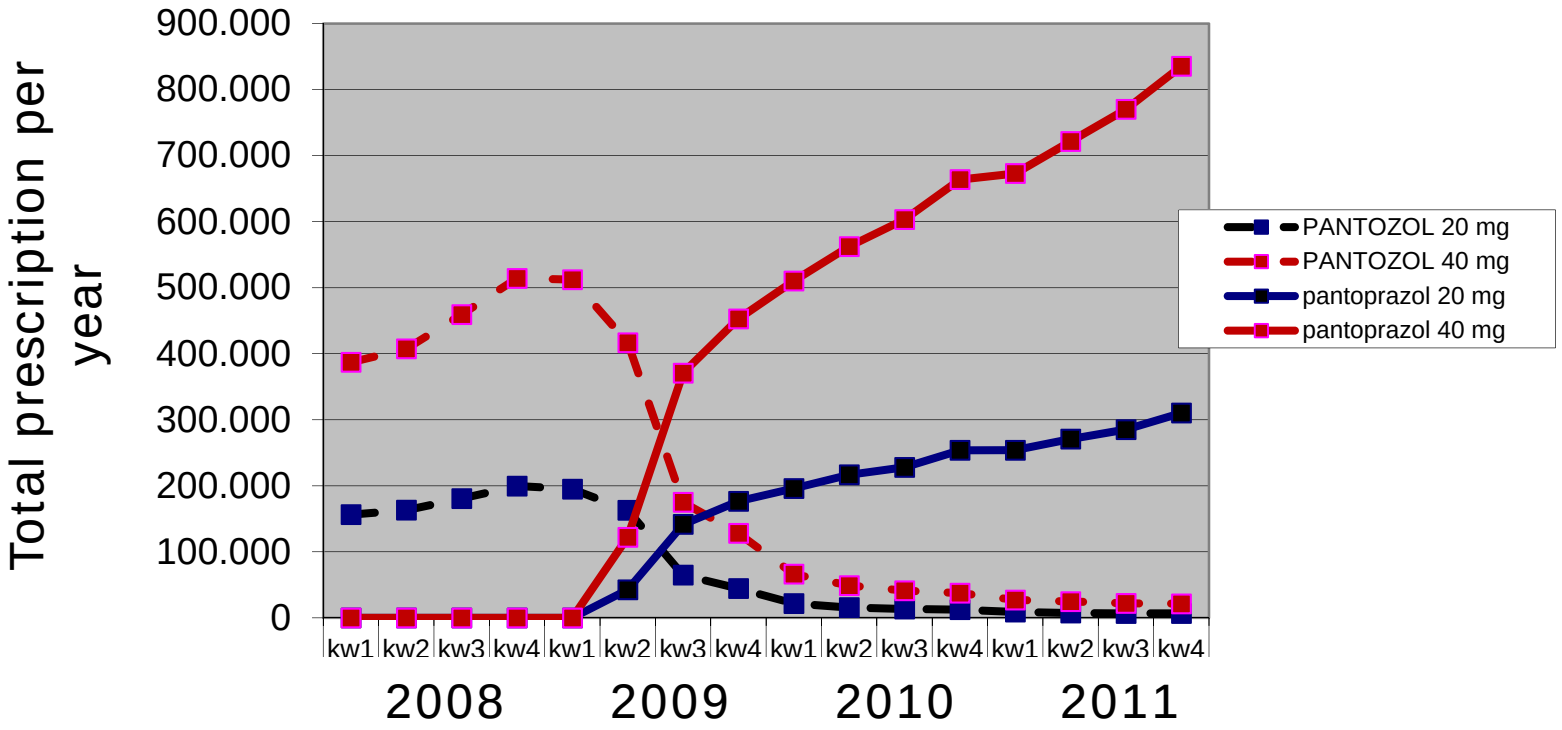
Generic Drugs in Society

Background. The Regulator's dilemma?

