of treatment
Alterations in dosage may be made according to the patient's response.

The optimal dosage of apomorphine varies between individuals but, once established, remains relatively constant for each patient.

Precautions on continuing treatment
In clinical studies it has usually been possible to make some reduction in the dose of levodopa and other anti-Parkinson medications; this effect varies considerably between patients and needs to be carefully managed by an experienced physician.

Once treatment has been established domperidone therapy may be gradually reduced in some patients and discontinued altogether whenever possible.

Paediatric population
APO-go POD is contraindicated for children and adolescents under 18 years of age (see Section 4.3).

Elderly
The elderly are well represented in the population of patients with Parkinson's disease and constitute a high proportion of those studied in clinical trials of apomorphine. The management of elderly patients treated with apomorphine has not differed from that of younger patients. However, extra caution is recommended during initiation of therapy in elderly patients because of the risk of postural hypotension.

Renal impairment
A dose schedule similar to that recommended for adults, and the elderly, can be followed for patients with renal impairment (see Section 4.4).

Method of Administration

APO-go POD is for subcutaneous use.
APO-go POD is a pre-diluted solution intended for use without dilution as a continuous subcutaneous infusion by minipump.
APO-go POD is designed to be used with a pump (the Crono APO-go III Infusion Pump or the Crono PAR4 20 Infusion Pump) and the **Crono*Bell Sleeve***. These are CE marked medical devices.

A summary of the instructions for setting up the infusion can be found in Section 6.6.

Apomorphine must not be used via the intravenous route.

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.

4.3 Contraindications

In patients with respiratory depression, dementia, psychotic diseases or hepatic insufficiency.

Apomorphine treatment must not be administered to patients who have an 'on' response to levodopa which is marred by severe dyskinesia or dystonia.

Hypersensitivity to the active substance or to any of the excipients listed in Section 6.1.

The concomitant use of apomorphine with drugs of the $5HT_3$ antagonist class is contraindicated (including, for example, ondansetron, granisetron, dolasetron, palonosetron and alosetron), see Section 4.5.

APO-go POD is contraindicated for children and adolescents under 18 years of age.

4.4 Special warnings and precautions for use

Selection of Patients Suitable for APO-go POD:

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, may be transferred to continuous subcutaneous infusion by minipump. Patients who have frequent 'off' periods not controlled by oral/transdermal medication may also be commenced on continuous subcutaneous infusion by minipump without prior use of intermittent injections.

Patients selected for treatment with APO-go POD should be capable of setting up an infusion system themselves or else have a responsible carer able to set up an infusion system for them when required.

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 whenever 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 (see Section 4.4).

Apomorphine should be initiated in the controlled environment of a clinic. During the titration phase of apomorphine the patient should be supervised by a trained healthcare professional 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 POD treatment.

Posology

Determination of Threshold Dose
The threshold dose for continuous infusion should be determined as follows: Continuous infusion is started at a rate of 1 mg apomorphine (0.2 ml) per hour then increased according to the individual response each day. Increases in the infusion rate should not exceed 0.5 mg - 1.0 mg/hr per day. Once there is adequate control of motor symptoms, the infusion rate can remain stable and will usually range between 4 mg/hr and 6 mg/hr (0.8 ml and 1.2 ml). Some patients may obtain adequate symptom control with as little as 2 mg/hr and others will require as much as 8 mg/hr. Infusions should run for waking hours only (typically 16 hours per day). 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 day.The total daily dose should not exceed 100 mg.

Patients may need to supplement their continuous infusion with intermittent bolus boosts, as necessary, and as directed by their physician.

Establishment of treatment
Alterations in dosage may be made according to the patient's response.

The optimal dosage of apomorphine varies between individuals but, once established, remains relatively constant for each patient.

Precautions on continuing treatment
In clinical studies it has usually been possible to make some reduction in the dose of levodopa and other anti-Parkinson medications; this effect varies considerably between patients and needs to be carefully managed by an experienced physician.

Once treatment has been established domperidone therapy may be gradually reduced in some patients but successfully eliminated only in a few, without any vomiting or hypotension.

Paediatric population
APO-go POD is contraindicated for children and adolescents under 18 years of age (see Section 4.3).

Elderly
The elderly are well represented in the population of patients with Parkinson's disease and constitute a high proportion of those studied in clinical trials of apomorphine. The management of elderly patients treated with apomorphine has not differed from that of younger patients. However, extra caution is recommended during initiation of therapy in elderly patients because of the risk of postural hypotension.

Renal impairment
A dose schedule similar to that recommended for adults, and the elderly, can be followed for patients with renal impairment (see Section 4.4).

Method of Administration

APO-go POD is for subcutaneous use.

APO-go POD is a pre-diluted solution intended for use without dilution as a continuous subcutaneous infusion by minipump. APO-go POD is designed to be used with the pump (Crono APO-go III Infusion Pump) and the **Crono*Bell Sleeve***. These are CE marked medical devices.

The components required to set up the infusion are listed below:

- Infusion line
- **Crono*Bell Sleeve***
- Cartridge
- Pump (Crono APO-go III Infusion Pump) with collar attachment.

A summary of the instructions for setting up the infusion can be found in Section 6.6.

Apomorphine must not be used via the intravenous route.

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.

4.5 Interaction with other medicinal products and other forms of interaction

Patients selected for treatment with apomorphine are almost certain to be taking concomitant medicinal products for their Parkinson's disease. In the initial stages of apomorphine therapy the patient should be monitored for unusual undesirable effects or signs of potentiation of effect.

Neuroleptic medicinal products may have an antagonistic effect if used with apomorphine. There is a potential interaction between clozapine and apomorphine, however clozapine may also be used to reduce the symptoms of neuropsychiatric complications.

If neuroleptic medicinal products have to be used in patients with Parkinson's disease treated by dopamine agonists, a gradual reduction in apomorphine dose may be considered when administration is by minipump (symptoms suggestive of neuroleptic malignant syndrome have been reported rarely with abrupt withdrawal of dopaminergic therapy).

Based on reports of profound hypotension and loss of consciousness when apomorphine was administered with ondansetron, the concomitant use of apomorphine with drugs of the $5HT_3$ antagonist class is contraindicated (including, for example, ondansetron, granisetron, dolasetron, palonosetron and alosetron) (see Section 4.3).

Antiemetics with anti-dopaminergic actions (for example, haloperidol, chlorpromazine, promethazine, prochlorperazine, metoclopramide, levopromazine and droperidol) have the potential to worsen the symptoms in patients with Parkinson's disease and should be avoided. In addition, use of these anti-emetics could increase the risk of QT prolongation, hypotension and torsade de pointes arrhythmias.

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

Antihypertensive and Cardiac Active Medicinal Products
Even when co-administered with domperidone, apomorphine may potentiate the antihypertensive effects of these medicinal products (see Section 4.4).

It is recommended to avoid the administration of apomorphine with other drugs known to prolong the QT interval.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no experience of apomorphine usage in pregnant women.

Animal reproduction studies do not indicate any teratogenic effects, but doses given to rats which are toxic to the mother can lead to failure to breathe in the newborn. See Section 5.3.

APO-go POD should not be used during pregnancy unless clearly necessary and, if used, the risk of depressed respiration in newborns warrants close monitoring immediately following delivery.

Breast-feeding
It is not known whether apomorphine is excreted in human breast milk. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with APO-go POD should be made taking into account the benefit of breast-feeding to the child and the benefit of APO-go POD to the woman.

Fertility
There is no data on the effects of APO-go POD on fertility.

4.7 Effects on ability to drive and use machines

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 themselves or others at risk of serious injury or death until such recurrent episodes and somnolence have resolved (see also Section 4.4).

4.8 Undesirable effects

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/1,000)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not know (cannot be estimated from the available data)

System Organ Class	Very Common	Common	Uncommon	Rare	Very Rare	Not known
Blood and lymphatic system disorders			Haemolytic-anaemia, thrombocy-t openia	Eosinophilia		
Immune system				Allergic reactions		

disorders				(including anaphylaxis and bronchospasm)[1]		
Psychiatric disorders	Hallucina-tions	Neuro-psychiatric disturbances (including transient mild confusion and visual hallucina-tions)				Impulse control disorders[2], aggression, agitation
Nervous system disorders		Transient sedation[3], somnolence, dizziness/ light headedness	Dyskinesia[4], sudden sleep onset episodes[5]			Syncope, headache
Vascular disorders			Postural hypotension[6]			
Respiratory, thoracic and mediastinal disorders		Yawning	Breathing difficulties			
Gastrointestinal disorders		Nausea[7], vomiting[7]				
Skin and subcutaneous tissue disorders			Local and generalised rashes			
General disorders and administration site conditions	Infusion site reactions[8]		Injection site necrosis and ulceration			Peripheral oedema
Investigations			Positive Coombs' test			

[1] due to the presence of sodium metabisulfite
[2] includes: pathological gambling, increased libido, hyper-sexuality, compulsive spending or buying, binge eating and compulsive eating) see Section 4.4
[3] at the start of therapy may occur; this usually resolves over the first few weeks
[4] during 'on' periods, which can be severe in some cases, and in a few patients may result in cessation of therapy
[5] see Section 4.4
[6] postural hypotension is usually transient (see Section 4.4)
[7] particularly when apomorphine treatment is first initiated, sometimes as a result of the omission of domperidone (see Section 4.2)
[8] these may include subcutaneous nodules, induration, erythema, tenderness, panniculitis, and local reactions such as irritation, itching, bruising, pain

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

There is little clinical experience of overdosewith apomorphine by this route of administration. Symptoms of overdosemay be treated empirically as suggested below:-
-excessive emesis may be treated with domperidone
-respiratory depression may be treated with naloxone
-hypotension: appropriate measures should be taken, e.g. raising the foot of the bed
-bradycardia may be treated with atropine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-Parkinson drugs, Dopamine agonists.

ATC Code: N04B C07

Apomorphine is a direct stimulant of dopamine receptors and while possessing both D1 and D2 receptor agonist properties does not share transport or metabolic pathways with levodopa.

Although in intact experimental animals, administration of apomorphine suppresses the rate of firing of nigro-striatal cells and in low dose has been found to produce a reduction in locomotor activity (thought to represent pre-synaptic inhibition of endogenous dopamine release) its actions on parkinsonian motor disability are likely to be mediated at post-synaptic receptor sites. This biphasic effect is also seen in humans.

The efficacy and safety of apomorphine continuous subcutaneous infusion was evaluated in a randomised, placebo controlled, 12 week double blind study in patients with Parkinson's disease with motor symptoms not adequately controlled on oral/transdermal medication. Patients who entered the double blind phase (DBP) of the study were invited to re-consent to take part in an open label phase (OLP) for up to a further 52 weeks. A total of 107 patients were randomised at the start of the DBP and 84 patients went on to the OLP.

In both phases, patients began infusions with 1 mg/hour with rate increases of 0.5-1.0 mg/hr per day until either a maximum of 8 mg/hr or control of motor symptoms, whichever came first. Other antiparkinsonian drugs could be gradually discontinued in the first 4 weeks of treatment. In the DBP, each patient received a starting dose of apomorphine or placebo as subcutaneous infusion of 1 mg/hour during the first day of titration (Visit 3, Day 1). The hourly flow rate was adjusted by increasing daily by 0.5-1.0 mg/hour during Visit 3 (5-10 days as inpatient or outpatient) and up to Visit 6 (Week 4) of double blind treatment, to an expected steady state infusion rate of 3-8 mg/hour for 14-18 hours per day, depending on individual tolerability and efficacy.

