DELAYED ACCESS FOR PATIENTS WITH RARE DISEASES IN ASIA PACIFIC: FINDING A SOLUTION THAT WORKS

ISPOR Asia Pacific 2018 – Workshop W14

Tuesday 11th September 10.45am

Discussion Leaders: Dr Annabel Griffiths (Head of Rare Diseases, Costello Medical, UK)

Prof Ming-Chin Yang (Professor, National Taiwan University, Public Health, Taiwan)

Prof Shanlian Hu (Professor and Senior Consultant, Fudan University and Shanghai Health Development Research Center, China)

Prof Bertram Häussler (Chairman of the Board, IGES Institut GmbH, