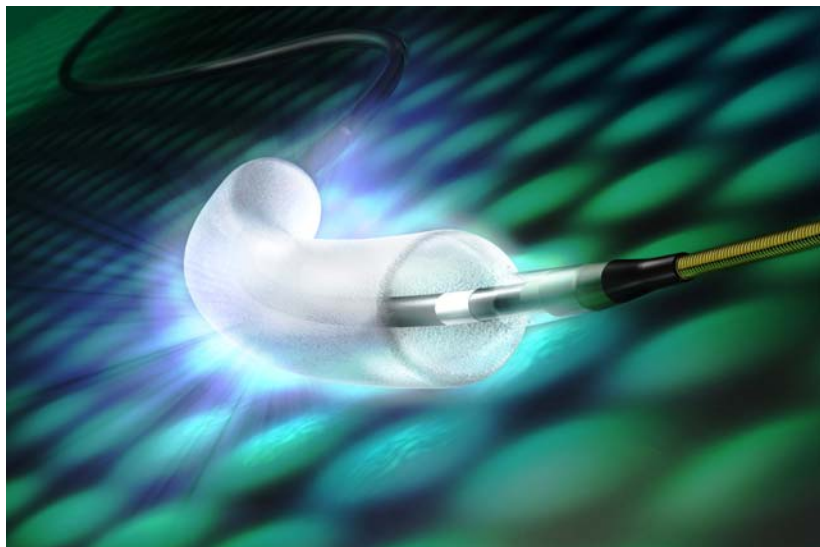


Drug Eluting Coronary Balloon Catheter (DEB) – to reduce In-Stent Restenosis (ISR = blockage of implanted stents)

1. Overview



SeQuent® Please – Drug Eluting Coronary Balloon Catheter (DEB)

Introduction / importance

- In Germany 380,000 coronary stents were implanted in 2007. Restenosis occurs in 10 to 20% of all stent implantations.
- Considerable costs are generated in case of re-interventions due to restenosis (additional stent and / or PTCA catheter, drug therapy).
- The possible annual savings with SeQuent® Please – Drug Eluting PTCA-Balloon are in the range of 50 to 60 million Euro.

Field of application

- In the so called interventional cardiology, blocked coronary arteries are diagnosed and treated in a minimally invasive way with catheters. It is a sub-discipline of cardiology. In most cases interventional therapy can be done instead of open heart surgery.
- The SeQuent® Please DEB offers the interventional cardiologists a more effective and cost-saving treatment of patients with ISR.

Mode of action

- Besides the mechanical expansion (re-opening) of the coronary artery, SeQuent® Please DEB provides a targeted drug delivery in the pathologically modified vessel segment. Thereby the risk of vessel wall proliferation triggered by arterial injury is decreased or inhibited. This reduced vessel wall proliferation leads to a lower restenoses rate in the treated vessel segment.

Special features

- The drug delivery for the ISR-treatment is not stent based but it is mediated by a short contact of the coated balloon catheter with the vessel wall.

2. Innovation

Technical description of the innovation

- SeQuent Please® is a conventional catheter for Percutaneous Transluminal Coronary Angioplasty (PTCA) whose balloon section at the distal end is coated with a homogenous matrix of Paclitaxel and contrast media (Iopromid). Paclitaxel is the pharmacologically active component of this matrix coating. Coated on numerous drug eluting stents Paclitaxel has already been used in coronary interventions for years. Paclitaxel inhibits cell division of smooth muscle cells by stabilizing the so called microtubules during mitosis.

Novelty value of the method / field of indication / market penetration

- The primary field of DEB application is coronary ISR. The clinical efficacy and safety of the DEB catheter for the indication of ISR was demonstrated in 3 randomized clinical trials (ISR I&II and PEPCAD II). The data regarding de novo lesions are very promising in small vessels (PEPCAD I).

Improvements compared to existing methods / history / efficacy

- In Germany 380,000 coronary stents were implanted in 2007.
- Re-interventions are to be expected in 8 to 20% of all interventions depending on the implanted stent type (i. e. bare metal stent or drug coated metal stent).
- Bare metal stents (BMS) require a post-procedural therapy with platelet aggregation inhibitors during one month.
- The requested post-procedural drug therapy after implantation of a drug eluting stent (DES) is usually extended to twelve months.