The primary efficacy endpoint was the least squares mean change in 'off' hours per day recorded in patient diaries comparing Day 0 and Week 12 in the modified intent to treat (mITT) population (n=105, 53 apomorphine and 52 placebo) using a mixed effects model for repeated measures (MMRM). The analysis of 'off' time showed a statistically significant reduction in 'off' time for patients treated with apomorphine compared to placebo (p=0.0047), (Table 1).

These data were supported by secondary endpoints in the DBP and in the mITT population of change in daily 'on' time without troublesome dyskinesia and Patient's Global Impression of Change (PGI-C), tested hierarchically. The PGI-C scale ranges from 1 (very much improved) to 7 (very much worse). The least squares mean change in daily 'on' time without troublesome dyskinesia showed a statistically significant increase for patients taking apomorphine compared to placebo (p=0.0022) (Table 1) and the PGI-C score was statistically significantly higher at Week 12 for apomorphine compared to placebo (p<0.0001) (Table 2).

Table 1: Summary of efficacy results from DBP of study comparing continuous subcutaneous infusion of apomorphine vs placebo

Treatment Group	n	Baseline Mean (SD) hours	Endpoint Mean (SD) hours	LS Mean (SE) of change hours	LS Mean (SE) of difference hours	p value
Primary endpoint: Change in daily 'off' time over 24 hours						
Apomorphine	53	6.69 (2.224)	4.06 (0.414)	-2.61 (0.414)	-1.87 (0.654)	0.0047
Placebo	52	6.79 (2.569)	5.92 (0.463)	-0.75 (0.463)		
Secondary endpoint: Change in daily 'on' time without troublesome dyskinesia over 24 hours						
Apomorphine	53	8.56 (2.329)	11.49 (0.423)	2.90 (0.423)	2.05 (0.666)	0.0022
Placebo	52	8.62 (2.477)	9.44 (0.476)	0.85 (0.476)		

Table 2: Number of patients by PGI-C score (DBP)

Status at Week 12 compared to baseline	Apomorphine (n=43)	Placebo (n=34)
Very much improved	3 (7.0%)	0

Much improved	12 (27.9%)	2 (5.9%)
Minimally improved	19 (44.2%)	6 (17.6%)
No change	3 (7.0%)	12 (35.3%)
Minimally worse	2 (4.7%)	10 (29.4%)
Much worse	4 (9.3%)	3 (9.7%)
Very much worse	0	0
p value (Wilcoxon Rank Sum Test)	<0.0001	

Eighty-four patients entered the OLP, 40 from the apomorphine group and 44 from the placebo group, and all received apomorphine starting the day after the DBP Week 12 visit, titrated again from 1 mg/hour to a maximum of 8 mg/hour or when motor symptoms were controlled, whichever came first. Results are summarised in Table 3 and show that patients who had been treated with apomorphine in DBP continued to experience a response for up to 52 weeks in the OLP and patients who had received placebo in the DBP (apomorphine naïve) responded to apomorphine and maintained a response for up to 52 weeks. The OLP was not powered for statistical analysis of these results.

Table 3: Summary of efficacy results in open label phase

Treatment Group	**n**	**OLP Baseline Mean (SD) hours**	**Week 52 OLP Mean (SD) hours**	**Mean (SD) of change hours**
Change in daily 'off' time over 24 hrs OLP Week 52 compared to OLP Baseline				
Apomorphine	40	4.1 (3.6)	3.4 (3.1)	-0.6 (3.1)
Apomorphine naive	44	6.2 (2.9)	2.8 (2.1)	-3.6 (2.3)
Change in daily 'on' time without troublesome dyskinesia OLP Week 52 compared to OLP Baseline				
Apomorphine	40	11.3 (3.8)	12.0 (3.3)	0.7 (3.2)
Apomorphine naive	44	9.3 (3.7)	12.2 (3.1)	3.0 (3.1)

The European Medicines Agency has waived the obligation to submit the results of studies with APO-go POD 5 mg/ml solution for infusion in cartridge in all subsets of the paediatric population in Parkinson's disease (see Section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption
Apomorphine is rapidly and completely absorbed from subcutaneous tissue, correlating with the rapid onset of clinical effects (4-12 minutes), and the brief duration of clinical action of the active substance (about 1 hour) is explained by its rapid clearance.

Distribution
After subcutaneous injection of apomorphine, its fate can be described by a two-compartment model, with a distribution half-life of 5 (±1.1) minutes.

Biotransformation
The metabolism of apomorphine is extensive and complex and involves enzymatic and non-enzymatic degradation pathways. Hepatic metabolism by glucuronidation and sulphonation occurs to at least ten per cent of the total. Extrahepatic metabolism involves intravascular oxidation, methylation and enteric sulfation.

Elimination
After subcutaneous injection of apomorphine, its fate can be described by a two-compartment model, with a distribution half-life of 5 (±1.1) min and an elimination half-life of 33 (±3.9) minutes.

Linearity/non-linearity
Apomorphine exhibits linear pharmacokinetics.

Pharmacokinetic/pharmacodynamic relationships
Clinical response correlates well with levels of apomorphine in the cerebrospinal fluid; the active substance distribution being best described by a two-compartment model.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional repeat dose subcutaneous toxicity studies, beyond the information included in other sections of the SmPC.

In vitro genotoxicity studies demonstrated mutagenic and clastogenic effects, most likely due to products formed by oxidation of apomorphine. However, apomorphine was not genotoxic in the *in vivo* studies performed.

The effect of apomorphine on reproduction has been investigated in rats. Apomorphine was not teratogenic in this species, but it was noted that doses which are toxic to the mother can cause loss of maternal care and failure to breathe in the newborn.

Carcinogenicity studies have been conducted in mice (short term) and rats (lifetime). Both studies demonstrated skin inflammatory changes at sites of repeated injection with the incidence of skin adenomas being increased at the highest dose administered. There was a higher incidence of testicular Leydig cell tumours in rats although the mechanism by which this occurs is not believed to be relevant in humans.

Environmental Risk Assessment (ERA)
Apomorphine is a well-established active substance. Apomorphine is unlikely to represent a risk to the environment following its prescribed use in patients.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium metabisulfite (E223)
Hydrochloric acid, concentrated (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years
Once opened, APO-go POD should be used immediately.
Any unused solution should be discarded after 48 hours and a new cartridge used.

6.4 Special precautions for storage

For storage conditions after first opening of this medicinal product, see Section 6.3.
Do not store above 30°C.

6.5 Nature and contents of container

A 20 ml Type I, clear glass siliconized cartridge with a chlorobutyl rubber stopper, aluminium seal (with purple flip-off cap) and siliconized chlorobutyl rubber plunger.
Each pack contains 5 cartridges containing 20 ml solution in a cardboard tray, inside an outer cardboard carton.
The CronoBell Sleeve is supplied separately in blister packs containing 5 CronoBell Sleeves.
Bundle packs of 25 and 50 cartridges are available:

- The 25 cartridge bundle packs consist of 5 packs, each containing 5 cartridges.
- The 50 cartridge bundle packs consist of 10 packs, each containing 5 cartridges..

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused solution should be discarded after 48 hours.

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.

After use, the infusion line, CronoBell Sleeve and cartridge should be discarded and disposed of in a 'Sharps' bin.

How to set up the infusion with APO-go POD:
Wash and dry your hands before handling any infusion equipment.
Make sure you have a 'Sharps' bin and these items before you begin:

- 1 x Infusion line
- 1 x **Crono*Bell Sleeve***
- 1 x Cartridge
- 1 x Pump (Crono APO-go III Infusion Pump or Crono PAR4 20 Infusion Pump), with collar attachment
- Tray

A box of single use sterile Luer caps may also be provided.

