



MEMO

TO: Health Care Professionals and Providers, Patients, Employees, Affiliates and Partners

FROM: Global Medical Office

DATE: September 24, 2020

SUBJECT: Further statement on the withdrawal of APEX time on POL 6.2

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Healthcare professionals strive for 'personalized medicine' in order to achieve the best outcome and safety in patients receiving renal replacement therapy. Fresenius Medical Care is dedicated to developing new products, therapies and services allowing physicians and nurses to prescribe and apply truly personalized treatments. Adapted Automated Peritoneal Dialysis (aAPD) reflects one cornerstone of individualized dialysis therapy, specifically designed to enable improvement in patients' fluid status, solute adequacy and eventually mortality from cardiovascular disease.

The aAPD concept is based on a profile of mixed PD cycles with individualized fill volumes and dwell times and was first proposed by Fischbach et al. in 1994 in children [1].

In a study cohort of adult patients published in 2011 [2], aAPD was applied by combining a sequence of short dwells (to enhance ultrafiltration volume (UF)) with long cycles (to ensure adequate solute clearance including large uremic toxins). This study indicated the following therapeutic advantages:

- Improved UF
- Better sodium removal
- Lower blood pressure
- Improved clearance of urea, creatinine, phosphate
- Reduced metabolic load

#### Original Accelerated Peritoneal EXamination (APEX)

The **original** APEX method was conceived by Dr. Christian Verger primarily as an alternative method to the conventional Peritoneal Equilibration Test (PET) for interpretation of peritoneal membrane transport characteristics [3]. Typically, 2 L of hypertonic glucose PD fluids are used. Essentially 5 samples of dialysis effluent are withdrawn over a timeframe of 2 hours. The time course of D/Purea and D/D0 glucose is determined from the sampled data. The point at which the D/Purea trace crosses the D/D0 glucose is known as the 'APEX' time.

#### APEX as implemented in PatientOnLine 6.2 (POL)

In order to leverage the data from routine tests such as the PET or PFT, another method of calculating the APEX time was developed. This avoided the need for a customer to perform an APEX test according to the **original** version for the sole purpose of obtaining an APEX time. This calculation method employed the existing models within the software POL to characterize the time courses of D/Purea and D/D0 glucose. It is also important to note that the use of PET or PFT data are typically collected over different time frames compared with the **original** APEX and PD fluids of different glucose composition may be used. On the one hand, the APEX time calculation provided in POL may be considered reasonable from the point of view of operational efficiency. However, on the other hand, when the resulting APEX time determined

by the POL method is compared against the APEX time from original APEX, discrepancies cannot be ruled out. This issue represents one of the reasons leading to the decision to remove the POL APEX time calculation from subsequent versions of POL.

### **The use of APEX time to establish optimal aAPD dwell durations**

While the effect of short and long PD cycles is understood in terms of UF and solute clearance, a systematic method to calculate the optimal dwell durations of an aAPD profile based on the APEX time was proposed by Fischbach et al. [2,4,5]. In the meantime, no further evidence has been generated that associates the application of this approach with clinical outcome benefit.

### **The Impact of the European Medical Device Regulation (EU MDR)**

The MDR soon comes into effect within the EU community; requiring a comprehensive clinical evaluation of all medical devices bearing a CE mark. Mandatory compilation of standardized clinical evaluations reports (CER) of all its products is a part of the holistic quality management approach of Fresenius Medical Care. Medical experts within our company concluded recently during the generation of the CER on the software POL that use of the APEX time to determine optimal aAPD dwell durations for individual patients required further evidence to meet with the criteria of the upcoming EU MDR. Following thorough analyses of potential options, it was decided to remove all calculations from POL that are related to APEX and that are subsequently used for aAPD profiling.

### **Recommendations for the deployment of aAPD going forward**

We would like to emphasize our continued commitment to personalized medicine. The PD-I.D.E.A study, which is a multi-center and international observational study primarily investigating the influence of aAPD treatment on hydration status, where different aAPD profiles are also investigated, will be concluded very soon and is expected to provide further insights (clinicaltrials.gov identifier: NCT02470598). Based on the results of this study, we anticipate planning further studies to investigate different aspects of the aAPD methodology.

Until further evidence of improved methodology becomes available, establishing the optimal dwell duration for aAPD profiles remains a matter of clinical experience and judgement of the attending physician.

Despite the withdrawal of the calculation of the APEX time, POL continues to support aAPD prescription and therapy monitoring on a number of fronts: the modelling capability of POL provides an estimate of the expected direction of Kt/V when prescribing aAPD profiles. UF information may be reviewed in POL for every PD cycle, providing important hints to assess the influence of short dwells in particular. If the clinician is in any doubt regarding the efficacy of a desired aAPD profile, the quality assurance (24-hour batch) tools in POL may be invoked as a cross check. POL provides a comprehensive portfolio of features, vital for the continued evolution of aAPD methodology and ongoing generation of evidence.

In case of further questions please contact:

Medical Information and Education, EMEA  
[Medinfo-EMEA@fmc-ag.com](mailto:Medinfo-EMEA@fmc-ag.com)

Dr. Fatih Kircelli

Medical Information and Education, EMEA

Global Medical Office



Dr. Dr. Elke Schulte

Medical Affaires / Medical Devices & Drugs

Global Medical Office

## References

- [1] Fischbach M, Desprez P, Donnars F, Hamel G, Geisert J. Optimization of CCPD prescription in children using peritoneal equilibration test. *Adv Perit Dial* 1994; 10: 307-9.
- [2] Fischbach M, Issad B, Dubois V, Taamma R. The beneficial influence on the effectiveness of automated peritoneal dialysis of varying the dwell time (short/long) and fill volume (small/large): a randomized controlled trial. *Perit Dial Int* 2011;31(4):450-8.
- [3] Verger C, Larpent L, Veniez G, Corvaisier B. [Monitoring of the peritoneal permeability in peritoneal dialysis]. *Rev Prat* 1991 Apr 21;41(12):1086-90. French.
- [4] Fischbach M, Zaloszc A, Schaefer B, Schmitt C. Adapted automated peritoneal dialysis. *Adv Perit Dial* 2014; 30:94-7.
- [5] Fischbach M, Załoszc A, Schaefer B, Schmitt CP. Optimizing peritoneal dialysis prescription for volume control: the importance of varying dwell time and dwell volume. *Pediatr Nephrol.* 2014;29(8):1321-7.