

C B G

M E B

DE LEVENSCYCLUS VAN EEN GENEESMIDDEL IS ONZE ZORG



Bert Leufkens
Voorzitter CBG

Never a dull moment at the MEB

- The MEB has classified ibuprofen 200 mg OTC to be available through grocery stores, while ibuprofen 400 mg OTC packs for longer duration of use than a week as pharmacy only, July 2009. How safe is this drug?
- The FDA has warned Canadian generic-drug maker Apotex because of multiple, serious deficiencies in good manufacturing practices (GMPs), July 2009. Can Dutch citizens trust generics?
- A clinical trial funded by Dutch public money compares Avastin and Lucentis in treating age-related macular degeneration (AMD), Sept 2009. Will the MEB assess the results?
- In Germany, the SPIEGEL has reported that Chancellor Merkel and other high level government officials would receive a non-adjuvanted flue vaccine, October 2009. Does the MEB also believe that the adjuvant is unsafe?

Never a dull moment at the MEB

TROUW MEDICIJNEN
dinsdag, 23 maart 2010
Volksgezondheid

Waakhond voor medicijnen moet opener worden

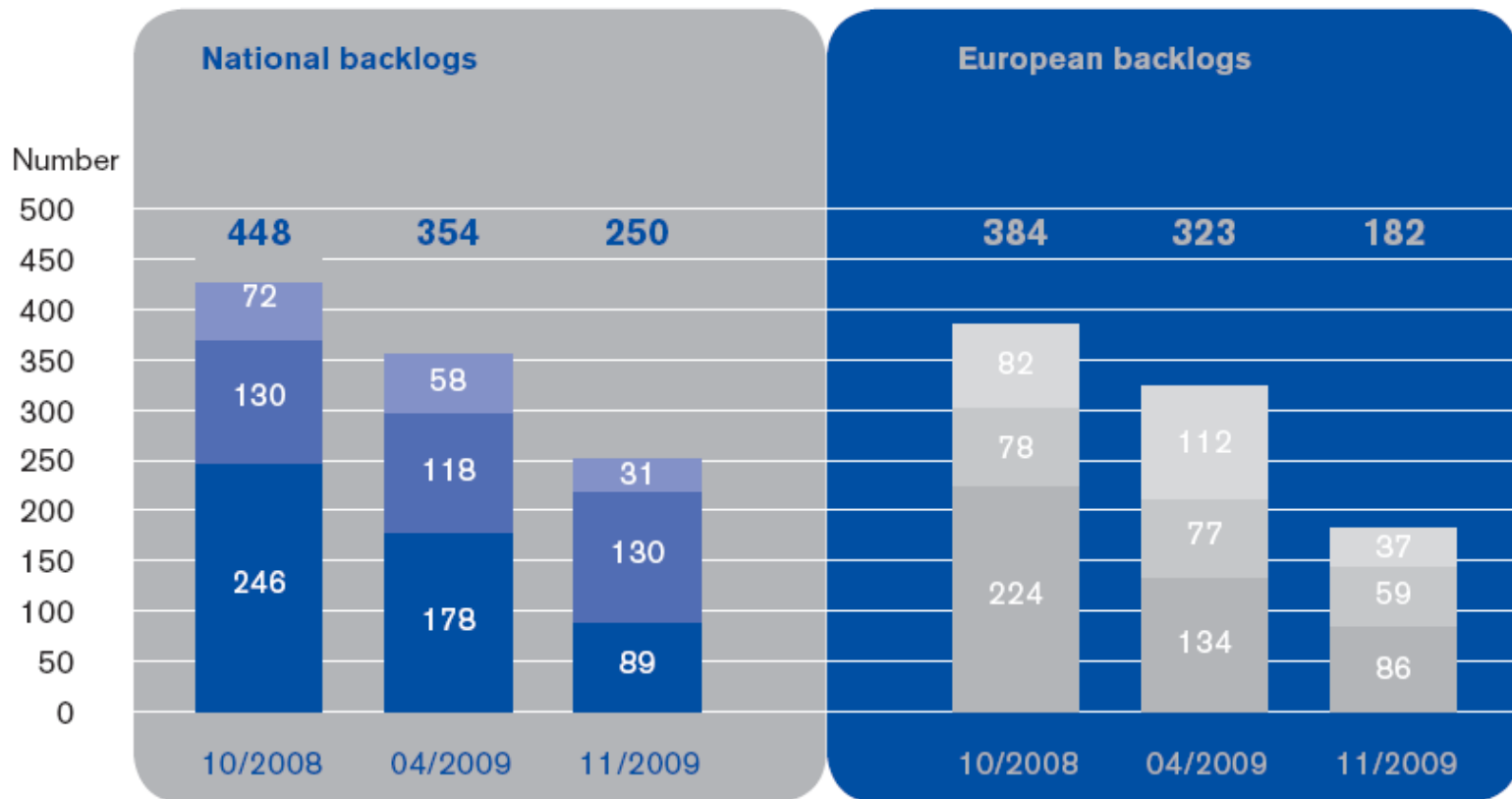
- Publiek wil meer weten over werking
- Farmaceuten vragen meeste info op