SeQuent Please: Benefits (for patients, physicians, hospitals, payers)

- Patients: Reduction/prevention of re-interventions, safer treatment, possible repeatable DEB-treatment significantly shortened drug therapy with less side effects
- Physicians: More effective ISR-treatment, easier treatment in general, better lesion accessibility, prevention of open heart surgery
- Hospitals: Prevention of re-interventions after failed revascularization of so called ISR
- Payers: Initially cost-neutral ISR-treatment with DEB compared to DES, enormous cost saving potential regarding re-intervention rates and significantly shortened post-interventional drug therapy with SeQuent® Please DEB

3. Cost-benefit analysis

The possible cost-savings with SeQuent Please DEB catheter are demonstrated based on a shortened drug therapy with platelet aggregation inhibitors. The number of DES interventions in ISR were calculated based on the number of implanted BMS and DES and their respective restenosis rates.

The possible cost-savings with SeQuent Please in Germany were calculated as follows:

Initial situation (2007)	BMS	DES	Total
Number of stents	250,000	130,000	380,000
ISR rate	20%	10%	
N° of stents with ISR	50,000	13,000	63,000
ISR treated with DES	80%	75%	
N° of DES interventions	40,000	9,750	~ 50.000*

Thus only in Germany 50,000* drug eluting stents were implanted as method of choice for the treatment of ISR in 2007.

- Cost-saving potential due to a shorter duration of accompanying drug therapy

The DGK¹ position paper recommends a 12 month post-procedural drug therapy with platelet aggregation inhibitors (e. g. Plavix®, Iscover®) if ISR are treated with DES. In case a DEB is used, only a 3 month drug therapy is sufficient, this leads to a difference of 9 months. With the daily drug costs of 2.02€/patient the cost savings are € 553 per patient in 9 months (= 274 days). This results in annual cost savings of € ~27.5 million for 50,000 ISR patients treated with DEB instead of DES.

- Cost-saving potential due to a lower re-intervention rate

Furthermore, cost savings can be realized due to a reduced number of re-interventions after failed revascularization. With the use of conventional DES the rate is about 18.0%^{2,3,4} versus 3.2%² with SeQuent Please. The difference of 14.8% is equal to ~7.400 patients. The costs of a re-intervention, according to DRG revenues, are 4,271.28 € per patient (average hospital stay). The difference in re-intervention rates results in an annual cost saving potential of ~31,6 million Euro.

- Combining the cost savings for drug therapy and re-interventions the use of SeQuent® Please results in an annual saving potential of ~59 million Euro.
- This cost benefit analysis was done with the assumption of equal occurrences of rare complications, e. g. thromboses or dissections, with both treatment options (DES and DEB).
- The updated DGK position paper⁵ considers SeQuent® Please as possible therapy form ISR.

Current reimbursement situation (DRG, "Hilfsmittelverzeichnis", ...)

- LBFW 2007 for Berlin € 2960, Association of health insurance providers for employees (= Verband der Angestellten Krankenkassen)
- "Fallpauschalen" catalogue diagnosis related group (DRG) F52B €1,490
- Platelet aggregation inhibitors (Clopidogrel, Iscover) public health insurance (GKV) price/day € 2.02 (Fricke et al., Herz', 20, 2005, Nr.4, S. 332-338)
- ¹Position paper of the German Society for Cardiology (DGK) regarding efficacy and safety of drug eluting coronary stents (DES), Der Kardiologe 2007 · 1:84–111
- ²FDAnews Device Daily Bulletin, Oct. 26, 2007 | Vol. 4 No. 211
- ³ Morice, MC et al., The REALITY Trial: A Randomized Controlled Trial, *JAMA*. 2006;295:895-904
- ⁴ Kastrati, A et al., Sirolimus-eluting stent or paclitaxel-eluting stent, *JAMA*. 2005 Jan12;293(2):165-71
- ⁵ Update of the DGK position paper, *Clin Res Cardiol* 97:548–563 (2008)