FACTSHEET

PolyActive™
A biodegradable polymer-based drug delivery system
PolyActive
PolyActive is a biodegradable polymeric drug delivery system. Its biodegradability, extensive safety record and linear release properties make PolyActive an excellent technology for the controlled release of proteins and lipophilic small molecules. Products based on PolyActive can be used for both local and systemic administration, and have applications in pharmaceutics and medical technology.

PolyActive composition
PolyActive represents a series of poly(ether ester) multiblock copolymers, based on poly(ethylene glycol), PEG, and poly(butylene terephthalate), PBT (Figure 1). A major advantage of this system is the ability to vary the amount and length of each of the two building blocks, creating a diverse family of customized polymers. Polymer matrix characteristics such as rate of controlled release, degradation, swelling and strength can be precisely controlled by the appropriate combination of the two copolymer segments.

Degradation of PolyActive
PolyActive degradation occurs by hydrolysis of ester bonds and oxidation of ether bonds. The rate of degradation depends on the selected polymer composition: polymers with higher PEG content show a faster degradation profile. In addition, the configuration of the PolyActive product also impacts the degradation rate; e.g. microspheres, in general, degrade faster than dense cylinders (Table 1).

Table 1
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<th>Configuration</th>
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<th>Example of active compound</th>
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PolyActive applications
Using PolyActive allows the development of burst-free drug delivery systems, and its hydrophilic nature conserves the stability of labile biopharmaceuticals, such as proteins. Products made from PolyActive can be processed into various shapes and configurations, thereby allowing them to be used in a wide range of applications.

Performance
Release rates from PolyActive can be tightly controlled. Adjusting the copolymer composition gives control over both the diffusive and degradation properties of the polymer, allowing control over the release rates of diverse molecules.
In vitro studies, a constant release of compounds has been achieved from PolyActive products without an initial burst effect, with release controllable from minutes to months (Figure 2).

Excellent in vitro – in vivo correlation
PolyActive release profiles show an excellent congruence between release in vitro in PBS and in vivo in rats. With the use of PLGA-based microspheres, in vitro and in vivo release profiles may differ considerably. In contrast to PLGA-based microspheres, protein diffusion through the PolyActive hydrogel is the main rate-controlling factor, and this process progresses similarly in vitro and in vivo. This induces an excellent in vitro-in vivo correlation.

Preserved stability of the encapsulated compound
A key issue in the design of controlled release systems for biopharmaceuticals, and in particular proteins, is the integrity of the encapsulated compound. Due to the presence of hydrophilic poly(ethylene glycol) segments, PolyActive exhibits a hydrogel character, providing a natural environment for compounds such as proteins. Unlike PLGA, degradation products of PolyActive do not create an acidic environment. An acidic environment may cause the released protein to lose its activity. PolyActive preserves the activity and stability of the embedded compound. Assessment of the activity of a model protein (lysozyme) after release from PolyActive shows that the PolyActive matrix and production process have no adverse effects on protein activity (Figure 3). This is a considerable benefit compared to PLGA-based systems which have shown an extensive reduction of lysozyme activity. The preservation of biological activity after release from PolyActive has been demonstrated both in vitro and in vivo with other therapeutically relevant proteins and peptides (Table 2).

PolyActive manufacturing
PolyActive microspheres, suitable for preclinical and clinical evaluation, can be produced under cGMP conditions in OctoPlus’ pilot plant in Leiden, the Netherlands. PolyActive is manufactured under a supply agreement on 10-20 kilogram scale under GMP conditions. Polymers containing 30-90 weight percent soft segment and PEG-blocks with molecular weights varying from 300-10,000 g/mole are currently available.

Application of PolyActive in human pharmacotherapy
OctoPlus uses PolyActive to develop its controlled-release alfa interferon product Locteron™. Locteron combines PolyActive microspheres with BLX-883, a recombinant alfa interferon produced by OctoPlus’ co-development partner Biolex Therapeutics in its patented LEX System™. Figure 4 shows plasma levels of alfa interferon after subcutaneous injection of Locteron in humans. The graph shows that the release from the PolyActive microspheres does not induce a so-called burst effect and is gradual during approximately two weeks. For more information on Locteron, please refer to our Locteron Factsheet.

Similar results have been obtained with other pharmaceutical proteins in animal studies. Table 2 shows several compounds evaluated in combination with PolyActive.

Safety and clinical data
In addition to over a decade of successful in vitro toxicity and biocompatibility assays, PolyActive has been used in implants in more than 5,000 patients and in over 2,000 animals (rats, rabbits, dogs, goats). An extensive biological safety report is available for the technology, and FDA and CE approval have been granted for two implantable orthopedic medical devices made from PolyActive.

Partner with OctoPlus for drug delivery with PolyActive
OctoPlus is actively pursuing new partnerships to develop products based on the PolyActive delivery system. As a medium sized organisation, we are flexible in constructing partnership agreements and open to take on some of the risk and cost for the development of promising compounds. Our priority is to build successful long-term drug delivery partnerships. Please feel free to contact us and discuss your ideas.
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