SmPC

Country : :	Lebanon
Date of approval	07.03.1998
Procedure:	National

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

APOKINON 30 mg/3 ml (1%), solution for injection in pre-filled pens

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Apomorphine hydrochloride .....30.00 mg
Sodium sulphite solution ..... 9 microlitres
Concentrated hydrochloric acid..... q.s. pH = 2.5 to 4.0
Water for injection ..... q.s. 3 ml
for one pre-filled pen.

3. PHARMACEUTICAL FORM

Solution for injection

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Adjunct treatment for severe fluctuations of dopamine treatment activity in Parkinson's disease (on-off phenomenon).

4.2. Posology and method of administration

Sub-cutaneous; discontinuous administration.

Start with a subcutaneous injection of 1 mg (or 20 µg/kg); increase by 1 mg steps in case of ineffectiveness until a releasing effect is obtained (reversal of the "off" period).

Dosage varies depending on the patient.
For a given patient, effective dosage usually is identical from one injection to another (see section 6.5).

4.3 Contraindications

This medicine is contraindicated in cases of:

- hypersensitivity to apomorphine,
- liver failure,
- mental deficiency,
- confusion,
- psychotic manifestations,
- combination with antiemetic neuroleptics (see section 4.5).

4.4 Special warnings and precautions for use

Drowsiness has been reported during treatment with apomorphine, and cases of sudden-onset sleep during treatment with dopaminergic agonists, particularly in patients with Parkinson's disease. Patients must be informed of the possibility of occurrence of these effects, and they should be warned to be cautious when driving motor vehicles or using machines during apomorphine treatment. Patients having experienced drowsiness or sudden-onset sleep should not drive vehicles or use machines. A reduction of doses or discontinuation of treatment may be considered.

As with all precision instruments, the pen must be maintained with care.

Avoid exposing the pen to dust and extreme temperatures. Make sure the cap is on the pen between two uses.

If the pen drops, verify that it operates correctly and that there is no leak of the medicine.

It is important for a member of the patient's family to also learn to use the pen in case the patient cannot carry out the injection him or herself.

Apomorphine must be used with care in cases of a history of psychic disorders following the administration of anti-Parkinson drugs, or of recent, severe cardiovascular disorders.

Digestive disorders and orthostatic low blood pressure can be avoided by administering domperidone by oral route: start domperidone 4 days before the start of apomorphine treatment, at the dose of 20 mg three times a day. Discontinue domperidone gradually, starting at the third week, by a 10 mg reduction every 3 days except if undesirable effects appear.

When administered discontinuously, apomorphine does not require a dosage reduction of other dopaminergic drugs.

Cases of compulsive gambling, hypersexuality and increased libido have been reported in patients with Parkinson's disease treated with dopaminergic agonists, particularly apomorphine. These cases have mainly occurred in

patients treated with high doses, and were generally reversible after reducing doses or discontinuation of dopaminergic agonist treatment (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Combination that is contraindicated:

+ **Antiemetic neuroleptics**: reciprocal antagonism of the dopaminergic agonist and neuroleptics.

  Use an antiemetic without extrapyramidal effects.

Combination that is not recommended

+ **Antipsychotic neuroleptics** (except clozapine): reciprocal antagonism of the dopaminergic agonist and neuroleptics.

  The dopaminergic agonist may cause or aggravate psychotic disorders. If it is necessary to administer neuroleptics to Parkinson patients treated with dopaminergic agonists, the latter should be reduced progressively until cessation (the abrupt cessation of dopaminergics may cause the "malignant neuroleptic syndrome").

4.6 Pregnancy and lactation

There are no reliable animal teratogenesis data available.
Currently, there are not enough clinically relevant data to assess a potential effect of apomorphine on malformations or foetal toxicity when it is administered during pregnancy.
As a result, it is recommended not to use this medicine in pregnant women, even if the age of the population makes pregnancy unlikely.

This medicine passes into mother's milk and so breast-feeding is to be avoided during its use.

4.7 Effects on ability to drive and use machines

Patients treated with apomorphine presenting drowsiness must be informed that they must not drive a vehicle or carry out any activity where a lapse of attention could expose them or others to the risk of a serious accident or death (e.g. use of machines). This applies until the drowsiness has disappeared (see section 4.4).