Marc Maliepaard, PhD
senior clinical assessor
College ter Beoordeling van Geneesmiddelen
Utrecht

Generics: changing prescriptions

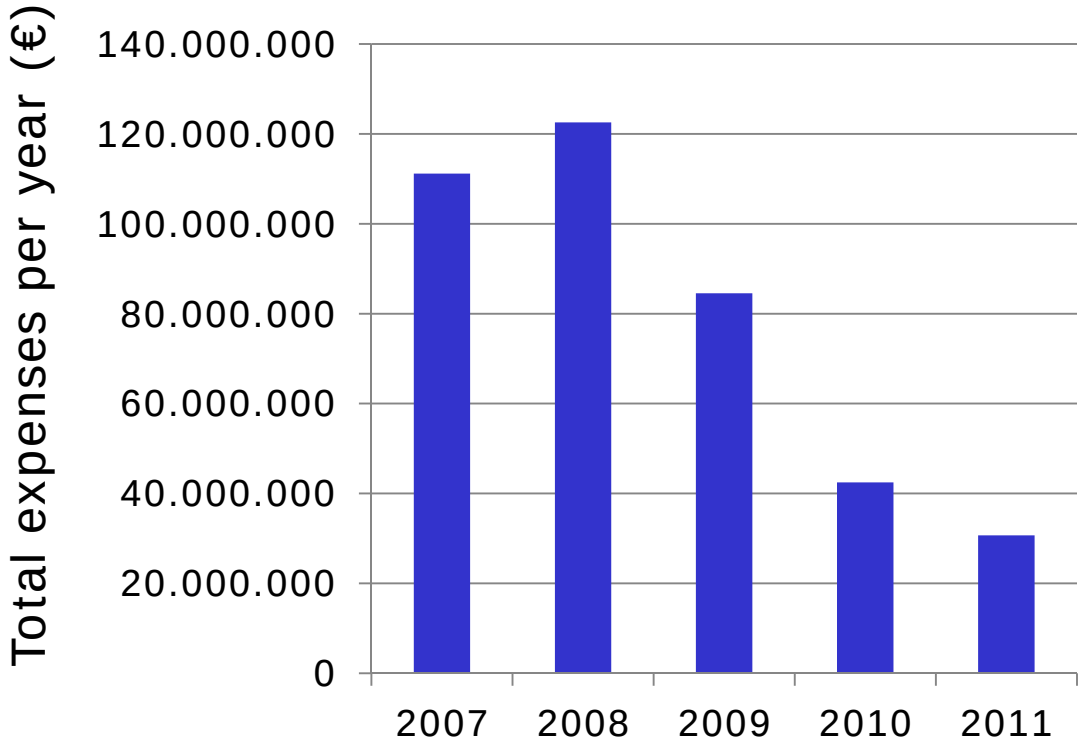
- Pantazol => pantoprazol



Bron: GIPdatabank 2012

Generics: costs

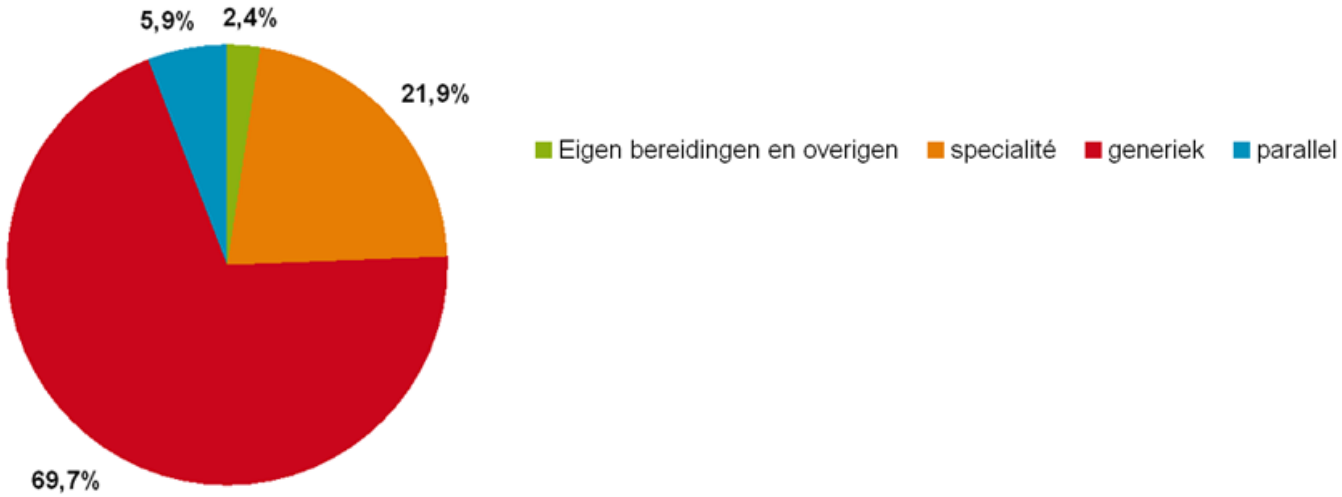
- Pantazol => pantoprazol



Bron: GIPdatabank 2012

Generics: % number of dispensed prescriptions

- 70% dispensed medicines in pharmacy is generic (2013)



- Generics only contribute 16% of the total costs for medicinal products

Generics: what is it about?