Van onze verslaggever

DEN HAAG – Het College ter Beoordeling van Geneesmiddelen (CBG), de toezichthouder in Nederland op medicinale pillen, poeders en drankjes, moet opener worden voor het publiek. Steeds vaker proberen patiënten en andere belangengroepen met de Wet Openbaarheid van Bestuur (WOB) in de hand informatie los te krijgen over de werking en bijwerkingen van geneesmiddelen.

Het CBG vindt zelf ook dat het wel wat transparanter kan, bleek gisteren tijdens een debat op het ministe-

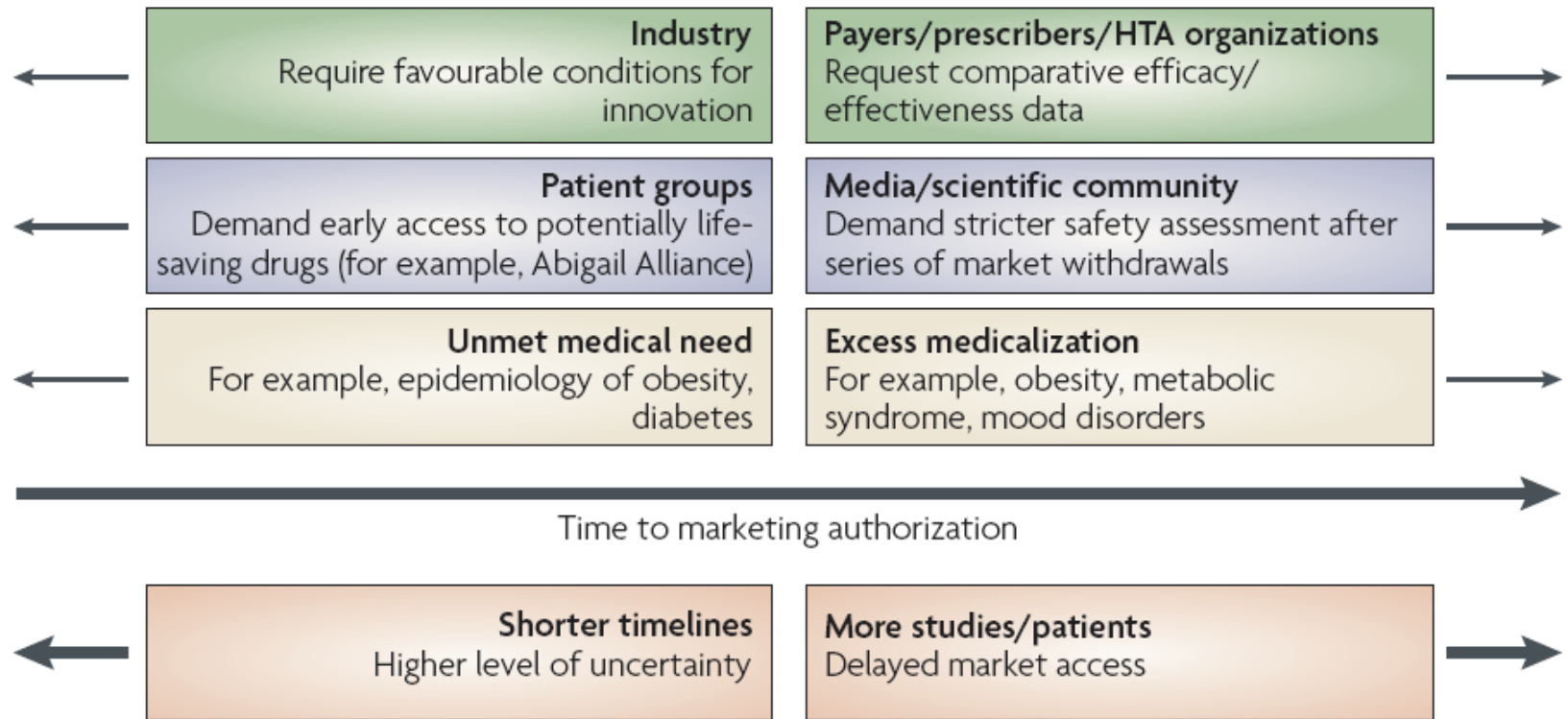
Never a dull moment at the MEB



Key questions in the lifecycle of a medicine

Question	Today's challenges
Robust definition and diagnosis of disease?	Psychiatric morbidities, sepsis somatic functional disorders,
Clinically relevant endpoints to evaluate drug effects?	6-MWT in PAH, MRI and multiple sclerosis
Identifiable target population (indication) that may benefit?	Biomarkers to identify responders and non-responders
What kind of comparison is useful, needed and feasible?	Placebo, active controls and dynamics in treatment options

The best moment to bring a product to the clinic?



Eichler HG, Pignatti F, Flamion B, Leufkens H, Breckenridge A. Balancing early market access to new drugs with the need for benefit-risk data. *Nat Drug Discov* 2008; 7: 818-26.

'Speerpunten' of the MEB:

- Pharmacovigilance
- Central nervous system
- Vaccines
- Female hormones
- Cardiovascular (including diabetes)
- Oncology/heamatology

Lifecycle approach means
'lifelong' responsibility
and aftercare !

Risk management throughout a product's lifecycle

- Continuous focus on B/R given 'signals' from ADR reporting, PSURs and 'landscaping' of the drug use environment (linked databases, registries).
- A high quality system of spontaneous reporting (Lareb) should be in place, link to Eudravigilance, WHO Vigibase.
- Implementation of RMPs, including post-authorization safety studies (PASS) and risk minimisation programs.
- Strengthening of the national involvement in the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) and other EMA initiatives.
- Thoughtful communication and transparency/trust building on decision making with prescribers, pharmacists and patients.

