PARKINSON'S DISEASE
Subcutaneous Delivery Route

Authors: C. Sinclair, M. Bendixen and P. K. Schøndorff

PARKINSON'S DISEASE

Parkinson's Disease (PD) is a progressively disorder neuropathologically characterized by the degeneration of dopamine producing neurons in the substantia nigra. Current pharmacological intervention in PD is symptomatic.

Disease characteristics can significantly reduce quality of life of the individual by impacting emotional wellbeing, mobility, activities of daily living, and the ability to communicate with others[1]. The key clinical features in Parkinson's disease are tremor, rigidity, bradykinesia and the individual may also present with impaired balance[2].

CONTINUOUS INFUSION

For patients, whose motor fluctuations are not optimally managed by oral medication, a more consistent maintenance of dopamine level is achieved by administering apomorphine by continuous subcutaneous infusion[3].

An evidence-based review of continuous subcutaneous apomorphine infusion (CSAI) concluded that subcutaneous apomorphine infusion is successful in reducing off time, dyskinesias[4,5] and improving HRQoL[6]. Nodule formation occur to some degree in the majority of patients treated chronically with apomorphine infusions[7] and thought to be a reaction to the drug itself[8].

NODULE FORMATION AND PREVENTION

Histologically, nodules consist of a focal panniculitis, without systemic eosinophilia, which could be due to a hypersensitivity reaction to either apomorphine or the preservative, but the histopathology of the nodules is poorly understood[8].

For most patients experiencing significant nodule formation, the difficulty in finding useable infusion sites was cited as the most significant problem[3]. Other factors are likely to contribute to nodule formation, and there may be a scope for lessening nodule formation and other tissue reactions by attending to factors such as[3,9]:

- Fine needle design
- Easy insertion technique
- Use of a wider area and rotation
- Improved hygiene

In a review of best practice, it was concluded that attention to cleanliness and injection site rotation are effective measures to reduce the incidence of nodule formation[10].

By auditing patients Jan Parsons found that fine needle design easy to place, resulted in fewer incidences of injection site problems with Neria™ needle. **A typic comment was:** easier to insert and do['es] not seem to have as many nodules[9].

Nodules can furthermore be avoided by use of ultrasound treatment and massage, transcutaneous electric nerve stimulation, Teflon, silicone patches or heparin creams or the use of higher apomorphine dilutions[10,11].

DRUG/ DEVICE STABILITY TESTS

According to Medical Device Regulations 2017/745 healthcare professionals must be able to rely on medical device manufacturers to perform adequate test to establish safe and effective use.

To ensure that ConvaTec Infusion sets during normal use with apomorphine do not have any negative influence on the stability of medication, drug/device stability tests have been carried out by external institutes like Teknologisk Institut.

SUBCUTANEOUS DELIVERY ROUTE

Each patient will have different symptoms, depending on their condition and the kind of treatment they may be having, and each patient must be considered on an individual basis. Compared to intrajejunal levodopa and deep brain stimulation, CSAI therapy is the least invasive of these three advanced therapeutic options, is reversible, practical to use and has shown significant efficacy for the management of the peak-effect dyskinesias and off-period non-motor-symptoms[12].

The most common sites for the infusion set to be inserted are abdomen and thigh. It is important to consider comfort, safety and the rotation of insertion sites.

It is recommended that some areas are avoided, including the following:

- Areas of lymphoedema or nodules;
- Areas of inflammation;
- Tumour sites;
- Close to broken skin;
- Bony prominences.

DRUG/DEVICE TEST METHOD

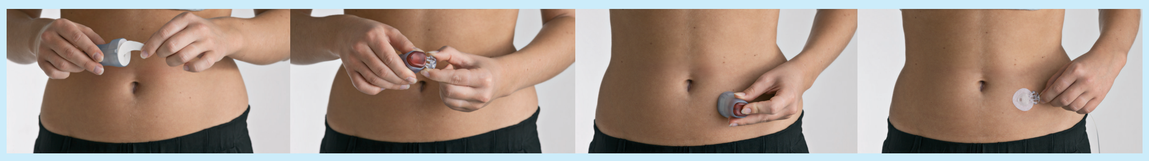
The stability test method used is a modified version of the USP assay (2008 USP Monographs: Apomorphine Hydrochloride). The USP assay method is a titration method and the method is found having fine linearity and precision.

Syringes with apomorphine was connected to pump simulator which was set to 0.1 ml per hour. Infusion set tubing was immersed in water bath of 37-0±0.2°C for 16 hours, samples collected and titration with 0.1N Perchloride acid took place until color change endpoint was obtained. Device Compatibility tests were conducted to detect any physical changes in infusion set, after being exposed to the drugs and in a test environment of 37°C[13,14,15].

Both drug and device tests concluded that the infusion sets are safe to use with apomorphine[16, 17].

NERIA™ GUARD/CONVATEC

ConvaTec offers a range of infusion sets for subcutaneous infusion which have all been drug/device stability tested for safe use with medication indicated for targeted disease areas. The latest development is the neria™ guard, an infusion set for fully automatic insertion by the touch of a button. neria™ guard has also been tested to be suitable for self-administration of apomorphine at home due to the simple insertion technique[18].



Berit Öqvist, Parkinson's Disease Patient in CSAI therapy:

I got the opportunity to try neria™ guard, which was new on the market and it was really an improvement. The biggest difference between the infusion set I had before, and neria™ guard is that I can press a button and the needle goes in. I don't have to press the needle in by myself."

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Aaholmvej 1-3, Osted | DK-4320 Lejre | Denmark