DRUG-ELUTING BALLOONS - US ANALYSIS AND MARKET FORECASTS
The table below provides the key metrics for drug-eluting balloons (DEB) for coronary and peripheral applications in the lower extremity in the US market.

### DEB for Coronary and Peripheral Applications*, Key Metrics in the US Market

<table>
<thead>
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<th>Diagnosed Prevalence (2012)</th>
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<tr>
<td>Coronary artery disease (CAD)</td>
<td>1.4 million</td>
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<tr>
<td>Peripheral artery disease (PAD)</td>
<td>1.5 million</td>
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<table>
<thead>
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<th>2012 DEB Market Sales ($m)</th>
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<tbody>
<tr>
<td>US</td>
<td>$0.00m</td>
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</table>

### Pipeline Assessment

- **Stage of clinical development**
  - Number of DEB in the early development stage: 3
  - Number of DEB in the preclinical stage: 1
  - Number of DEB in the early clinical stage: 8
  - Number of DEB in the late clinical stage: 3

### Key Events (2012–2019)

- **Commercial launch of DEB, such as IN.PACT and Lutonix DCB for PAD in the lower extremity, in 2015 in the US**
  - Level of Impact: ↑↑↑

- **Expected commercial launch of coronary DEB, such as Elutax SV, Lutonix DCB, Dior, and Magic Touch, in 2015 in the US**
  - Level of Impact: ↑↑

- **Commercial launch of DEB, such as Protégé, Pioneer, Danubio, Restore DEB, and Legflow DEB, in 2016 in the US**
  - Level of Impact: ↑↑

### 2019 DEB Market Sales ($m)

| US                                  | $121.8m      |

Source: GlobalData

Peripheral applications include arteries in the lower extremity such as the iliac, femoropopliteal, and infrapopliteal arteries.

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**Sales of Drug-Eluting Balloons by Region**

DEB are currently not available for sale in the US and are expected to enter the market beginning from 2015 and specifically for peripheral applications. The sales of DEB for coronary artery disease (CAD) and peripheral artery disease (PAD) in the lower extremity in 2015 in the US are estimated to be $13.5m.

DEB can be used for select coronary and peripheral indications, including in-stent restenosis (ISR), small-vessel disease, bifurcation lesions, and femoropopliteal artery and below-the-knee (BTK) lesions. DEB angioplasty can improve the clinical outcomes for these select indications and the quality of life for patients suffering from these debilitating diseases.

By the end of the forecast period, sales of DEB will grow to $122m at a Compound Annual Growth Rate (CAGR) of 73% from 2015-2019.

The key drivers for this market during the forecast period are:

- The rising prevalence of CAD and PAD
- The need for effective therapies that reduce the risk of complications such as restenosis and thrombosis, and the need for target lesion revascularization (TLR) associated with bare metal and drug-eluting stenting
Executive Summary

- The cost savings for healthcare payers resulting from the reduced need for repeat revascularization procedures and prolonged dual antiplatelet therapy
- Reducing the need for stent-in-stent procedures, where DEB can become the gold standard of treatment for ISR
- The technical feasibility of future interventions
- The approval and launch of coronary and peripheral DEB, such as IN.PACT, SeQuent Please, Lutonix DCB, Dior, Protégé, Elutax SV, and Magic Touch, in the US

US Drug-Eluting Balloons Market

Percutaneous coronary interventions (PCI) and endovascular therapies, such as angioplasty and stenting, are widely used in clinical practice to treat patients with CAD and PAD. DEB are an emerging, innovative technology that can be effectively used for the treatment of select coronary and peripheral indications, including ISR, small-vessel disease, bifurcation lesions, and superficial femoral artery (SFA) and BTK lesions. The peripheral market in the lower extremity presents greater opportunity and value for DEB, where they have the potential to become primary therapy for femoropopliteal and infrapopliteal artery disease.

As DEB receive approval and enter the US market, the coronary and peripheral DEB markets are expected to grow steadily. By 2019, the coronary and peripheral markets for DEB are estimated to be $42m and $79m, respectively. The DEB for peripheral applications accounts for over 60% of the overall DEB market.

