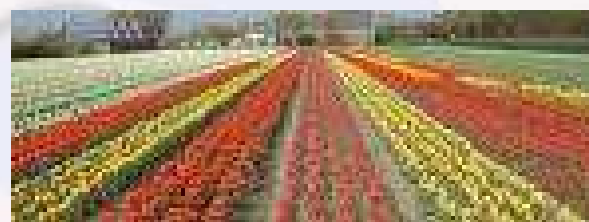


Orphan drug regulation and national strategies: complementary actions



Sonja van Weely

**Dutch *Steering Committee* on
Orphan Drugs**

Regulation (EC) 141/2000 for Orphan medicinal products

- **Incentives for development and marketing of orphan medicinal products for the European Union, meant for diagnosis, prevention or treatment for rare conditions**
- **However, availability and access for patients is different in the EU member states**
- **Multiple reasons, e.g.**
 - **National procedures for reimbursement**
 - **Companies do not market their product in small countries as the first step**
- **Other actions are needed to improve the possibilities for reimbursement for orphan drugs**

National actions/plans/strategies are needed

- **Especially needed for patients with rare disorders for whom no therapy is available**

- **Building blocks of the Council Recommendation (2009/C 151/02) on an action in the field of rare diseases:**
 - **Definition, codification and inventory**
 - **Research**
 - **Centres of expertise and European reference networks**
 - **Gathering expertise at European level**
 - **Empowerment of patient organisations**
 - **Sustainability of infrastructures in the field of information, research and healthcare for rare diseases**

Parallel developments in Europe and in The Netherlands

European Community:

- Consultations with stakeholders on possible legislative procedures (starting in 1995)



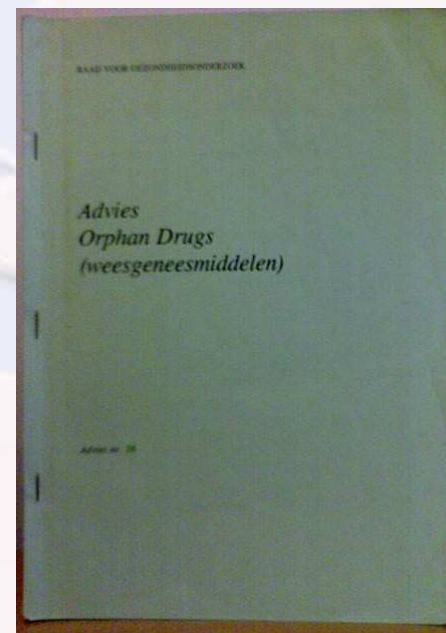
- Regulation (EC) 141/2000 on orphan medicinal products and Rare disorders



- Committee for Orphan Medicinal Products at the European Medicines Agency

The Netherlands

- Consultations with stakeholders starting in 1998:



Advice from Dutch Advisory Council on Health research (RGO)

Main recommendations of the RGO and resulting government policy

- **Make an inventory of and coordinate ongoing initiatives, stimulate new initiatives ▶ via a national organisation**
- **Stimulate research and development ▶ create financial support, tax agreements, fee waivers, a reimbursement policy**
- ***Steering committee established in 2001***
- **Some proposals accepted or in preparation, some dismissed**

Dutch *Steering Committee* on Orphan Drugs

- **Installed in 2001 by Dutch Minister of Health, Welfare and Sport**
- **Financed by this ministry**
- **Independent**

- **Eleven members on personal title from:**
 - **Two umbrella organisations of patients' support groups**
 - **Two medical university professors**
 - **University pharmacist (Children's hospital)**
 - **Two umbrella organisations of pharmaceutical industry**
 - **Dutch Medicines Evaluation Board (MEB)**
 - **Health Care Insurance Board (CVZ)**
 - **Health Insurance Company (since 2005)**
 - **Chair – clinical pharmacologist/former chair of MEB**

- **Observers from:**
 - **Ministry of Health, Welfare and Sport**
 - **Dutch member of the COMP/EMA**