4.8 Undesirable effects

- drowsiness has been reported during treatment with apomorphine,
- nausea, vomiting,
- orthostatic low blood pressure,
- fatigue, pallor, salivation, perspiration,

- psychic disorders requiring dosage reduction, even treatment interruption,
- pruritus at the point of injection,
- because of the presence of sulphite, there is a risk of allergic reaction, including anaphylactic reactions and bronchospasms,
- cases of compulsive gambling, hypersexuality and increased libido have been reported since Apokinon has become available (see section 4.4).

4.9 Overdose

- Severe respiratory depression: treatment with naloxone.
- Bradycardia: treatment with atropine.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ANTIPARKINSON DRUGS, DOPAMINERGIC AGENTS, ATC code: N04BC07
(N: nervous system)

Apomorphine: dopaminergic agonist stimulating D1 and D2 receptors.
In the substantia nigra, apomorphine exerts an antiparkinson effect by stimulating post-synaptic dopaminergic receptors.
It has a powerful emetic effect by stimulating dopaminergic receptors in the area postrema.

5.2 Pharmacokinetic properties

When administered parenterally, action is rapid (2 to 10 minutes). The average elimination half-life is 34 minutes. The duration of action is short (45 to 90 minutes depending on the patient).
Apomorphine is metabolized by conjugation with glucuronic acid.
It is excreted in the urine primarily in glucuronide form.

5.3 Preclinical safety data

6. PHARMACEUTICAL PARTICULARS

6.1 Incompatibilities

6.2 Shelf life

2 years in the initial conditions of storage.
30 days after the first use.

6.3 Special precautions for storage

Store at a temperature lower than 25°C.

6.4 Nature and contents of container

3 ml in a cartridge (glass) with an injection pen; box of 1

6.5 Instructions for use, handling instructions

How the pen is supplied and used is described in the document given to the doctor and in the leaflet.

1°/ Description of the APOKINON pen

The pen is supplied without a needle. Use needles for injector pens, preferably 28G. The pen is supplied with a cartridge containing 3 ml (30 mg) of apomorphine and so is ready to use.

The dose prescribed by your doctor is adjusted using the mark on the dosage button, graduated from 1 to 10. The number selected sets the dose, for example if you select 5 then the dose of 5 mg will be injected. Doses can be selected in 1 mg steps.

The pen can be used for several injections. The cartridge cannot be recharged and the pen is discarded when the cartridge is empty or if the remaining quantity of apomorphine is not sufficient.

2°/ Using the pen

a) Installing the needle

Place a needle, a cotton ball and alcohol on a clean surface. Take a pen. Remove the cap from the pen. Disinfect the membrane with the cotton moistened with alcohol. Remove the paper film from the needle. Hold the pen and screw the needle all the way onto the membrane. The needle must be fully inserted into the pen.

b) Adjusting the dose

The dose to inject is indicated by numbers from 1 (1 mg) to 10 (10 mg). Simultaneously push and turn the dosage button clockwise until the blue line is opposite the number corresponding to the prescribed dose. **Verify the dose selected**.
The clicks you hear mean only that the blue mark is lined up with the selected number.
Important:

- When using the pen for the first time, if the prescribed dose is 1 mg (dose "1") and only in this case, do not inject this first dose, but empty it (for example, into a paper towel)
- If you go past the desired dose, simply continue to push and turn the dosage button in the same direction until the desired dose is reached.

c) Injection

Arm the pen by gently pulling the dosage button until it stops. The graduation mark corresponding to the chosen dose appears on the end of the cartridge.
Never try to modify the dose when the pen is in "armed" position. In case of an error when selecting the dose, dispose of the incorrect dose, for example into a paper towel, then select the correct dose described above under "adjusting the dose".
Disinfect the skin where the injection is to be performed. Remove the needle cap. Remove the protective film.
Insert the needle at the injection site. To inject, push the dosage button all the way, preferably with your thumb. Once the button stops, count to 3 before removing the pen.
Place the needle cap on the used needle.
Hold the pen firmly and unscrew the needle with its cap counterclockwise. Discard the needle and its cap. Put the cap on the pen. The pen is ready for the next use.

d) Subsequent uses of the pen

- Adjusting the dose

In general, the first dose selected remains unchanged for subsequent uses. You can check again that the blue mark is lined up with the number corresponding to the prescribed dose.

- Injection

Gently pull the dosage button all the way out. If the dose to inject is available, the mark corresponding to the chosen dose will appear on the end of the plunger. Install the needle, referring to the section on the first use.

If the dose to inject is not available, the mark corresponding to the chosen dose will not appear on the end of the plunger. Place the cap on the pen and discard the pen. Use a new pen to inject the prescribed dose.