Infusion line

CronoBell Sleeve

Cartridge

Luer cap

Crono APO-go III Infusion Pump with collar attachment

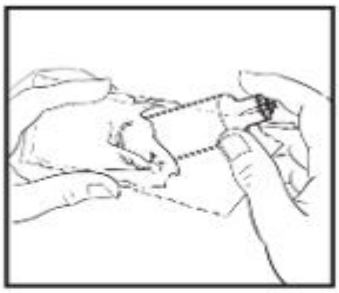
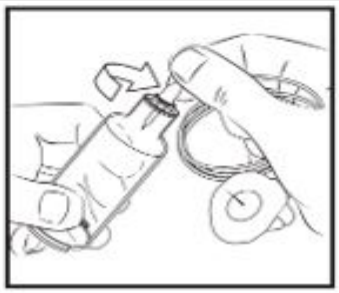
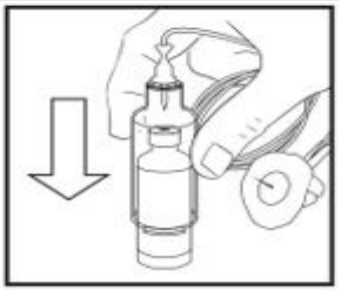
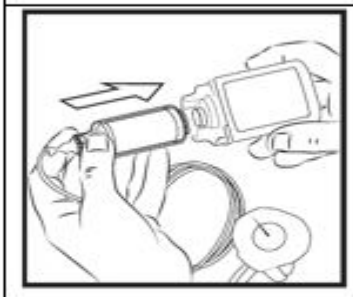
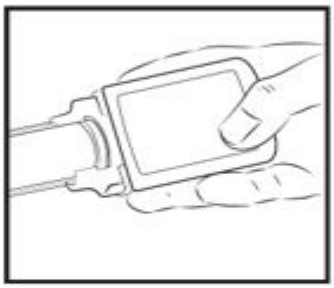
Or

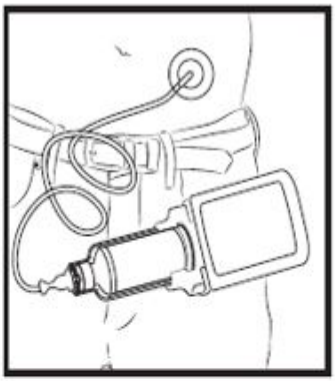
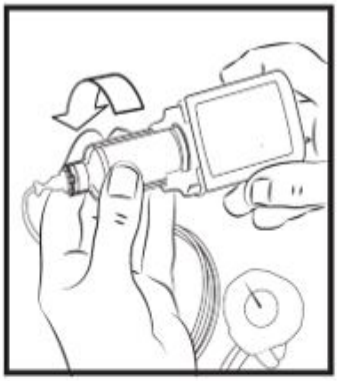
Crono PAR4 20 Infusion Pump with collar attachment

Please note that there are three different scenarios on how to use and change the cartridge and are shown in the steps below.

Instructions for using the cartridge for one day

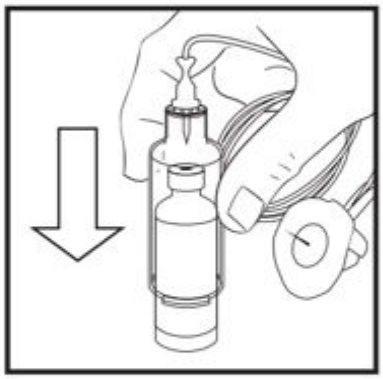
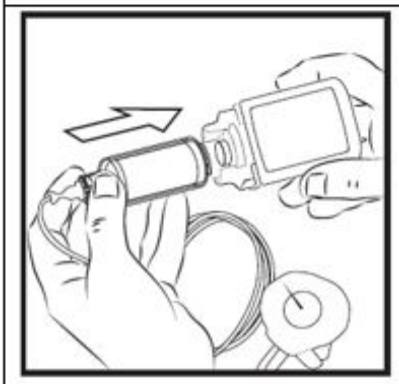
Please follow the steps below if using the cartridge for one day, without changing the cartridge during the day:

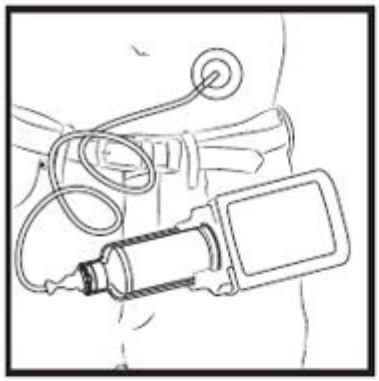
		
1. Wash and dry your hands	2 Remove plastic cap from the cartridge and discard.	3. Remove CronoBell Sleeve from its sterile packaging.
		
4. Connect the infusion line to the top of the CronoBell Sleeve and turn clockwise until tight.	5. Place the cartridge on a flat surface and push the CronoBell Sleeve firmly down onto the cartridge until the rubber bung in the top of the cartridge is pierced.	6. The CronoBell Sleeve (with cartridge and infusion line) is now ready to be connected to the pump.
		
7. Slide the CronoBell Sleeve (with cartridge inside) into the collar on the pump aligning the outer lip on the CronoBell Sleeve with the gap in the collar of the pump.	8. Once inserted, turn the CronoBell Sleeve (with cartridge inside) clockwise until it clicks into place.	9. If instructed by your healthcare professional, the infusion line can be primed. Insert the infusion line, as directed by your healthcare professional. Please refer to the APO-go Skin Management Guide.

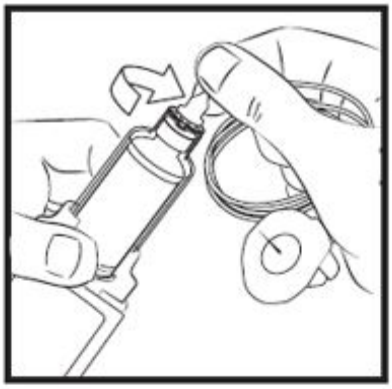
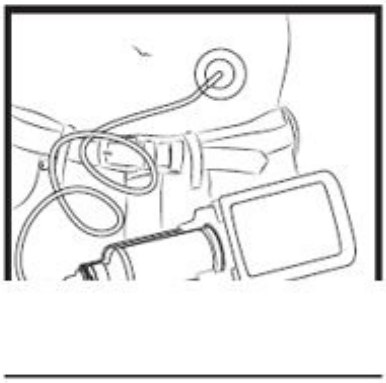
		
10. Once the infusion line needle is inserted into the body, the pump can be switched on and the infusion started. At the end of the infusion stop the pump and detach the infusion line from the body/patient. The infusion is generally stopped before sleeping.	11. Ensure the pusher of the pump is fully retracted, once this is done the CronoBell Sleeve (with cartridge inside) and the infusion line can be turned and detached.	12. Dispose of the CronoBell Sleeve (with cartridge inside) and the infusion line in a sharps bin

Instructions for using the same cartridge over 2 days

Please use the following steps if using the cartridge up to a maximum of 48 hours:

		
1. Wash and dry your hands	2 Remove the plastic cap from the cartridge and discard.	3. Remove the CronoBell Sleeve from its sterile packaging.
		
4. Connect the infusion line to the top of the CronoBell Sleeve and turn clockwise until tight.	5. Place the cartridge on a flat surface and push the CronoBell Sleeve firmly down onto the cartridge until the rubber bung in the top of the cartridge is pierced.	6. The CronoBell Sleeve (with cartridge and infusion line) is now ready to be connected to the pump.
		
7. Slide the CronoBell Sleeve (with cartridge inside) into the collar on the pump aligning the outer lip on the CronoBell Sleeve with the gap in the collar of the pump.	8. Once inserted, turn the CronoBell Sleeve (with cartridge inside) clockwise until it clicks into place.	9. If instructed by your healthcare professional, the infusion line can be primed. Insert the infusion line, as directed by your healthcare professional. Please refer to the APO-go Skin Management Guide.

