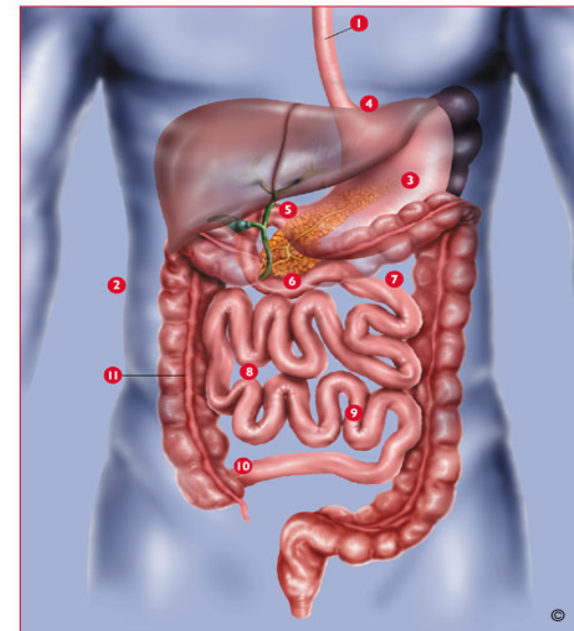


Oral Drug Delivery Market- Modified-Release to be “Adding Value” Strategy

БАФТ
София
Септември 2011

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The Human Digestive System



Oral Drug Delivery- Modified Release

Tailoring Release for Modified Release



Ascending



Delayed / Sustained



Enteric



First Order



Intestinal



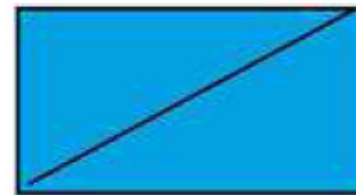
Modified Enteric



Biphasic



Pulsatile



Zero Order



Oral Drug Delivery- Modified Release

- Еволюционна промяна в генеричната индустрия формираха една нова R&D стратегия, обозначавана най-често като “Adding Value” към жизнения цикъл на продукт ;
- Фактори, отнасящи се до генеричните фирми в създаването на тази стратегия:
 1. Променената роля на генеричните лекарства в съответствие с еволюцията на фармацевтичния свят;
 2. Качество на генеричните лекарства, сравнимо с това на оригиналните с търговски марки.
 3. Доказано съответствие с нарасналите регулативни изисквания.
 4. Икономически натиск от страна на здравно-осигурителните системи, основан на повишени разходи вследствие увеличаване на възрастното население.
 5. Икономически натиск като резултат от ожесточена ценова конкуренция между самите генерични фирми.



Oral Drug Delivery- Modified Release

- Тази стратегия се използва също и от етичните фармацевтични фирми, разработващи оригинални лекарства.
- Фактори, отнасящи се до иновационните фирми:
 1. Завишените R&D разходи за откриване на нови лекарствени вещества;
 2. Предстояща атака на изтичащите патенти и търсене възможности за компенсиране на загубите, т.е. поддържане на "post-patent value" на продукта.
 3. Завишаващите се изисквания на потребителя, фармакоикономика.
- Всички фармацевтични фирми оценяват, че технологиите Modified-Release Drug Delivery са едно силно **стратегическо средство** на маркетинга за диференциране продуктите и удължаване на техния жизнен цикъл, като по този начин се преодоляват предизвикателствата на пазара.

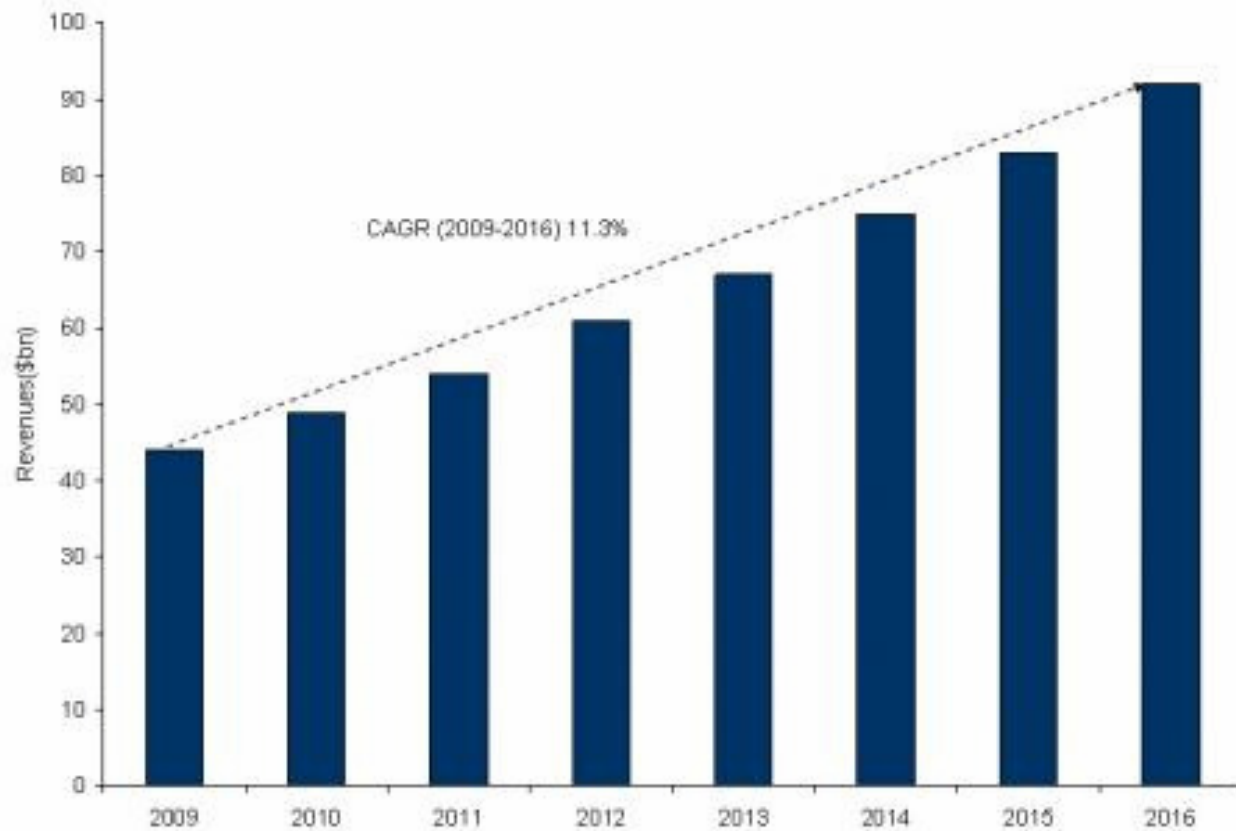


Oral Drug Delivery- Modified Release

- This has resulted in significant growth in the drug delivery market over the last few years. According to GBI Research, the overall drug delivery market is forecasted to grow to \$199 billion in 2016 from \$101 billion in 2009, at a CAGR of 10.3%.
- Central Nervous System (CNS) agents, hormone-related agents and gastrointestinal agents are among the key therapeutic areas witnessing the use of innovative drug delivery methods, and this trend is expected to grow in the coming years.
- The oral drug delivery market remains the largest segment of the overall drug delivery market, with more than 52% of the market share. It is presently valued at \$49 billion and is expected to reach \$92 billion by 2016, at a CAGR of 11.3%. The growth in the oral drug delivery market shall be driven primarily by newer technologies enabling controlled release formulations of oral drugs and oral formulations of injectable only drugs.