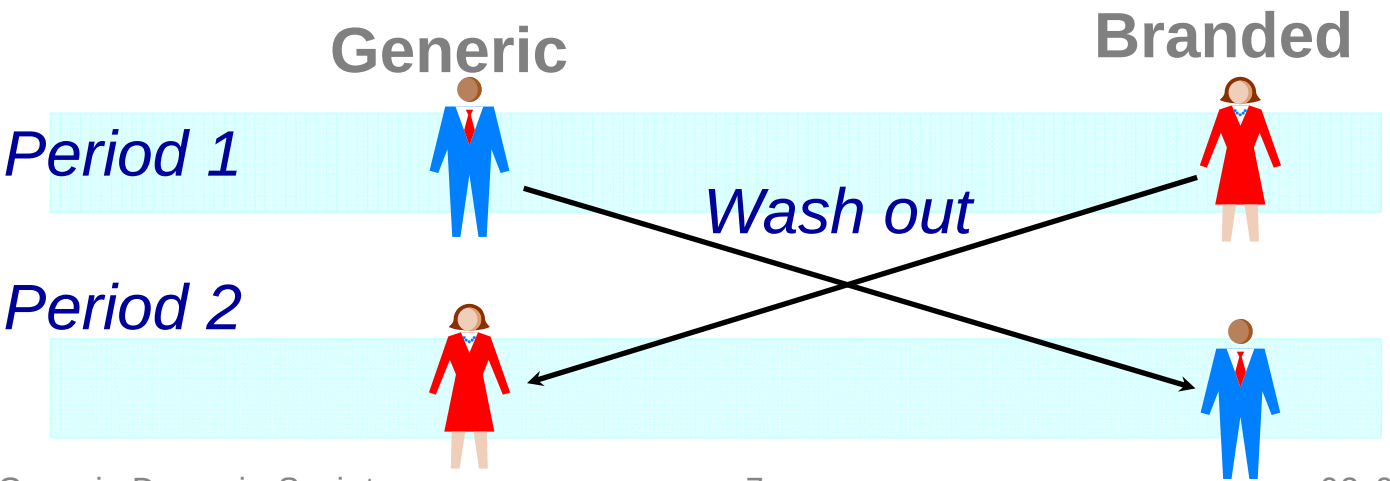
- … a generic medicinal product is a medicinal product which has:
- the **same qualitative and quantitative composition** in active substances as the reference product,
- the **same pharmaceutical form** as the reference medicinal product,
- and whose **bioequivalence** with the reference medicinal product has been demonstrated by appropriate bioavailability studies.

Bioequivalence

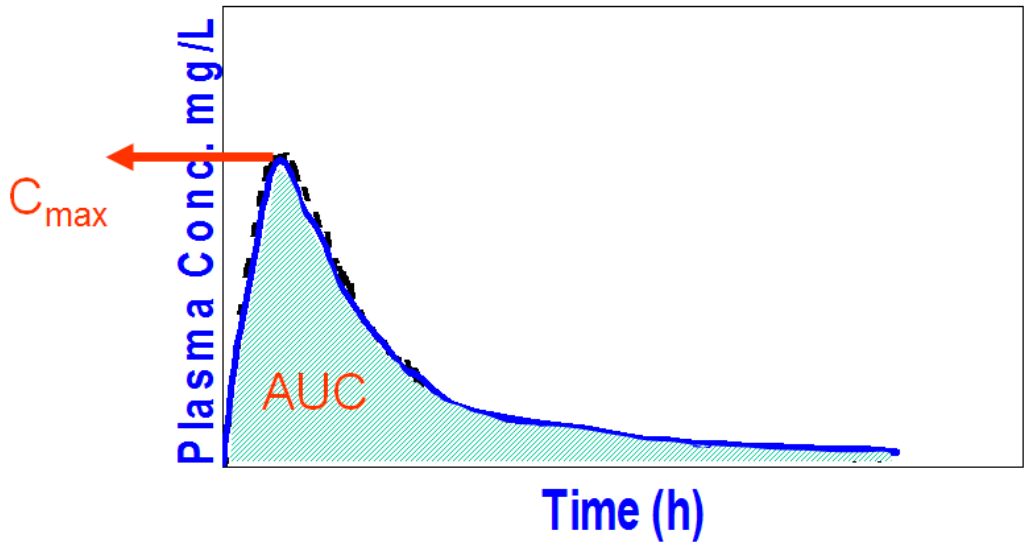
- Basic principle: **Exposure** to active substance of generic and branded product in plasma is **equal**:
- Efficacy and safety characteristics of branded branded is applicable to the generic product! **Therapeutically equivalent.**
- From then **switching branded-generic is possible**.