B/R as a function of appropriate use

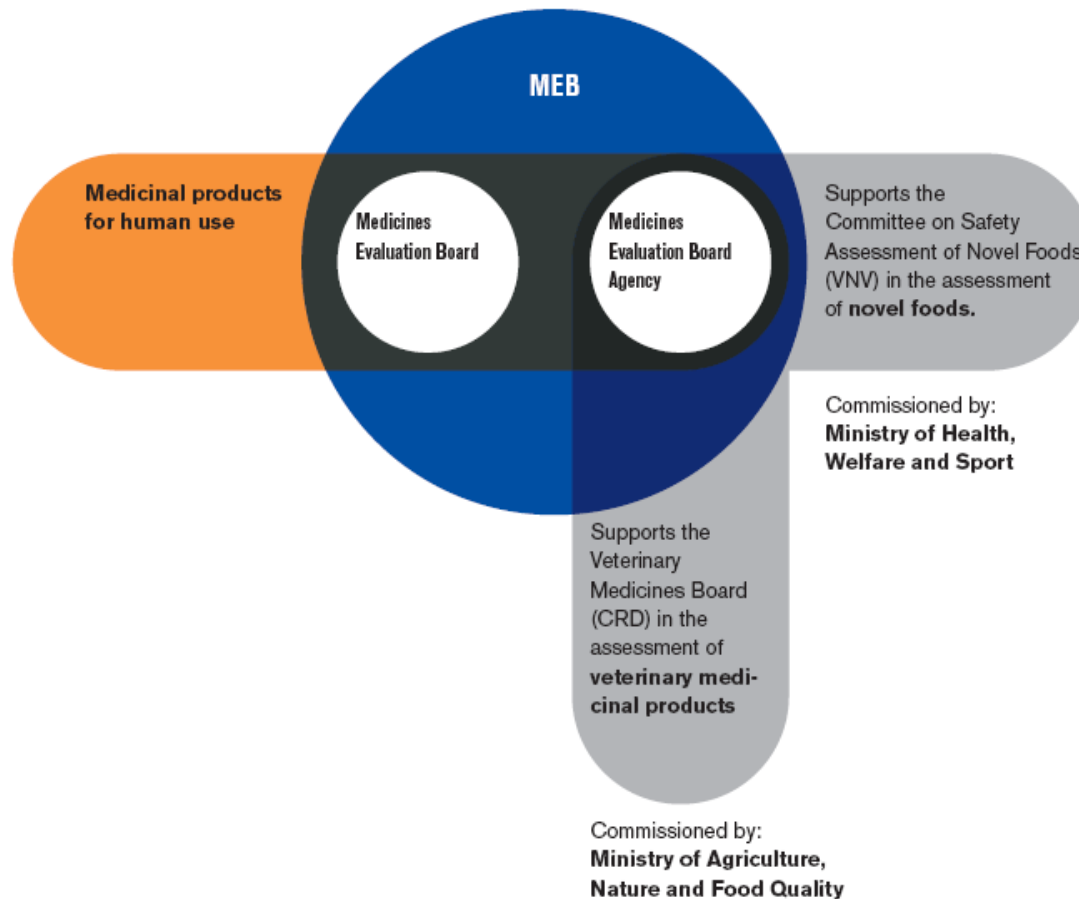
Rimonabant and CNS events	MABs and risk of infections, PML	Sibutramine and CV events
Known effect, B/R initially positive	Rare, difficult to see, but very severe	Known effect, B/R uncertain at start
Patterns of use, too short duration of use	Outcome masked by indication	SCOUT study driver B/R assessment
Complex outcome measurement	Ascertainment and traceability exposure	Difficult to define a group that may benefit
Risk minimization insufficient	Risk minimization insufficient	Risk minimization insufficient
Confounding by underlying disease	Differential weighing of B/R per indication	RR of 1.2 enough to suspend

Biomarkers variation in eff
 Knowledge Mgmt
Access to computational data b
 Risk-Benefit - Role of Patient
 Mechanism of Disease - Funding
 Regulators looking at therapeutic ^{value}
 Unmet needs - Who should deter
 Role of patients ^{PH perspective} group + funding
 how to involve
 - learning from failures / off label ^{of variable} use
 Transparency in Advice & Regulatory
 scientific information -
 society / company dialogue -
 Pharmacoeconomic burdens
 Conditional approval with Phase
 Access Issues (Mondrian)
 Utilization Innovation + therapeutic out
 Phase 4

system: The Escher-project



The MEB at a crossroad



What is at the top of our radar screen?

- Further innovation in Scientific Advice and regulatory dialogue, both nationally and together with EMA. (Regnstrom J et al. *Eur J Clin Pharmacol* 2010; 66: 39-48.)
- Maintaining consistency in regulatory decision making, nationally and in alignment with European partners.
- Strengthening of sustained knowledge management and learning, alignment with experts, academia and the clinic (e.g. orphan drugs, advanced therapies, pediatrics).
- How to handle the increasing number of GMP and GCP problems? A systems approach or case-by-case?
- Increasing emphasis on public health driven 'risk based' assessment of B/R, SmPC and patient information updates of existing products ('aftercare is a continuum').

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