The adoption of DEB is expected to increase in the future as the next generation of DEB platforms enters the market, long-term clinical data become available, appropriate reimbursement rates are established, and high selling prices decrease. In addition, the tendency to use multiple DEB per procedure, especially for femoropopliteal and infrapopliteal applications, will drive the DEB market in the US.

Within the peripheral DEB market in the lower extremity, the femoropopliteal revascularization market for DEB has the largest market share, accounting for nearly 50% of the peripheral DEB market, followed by that for infrapopliteal (BTK) revascularization.

Unlike in the femoropopliteal and BTK artery markets, DEB are not expected to be widely used to treat patients with iliac artery disease. Stenting remains the treatment of choice for treating the iliac arteries, given its high procedural and clinical success. The femoropopliteal and infrapopliteal DEB markets are approximately three times that of the iliac market in the US.
Executive Summary

Unmet Needs Remain a Challenge

Although stent technologies have evolved over the years, complications such as thrombosis and restenosis, negative vessel remodeling, delayed endothelialization and healing, lack of homogenous drug distribution, and the need for prolonged dual antiplatelet therapy remain. Patients with ISR who are treated with drug-eluting stents (DES) have high risk of clinical failure, where performing stent-in-stent procedures leads to the formation of multiple layers of metal and increases the risk of chronic inflammation and recurrent stenosis. Currently, there is no effective therapy for treating patients with ISR, a challenge that DEB can address. In addition, treating small coronary vessel disease and the side branches of coronary bifurcations is challenging, given that these lesions are associated with a high risk of restenosis, and outcomes with stenting are suboptimal.

In the peripheral vasculature, treating the femoropopliteal and infrapopliteal arteries is difficult, given the diffuse nature of the atherosclerotic disease, long lesions with heavy calcifications, and exposure to high external forces.

For patients with severe critical limb ischemia (CLI), effective therapies are needed to prevent major amputation, which can reduce the quality of life for these patients.

Low-profile drug-delivery systems need to be developed to reduce the risk of restenosis and thrombosis, and improve long-term patency. Effective therapies need to be developed to treat complex lesions and challenging patient populations, such as chronic total occlusions (CTOs), long lesions, diabetes mellitus, and acute myocardial infarction (heart attack). In addition, the high restenosis rates associated with standard balloon angioplasty warrant the development of effective alternative therapies. With DEB, the antiproliferative benefits of a DES are maintained without the complications of a permanent implant left behind or late stent thrombosis.

Key Players in the Global Drug-Eluting Balloon Market

As illustrated in the figure below, the global DEB market for treating CAD and PAD in the lower extremity is a small but dynamic market with several key players, including Medtronic, B. Braun, Eurocor, C.R. Bard, Biotronik, and Cook Medical. The competitive landscape consists of large, mid-size, and small companies that have developed DEB to target specific patient populations within the coronary and peripheral markets. Companies such as Blue Medical, Cardionovum, and Minvasys are strong potential competitors in the market.

DEB developed by these companies have received the CE (Conformité Européene [European Conformity]) Mark and are commercially available. These companies have not yet received FDA approval and launched in the US market.
Companies such as Medtronic are leading the race to launch DEB in the US by 2015, specifically for peripheral applications.

GlobalData believes that as the next generation of DEB enters the market, the current key players will need to retain and acquire market share by improving the clinical performance of their existing products.

Global DEB Market for Treating CAD and PAD in the Lower Extremity, Company Share (%), 2012

“Others” category includes the companies Blue Medical, Cardionovum, Minvasys, and Acrostak.

Source: GlobalData

US Drug-Eluting Balloons Market Future Outlook

DEB provide short-term, homogenous local drug delivery and enhanced vessel healing, with no permanent metal implant left behind. In the future, DEB can become the gold standard of treatment for coronary and peripheral ISR. In interventional cardiology, optimizing the outcomes of stenting with DEB does not have the same value as in the peripheral market. In the coronary market, there are already excellent DES that provide optimized treatment for the patient, where DES are considered to be the standard of treatment. DEB-only or DEB with stenting approaches can be used to treat niche coronary indications, such as small-vessel disease, bifurcations, and CTOs. However, in endovascular therapy, DEB can become a primary treatment for femoropopliteal artery and BTK lesions, where stenting is associated with high rates of restenosis and poor outcomes.