Bioequivalence study

- Pharmacokinetic data are used to demonstrate therapeutic equivalence
- Single dose, two-way cross-over bioequivalence study in healthy volunteers



Bioequivalence



- **Ratio** test/reference for AUC en C_{max} is determined for each subject
- Statistical analysis: ANOVA, based on log-transformed data.
- The **90% confidence interval** for the ratio in whole study population should be within **80.00-125.00 %** borders

Narrow therapeutic drugs. Consistency in the EU?

- EMA

Substance	Acceptance limits 90% CI for AUC and C_{max}
ciclosporin	Fasted and fed: **90-111% for AUC and C_{max}**
tacrolimus	Fasted: **90-111% for AUC**, 80-125% for C_{max}
sirolimus	Fasted and fed: **90-111% for AUC**, 80-125% for C_{max} .
everolimus	Transplant indication: fasted and fed: **90-111% for AUC**, 80-125% for C_{max}. Oncology indication: No NTI.

Narrow therapeutic drugs. Consistency in the EU?

- Denmark

Substance	Acceptance limits 90% CI
aminophylline / Theophylline	90.00-111.11 %
lithium	90.00-111.11 %
thyroxine	Cannot be substituted
vitamin K antagonists	90.00-111.11 %
anti-epileptics apart from levetiracetam and benzodiazepines	90.00-111.11 %
Certain immunosuppressants: cyclosporine tacrolimus	Cannot be substituted
antiarrhythmics	90.00-111.11 %
centrally acting anorectics	90.00-111.11 %
tricyclic antidepressants	90.00-111.11 %

https://laegemiddelstyrelsen.dk/en/licensing/licensing-of-medicines/marketing-authorisation/application-for-marketing-authorisation/bioequivalence-and-labelling-of-medicines-with-regard-to-generic-substitution

Narrow therapeutic drugs. Consistency in the EU?

- UK, MHRA

GOV.UK

tics:

- ensure that the patient is **maintained on a particular clinical** or carer that cturer's

Antiepileptic drugs: new advice on switching between different manufacturers' products for a particular drug

From: Medicines and Healthcare products Regulatory Agency
Published: 14 November 2013
Therapeutic area: Neurology

https://www.gov.uk/drug-safety-update/antiepileptic-drugs-new-advice-on-switching-between-different-manufacturers-products-for-a-particular-drug


Malariamedicijnen van Sandoz en Teva geschorst
De malariamiddelen Atovaquon/Proguanil HCl van Sandoz en van Teva mogen niet meer verkocht worden. Niet omdat ze onveilig of niet effectief zijn, maar omdat het onderzoek voor de registratie niet op de juiste wijze is uitgevoerd.
UA Uitsluitend voor Apothekersassistenten
31 aug 2016 Pagina : 9
esmiddelen moet beter'
op generiek
Zorg. Inspectie roept op tot terughalen van malariamedicijnen
Metro ed. Amsterdam
26 jul 2016 Pagina : 7
van generieke medicijnen
Leveringsprobleem medicijnen steeds hinderlijker
Medisch Contact
12 jan 2017 Pagina : 10
schering en inslag
'Uw medicijn is op'
Gezondgids Consumentenbond
30 apr 2016 Pagina : 32


DE VERLEIDERS
slikken en stikken
Medicijnwissel:
80%
100%
125%
SLIKKEN EN STIKKEN
Momenteel te zien in Koninklijk Theater Carré. Wegens succes zijn er extra voorstellingen toegevoegd in het DeLaMar Theater. Bekijk de speellijst hier.
HOME
ELLENDE OP RECEPT
VRIJDAG 9 NOVEMBER 2012 DOSSIER: FARMACEUTISCHE INDUSTRIE

The Regulator's dilemma?

- **YES!**

- Opinions from clinicians
- Patients
- Regulatory Science at CBG.
  - Generic-generic exchange, prediction exposure individual level, risk minimization, shortages
- Pharmacy
- Communication to prescriber and consumer