Mission of the *Steering Committee*

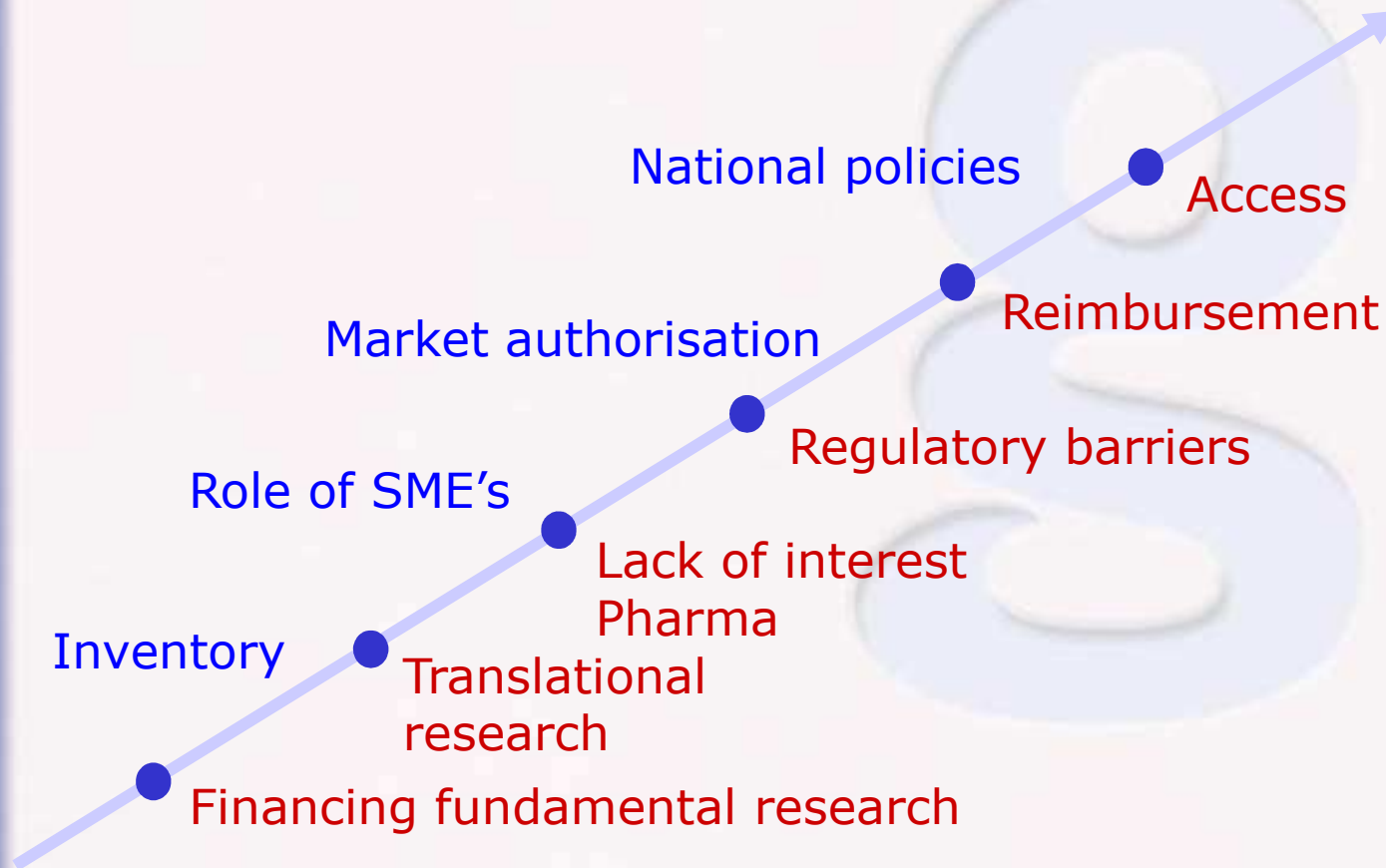
The *Steering Committee* on Orphan Drugs has the following mission:

- Encourage the development of orphan drugs
- Improve the situation of patients with a rare disease, especially strengthen the transfer of information on rare diseases

Strategies on availability and access of orphan drugs

- **Research**
- **Reimbursement**
- **Information**

Key issues in Orphan Drug development



Research and Technology

Four year programme with total budget of EUR 0.5 million

Aim:

- **To encourage the development of orphan medicinal products in The Netherlands and elsewhere**

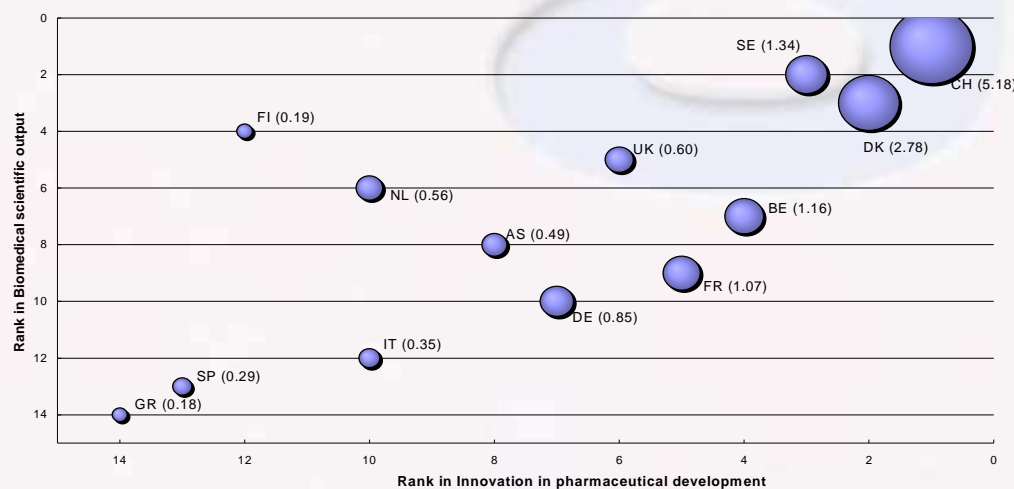
- **Two projects:**
 - 1. 'Orphan product developer': acts as mediator between Dutch universities, university medical centers, technology transfer points, SME's and other pharmaceutical companies**

 - 2. PhD student – research on rare diseases and orphan drugs**



Project 2: a PhD-project (1)

- Main deliverable: thesis
- Identification of success factors for enhancing the development of orphan drugs: for example
 - basic biomedical research
 - strong pharmaceutical innovation in general, including patent applications, R&D expenditure and the existence of small and medium enterprises "



Project 2: a PhD-project (2)

- **Second main deliverable:
The Development of a Proposal for a Scientific Programme:**
 - **To encourage precompetitive translational research with the ultimate goal to develop treatments (key words: focus and mass, involvement of patients, perspective on participation of industry)**
 - **To encourage international collaboration and participation in E-Rare (European project on rare disease research)**
 - **The programme will start in 2011; 13.6M€ available**

Strategies on availability and access of orphan drugs

- Research
- **Reimbursement**
- Information

Definition of a rare disease used for reimbursement

- **A life-threatening or chronically debilitating condition affecting not more than 5 in 10,000 persons in the European Community (EC)**
- **Exception: In case of off-label use of registered medicinal products for patients with a prevalence of less than 1:150,000 inhabitants in The Netherlands: reimbursement despite the fact that the product is not registered for the specific rare indication**

Dutch assessment for reimbursement of (orphan) drugs

- In principle similar procedure of assessment for orphan and non-orphan drugs by a specific committee of the Health Care Insurance Board
- Contents of extramural reimbursement dossier:
 - Pharmacotherapeutic evidence (therapeutic added value):
 - Pharmaco-economic evaluation (dispensation for orphan drugs!)
 - Budget impact

Reimbursement of medicines (1)