Device manufacturers are developing innovative DEB platforms to improve the mechanical properties of DEB, minimize drug loss and trauma to the vessel wall, incorporate limus-based anti-proliferative drugs, and ensure efficient drug delivery. GlobalData believes the adoption of innovative technologies, such as DEB, will increase steadily as these products launch in the US market. However, widespread adoption will depend on the availability of long-term clinical and cost-effective data and appropriate reimbursement rates and decrease in selling prices.
Executive Summary

What Do Physicians Think?

Physicians are optimistic about the adoption of DEB for treating CAD and PAD in the lower extremity in the future.

“I am very enthusiastic and positive about this technology. With DEB, there are advantages linked to, I would say, every aspect that is characterizing and limiting DES….With DEB, there is no substance that is potentially stimulating an inflammatory reaction, where there is [a] risk of thrombosis or restenosis.”

Key Opinion Leader

“I think that DEB will get cheaper, given the increased competition, and they will be used for indications where [the] outcomes of stenting are unsatisfactory….These factors will drive the use of DEB.”

Key Opinion Leader

Physicians want to see long-term clinical data to evaluate and compare the clinical effectiveness of DEB.

“We want to see clinical trials with good data…we want to use devices that are cost-effective and best for the patient.”

Key Opinion Leader

“The clinical data subset is very weak right now. That is why the technology is lagging behind…we do not have any robust clinical data to support the use of DEB in these clinical situations. Until we have these data, it will be very difficult to have any strong indication in the future as well.”

Key Opinion Leader

“We need to have more clinical data to support this idea. If the data is positive and they [DEB] are better than DES in these lesion subsets, then it will change the whole paradigm and everyone will use DEB.”

Key Opinion Leader

The current design of DEB platforms needs to be improved to increase the predictability of the treatment and increase adoption in clinical practice.

“I think the next development step will be to design DEB that is as much as possible similar to the best-in-class standard angioplasty balloon. DEB need to be developed with better trackability…[in order to] favor advancement of the device through complex anatomy.”

Key Opinion Leader

“To adopt DEB into my practice, I need to see clinical data that it works. I need to see data that demonstrates DEB technology is reliable, where every time you treat a patient with a DEB, it is going to work similarly.”

Key Opinion Leader
Executive Summary

As cost-containment policies are implemented, the widespread adoption of expensive DEB technologies is questioned.

“I think price and access to devices are going to be issues. The current financial environment in healthcare is very uncertain….I would not be surprised that in a year or two, we will be told to prove [that] using one device over another [is better] for cost-containment purposes.

Key Opinion Leader

“DEB need to come down in price…. The cost of devices per patient should not exceed $600 to $800 in total [in order] to provide [an] incentive to hospitals and increase adoption.”

Key Opinion Leader
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2 Introduction

Coronary artery disease (CAD) and peripheral artery disease (PAD) are global public health and socioeconomic issues that affect millions of lives each year. Percutaneous coronary interventions (PCI) and endovascular therapies, such as stenting and angioplasty, have been widely adopted to treat CAD and PAD in the lower extremity. Vascular stents, such as bare metal and drug-eluting stents are often used in clinical practice to treat coronary and peripheral artery lesions. However, for indications such as in-stent restenosis (ISR), small-vessel disease, coronary bifurcations, and femoropopliteal artery and below-the-knee (BTK) lesions, stenting is associated with poor clinical outcomes, reiterating the need for alternative therapies. In addition, implanting permanent stents, such as drug-eluting stents (DES) and bare metal stents (BMS), into the vessel can increase the risk of chronic inflammation, restenosis, and thrombosis.

Emerging technologies, such as drug-eluting balloons (DEB), address the challenges and complications of stenting in these subsets of lesions. DEB provide fast, short-term, homogenous, local drug delivery, preserve the anatomy of the vessel, promote enhanced vessel healing, and reduce the need for prolonged dual antiplatelet therapy without leaving any metal behind. Medical device companies have developed a range of DEB for coronary and peripheral applications in the lower extremity. The majority of these DEB have paclitaxel as the antiproliferative drug of choice, with different drug coating technologies and balloon/catheter designs. In this report, DEB are defined as drug-coated angioplasty balloon catheters.

This report focuses on the DEB market for treating CAD and PAD in the lower extremity in the US. This report identifies the unmet needs in the market for treating CAD and PAD in the lower limb, provides an understanding of physicians' perceptions and decision-making process in using DEB, and evaluates the adoption of DEB in the future. From GlobalData’s analysis, it is evident that the current adoption of DEB for coronary and peripheral applications is slow in the EU, APAC and SA. Currently DEB are not available in the US. However, adoption of DEB is expected to increase steadily as this technology enters the US market. To successfully market DEB, companies need to design novel platforms that address the challenges in treating femoropopliteal and infrapopliteal artery lesions, coronary bifurcations, and small-vessel disease, and show that they have superior clinical performance to the stents that are used to treat these lesions.
Introduction

2.1 Catalyst

Minimally-invasive techniques, including stenting and angioplasty, have become the standard of care for patients with CAD and PAD in the lower extremity. Modern developments in endovascular interventions have led to a paradigm shift in the treatment of PAD in the lower extremity towards endovascular therapy. Although vascular stents, including bare metal, drug-eluting, and covered stents, offer treatment solutions for patients, they do not provide sustained clinical outcomes in lesions such as ISR, small-vessel disease, coronary bifurcations, and superficial femoral artery (SFA) and BTK lesions. In the peripheral vasculature, the femoropopliteal and infrapopliteal arteries are challenging to treat, given the diffuse nature of the atherosclerotic disease and long and heavily-calcified lesions. In the femoropopliteal arteries, the high plaque burden, slow vascular flow, and exposure to high mechanical forces increase the risk of stent compression and fracture. Alternative effective technologies need to be designed to address these unmet needs.

Compared with the coronary and peripheral vascular stent markets, the DEB market is a much smaller market. However, it is a dynamic market that allows device manufacturers to develop a range of platforms to target different coronary and peripheral indications. Low-profile DEB technologies are being developed to reduce the risk of complications of stenting such as restenosis and thrombosis, improve long-term vessel patency, and reduce barotrauma to the vessel. DEB-only and DEB as an adjunct therapy can be used to treat complex and challenging lesions and optimize stenting. Given the lack of effective therapies, DEB can become the gold standard of treatment for coronary/ peripheral artery ISR. In addition, DEB may become a primary therapy for treating peripheral lesions in the lower extremity, where stenting can be used as a “bailout” strategy.

As more long-term clinical data that demonstrate the superior therapeutic benefits of DEB and reimbursement become available, the adoption of DEB by the medical community will increase steadily in the future, especially in the US. As CAD and PAD present enormous global public health and socioeconomic issues, and use of stents continues to increase, it is important to find effective treatment modalities that ensure long-term quality results for patients.
13.7 About MediPoint

MediPoint is the flagship product for GlobalData’s Medical team. Each MediPoint report is built from the ground up by our team of healthcare analysts in the US and UK. Each report includes input from experienced physicians and leading key opinion leaders (KOLs). Running throughout each report in the series, “What Physicians Think” quotes provide a unique insight into how healthcare professionals are reacting to events within the industry, and what their responses could mean for industry strategists.

13.8 About GlobalData

GlobalData is a leading global provider of business intelligence in the healthcare industry. GlobalData provides its clients with up-to-date information and analysis on the latest developments in drug research, disease analysis, and clinical research and development. Our integrated business intelligence solutions include a range of interactive online databases, analytical tools, reports, and forecasts. Our analysis is supported by a 24/7 client support and analyst team. GlobalData has offices in New York, Boston, London, India, and Singapore.

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