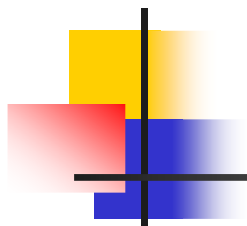
Oral Drug Delivery- Modified Release

Oral Drug Delivery Market Forecast (2009-2016)



Source: GBI Research

Oral Drug Delivery- Modified Release Bulgaria



Product	Sales 2010 [Eur]
Preductal MR 35 mg modified-release tablet (Trimetazidine dihydrochloride)	5 587 001
Tertensif SR 1.5 mg prolonged-release tablet (Indapamide)	4 385 980
Betaloc ZOK 50, 100 mg prolonged-release tablet (Metoprolol succinate)	4 220 976
Diaprel MR 30 mg modified-release tablet (Gliclazide)	2 713 444
Klacid SR 500 mg modified-release tablet (Clarithromycin)	1 281 628
Seroquel SR 200 mg, 300 mg prolonged-release tablet (quetiapine)	2 495 984
Agapurin 600 mg, 400 mg retard prolonged-release tablet (Pentoxifylline)	2 222 045
Omnitoc Tocas 0.4 mg prolonged-release tablet (Tamsulosin hydrochloride)	2 365 214
Depakine Chrono 500 mg prolonged-release tablet (Sodium valproate)	2 314 371
Auronal 2.5, 5, 10 mg prolonged-release tablet (Felodipine)	2 259 359

Oral Drug Delivery- Modified Release

Recent Trends : Quetiapine OD

- **Seroquel XR Tablets**, 50, 200, 300 and 400mg,
AstraZeneca Pharmaceuticals LP, USA
- **Technology:**
 - Film Coated Matrix tablets comprising Hypromellose as a release controlling polymer with diffusion and erosion controlled release.
- **Composition patent** claiming Gelling agents in combination with Quetiapine. Constraint of use of any of the following polymers like HPMC, HPC, Polyox, Carbopol, HEC, Ethylcellulose.



Oral Drug Delivery- Modified Release

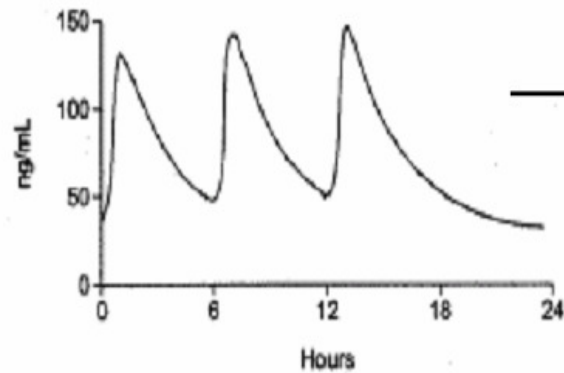
Recent Trends : Extended release formulation of Bupropion

- **Bupropion** is used in the treatment of major depressive disorder.
- **Conventional** formulation has to be administered 3 times daily
- **Initially 150 mg** ER formulation was introduced for bid regimen
- **Later on 300 mg** ER formulation was introduced for **once daily** regimen
- For ER formulation provide similar C_{max} and AUC values as compared to immediate release formulation at steady state.

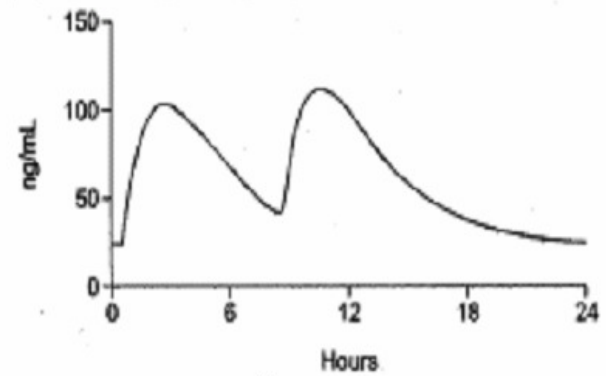
Oral Drug Delivery- Modified Release

Recent Trends : Extended release formulation of Bupropion

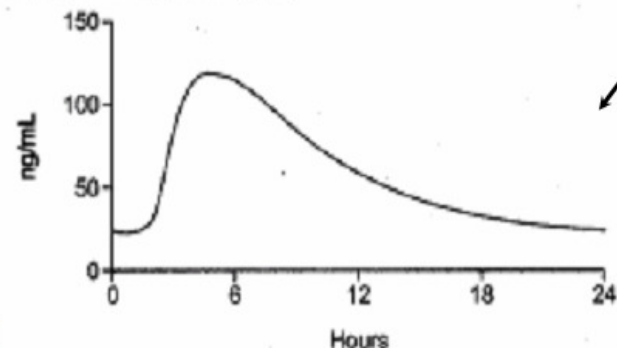
Bupropion IR (100 mg tid)