- **Medicines in Primary Care and Out-patient Setting:**
 1. **Average of prices in UK, Germany, Belgium, France**
 2. **Health Care Insurance Board advises on reimbursement, but the government decides ►**
 3. **Medicines are put on one of the following Lists:**
 - **List 1A Medicines put into groups; with upper limit of reimbursement**
 - **List 1B Unique medicines, fully reimbursed, no upper limit of reimbursement**
 - **List 2 Limitative preconditions for reimbursement**
- **Unique orphan drugs are on List 1B**

Reimbursement of medicines (2)

- **In-Hospital treatment:**
 - **Diagnosis/treatment combinations (DBC's)**
 - **In case there is no DBC and the prescriber in the hospital decides to prescribe the medicine, the hospital has to pay for it by the hospital budget**
- **Policy Rules for Expensive Medicines and for Orphan Drugs**

Policy rules (1)

- **Only for In-Hospital treatment**
- **Conditional reimbursement for four years**
- **Additional evidence on (cost)-effectiveness has to be obtained in these four years**
- **New research programme for collecting more data on (cost-) effectiveness**
- **Start of the first projects: 1-10-2008**

Policy rules (2)

- **In the case of policy rule for orphan drugs:**
 - **European Orphan Drug Designation Status mandatory**
 - **Only in University Hospitals - to improve expertise building**
 - **Threshold for application for policy rule for orphan drugs: Expenditure on an orphan drug exceeds 600,000 € in the individual university hospital**

Policy rules: reappraisal after four years

- **Health Care Insurance Board reappraises the available evidence on efficiency in daily practice upon four years:**
 - **Therapeutic value**
 - **Actual costs of the medicinal product**
 - **Cost-effectiveness**
 - **Efficient prescription**

Strategies on availability and access of orphan drugs

- Research
- Reimbursement
- **Information**

Information on availability of (orphan) drugs

- Brochure for clinicians and pharmacists

and

- Brochure for patients



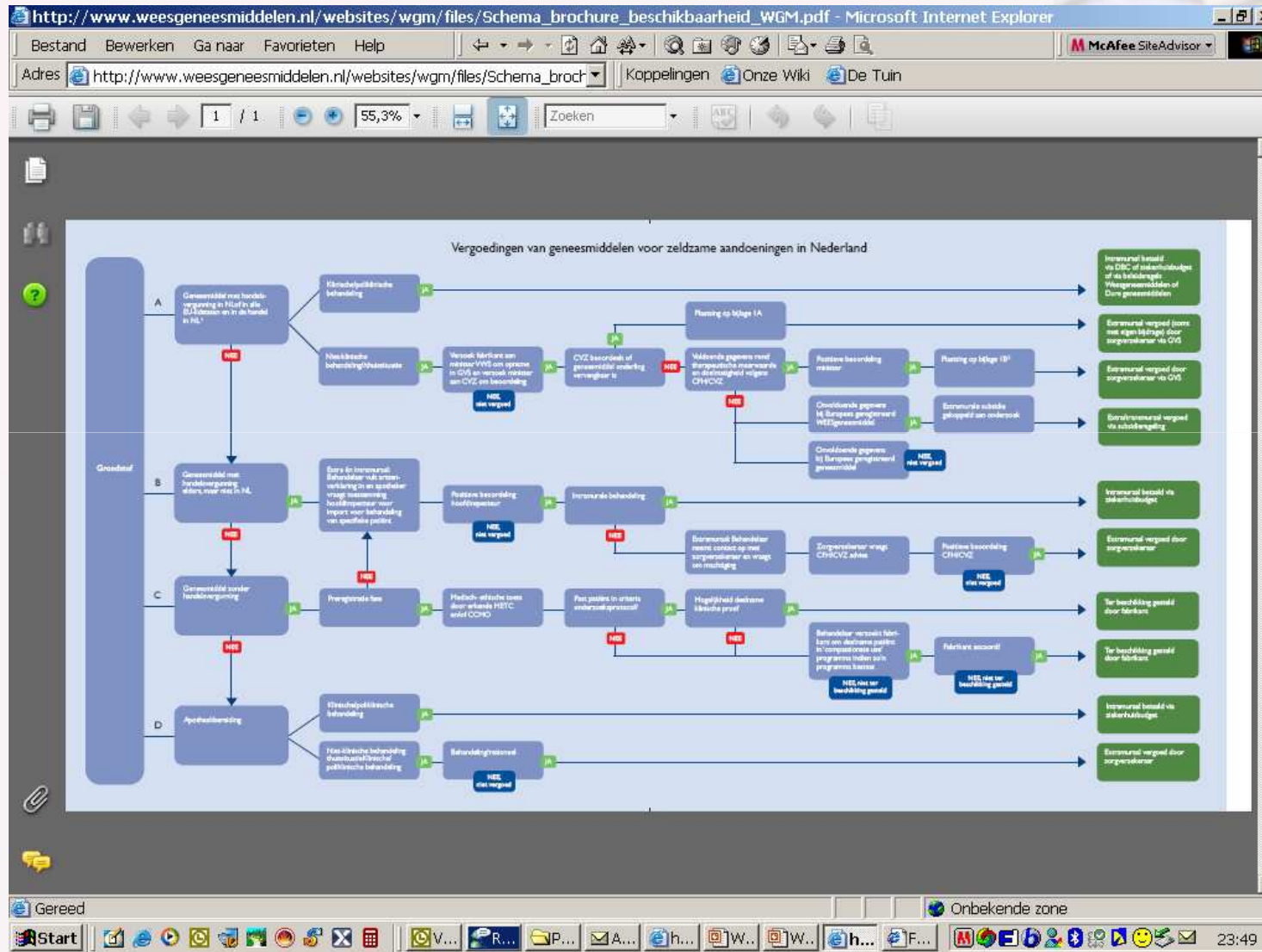
- In collaboration with the Dutch Royal Society of Pharmacists: website with information on aspects of European registered orphan medicinal products (www.farmanco.knmp.nl/weesgeneesmiddelen)

