



HESylation Innovative Drug Delivery

Innovative formulation and drug delivery play a crucial part in optimising drug characteristics, such as pharmacodynamics, side effect profiles or water solubility.

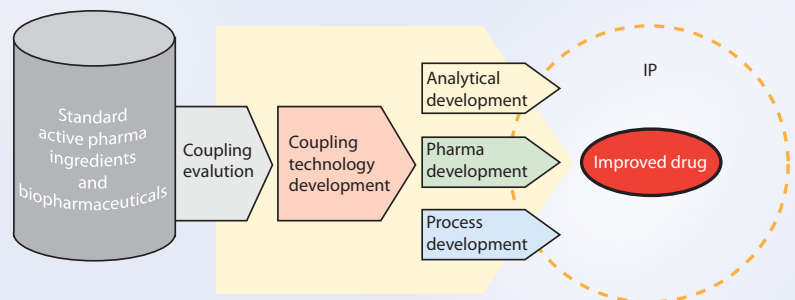
Fresenius Kabi has developed a new drug delivery technology with superior properties: the HESylation technology.

HESylation utilises hydroxyethyl starch ("HES") derivatives linked to drug substances in order to modify the drug characteristics. This modification enables the prolongation of the circulation half-life by increasing the stability of the molecule, as well as by reducing renal clearance, resulting in an increased biological activity.

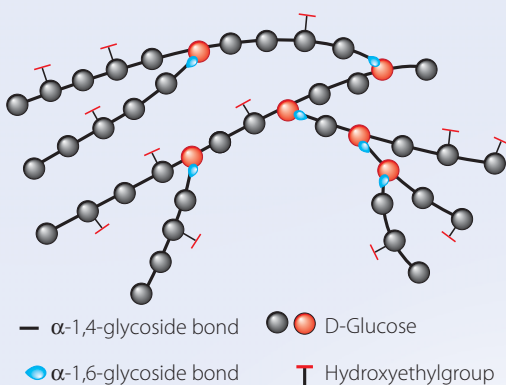
Fresenius Kabi has a broad portfolio of patents and patent applications covering coupling chemistry, special linkers and HESylated drugs on a target-by-target basis.

HESylation: the objectives

- **Enhanced Therapeutic Value through**
 - Extended circulating life
 - Improved efficacy
 - Reduced toxicity
 - Reduced immunogenicity
 - Improved solubility
 - Improved stability
- **Life Cycle Management through**
 - Patent prolongation
 - Proprietary patent position for (new) targets



HESylation: the polymer



HydroxyEthyl Starch (HES)

- A modified natural carbohydrate polymer derived from waxy maize starch
- Widely used in clinical practice for many years a/o as a blood plasma volume expander and in hemodilution
- Outstanding safety and biocompatibility record
- Various coupling strategies to target molecules available f/i through lysine, cysteine, terminal amino, or glyco-structures
- Molecular characteristics of HES can be varied through well controlled processes

HESylation: the target

- **Large therapeutic molecules such as**
 - Proteins
 - Peptides
 - (other) biomolecular therapeutics
- **Small molecule drugs**