	**How to put the pump with cartridge and CronoBell sleeve away for the night (steps 11-13)**	
10. Once the infusion line needle is inserted into the body, the pump can be switched on and the infusion started. At the end of the infusion stop the pump. The infusion is generally stopped before sleeping.		11. Wash and dry your hands as in step 1 and detach the infusion line from the body/patient. Place the pump standing upwards on the tray with the cartridge/sleeve still attached. Detach the infusion line from the pump and dispose of in the sharps bin. Wipe any spillage with the alcohol wipe.
		**How to start the infusion the following morning (steps 14-17)**
12. Screw the sterile Luer cap onto the CronoBell Sleeve (leaving cartridge inside).	13. Place the tray with the infusion pump in a safe place. Store below 30°C and do not refrigerate. Keep out of reach from children.	

		
14. The following day, wash and dry your hands.	15. Unscrew the Luer cap and dispose of in the bin. Clean the top of the CronoBell Sleeve with an alcohol wipe. Immediately, take a new infusion line and connect to the top of the CronoBell Sleeve (with cartridge still inside) by turning clockwise until tight.	16. If instructed by your healthcare professional, the infusion line can be primed. Insert the infusion line, as directed by your healthcare professional. Please refer to the APO-go Skin Management Guide.
		
17. Once the infusion line needle is inserted into the body, the pump can be switched on and the infusion restarted. At the end of the infusion stop the pump and detach the infusion line from the body/patient.	18. Ensure the pusher of the pump is fully retracted, once this is done the CronoBell Sleeve (with cartridge inside) and the infusion line can be turned and detached.	19. Dispose of the CronoBell Sleeve (with cartridge inside) and the infusion line in a sharps bin.

Instructions for changing the cartridge during the day

If you are using the cartridge for more than one day, it may be necessary to use a new cartridge when the old one finishes. Please use the following steps when changing the cartridge during the day:

		
1. Wash and dry your hands.	2. Remove the plastic cap from the new cartridge and discard.	3. Remove the CronoBell Sleeve from its sterile packaging.
		
4. Place the cartridge on a flat surface and push the CronoBell Sleeve firmly down onto the cartridge until the rubber bung in the top of the cartridge is pierced.	5. The CronoBell Sleeve (with cartridge) is now ready to be connected to the pump. Wipe any spillage with the alcohol wipe.	6. Stop the infusion.
		
7. Detach the infusion line from the used CronoBell sleeve (with cartridge inside), leaving the infusion line in the skin.	8. Wipe the end of the infusion line with a new alcohol wipe. In order to prevent contamination, do not touch the end of the infusion line except to wipe it.	9. Connect the infusion line to the new CronoBell Sleeve (with cartridge inside).

		
10. Ensure the pusher of the pump is fully retracted, once this is done the used CronoBell Sleeve (with cartridge inside) can be turned and detached.	11. Dispose of the used CronoBell Sleeve (with cartridge inside) in a sharps bin.	12. Slide the new CronoBell Sleeve (with cartridge inside) into the collar on the pump aligning the outer lip on the CronoBell Sleeve with the gap in the collar of the pump.
		
13. Once inserted, turn the CronoBell Sleeve (with cartridge inside) clockwise until it clicks into place.	14. The pump can be switched on and the infusion started.	

Note: Different infusion lines require different insertion techniques. The choice of needle will be determined by the physician.

User guides for the pump and CronoBell Sleeve are provided for the healthcare professional, refer to these for details on how to set up APO-go POD for continuous infusion and additional bolus dosing.

There are differences in the pump used to administer this product and some other apomorphine products on the market. Therefore, if the patient switches from or to a different product, re-training under the supervision of a healthcare professional is required.

After use, the infusion line, CronoBell Sleeve and cartridge should be discarded and disposed of in a 'Sharps' bin. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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D-61118 Bad Vilbel
Germany

8 MARKETING AUTHORISATION NUMBER

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Date of first authorisation: 13th November 2020

10 DATE OF REVISION OF THE TEXT

September 2023