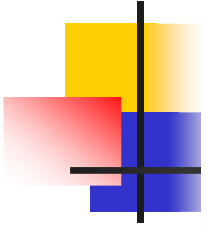
Bupropion SR (150 mg bid)



Bupropion XL (300 mg qd)



Oral Drug Delivery- Modified Release

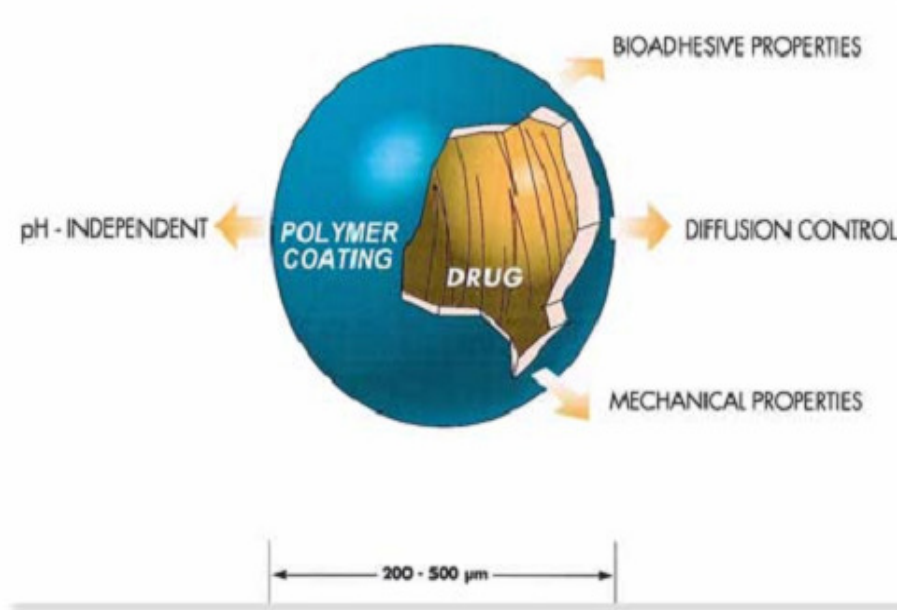


Carvedilol ER

- **Innovator – Coreg CR™** (carvedilol phosphate) extended-release capsules 10, 20, 40 and 80 mg GlaxoSmithKline
- **COREG CR** utilizes Flamel's proprietary Micropump® technology. Micropump® is a controlled release and taste-masking technology for the oral administration of small molecule drugs.
- **COREG CR** hard gelatin capsules are filled with carvedilol phosphate immediate-release and controlled-release microparticles that are drug-layered and then coated with methacrylic acid copolymers.
 - IR component as micro particle – 12.5% of dose
 - Micropump IIa – (37.5% of dose)- Releases content at pH 5.5
 - Micropump IIc – (50 % of dose)- Releases content at pH 6.4-6.8

Oral Drug Delivery- Modified Release

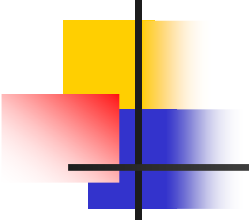
Carvedilol ER



- Technology consist of 5000- 10000 microparticles per capsule.
- 200-500 micron particles released in stomach, and pass into small intestine, where each microparticle release drug by osmotic pressure at adjustable rate over an extended period.

Oral Drug Delivery- Modified Release

Recent Trends : LEDDS Technology

- 
- Liquid and Emulsion Drug Delivery System (LEDDS)
 - Enabling Oral Controlled Release
 - 1.Liquids/Emulsions/Suspensions
 - 2.Customise drug release profile
 - Controlled
 - Sustained
 - Pulsatile
 3. Format flexibility