werkzame stof	merknaam	status	registratiedatum
Agonicecifil	Relegel	geregistreerd	08-2001
Agonicecifil beta	Fabryzyme	geregistreerd	04-05-2001
Agonicecifil alpha	Muczyme	geregistreerd	21-03-2004
Agonicecifil	Agard	geregistreerd	16-11-2004
Kriemtschilde	Trisox	geregistreerd	05-03-2002
Kriemtschilde	Cytidene	geregistreerd	15-02-2007
Rosentan	Tracleer	geregistreerd	15-09-2002
Busifin	Busifin	geregistreerd	09-07-2003
Conglutine	Cartago	geregistreerd	24-01-2003
Cefoxitil	Onsenal	geregistreerd	17-10-2003
Cladribine	Libi	geregistreerd	04-04-2004
Clifofabine	Evotra	geregistreerd	29-05-2004
Dalacin	Spricel	geregistreerd	20-11-2004
Dufrenoyl	Eufle	geregistreerd	28-08-2004
Duvelizumab	Savene	geregistreerd	28-07-2004
Gallifone	Naglazyme	geregistreerd	25-01-2004
Hydroxychloroquine	Hydro	geregistreerd	13-02-2005
Isoproterenol	Pedia	geregistreerd	29-07-2004
Kanamycin	Blarneo	geregistreerd	01-01-2007
Koprost	Venavist	geregistreerd	16-09-2003
Malvidin	Givoc	geregistreerd	11-11-2003
Marimastat	Aldarapine	geregistreerd	05-06-2003
Migastat	Zaveca	geregistreerd	20-11-2002

Situation

Essential actions to be done by practitioner and pharmacist

Way of reimbursement



Conclusions

- **Orphan Drug Regulations and national plans/strategies should complement each other**
- **The Netherlands has chosen to develop strategies involving:**
 - **Multidisciplinary approach**
 - **Inventory of existing situation**
 - **Performing research to come up with solutions and to monitor the solutions**
 - **Disseminate information to several stakeholders**

wgm

STUURGROEP WEESGENEESMIDDELEN



Muchas Gracias!

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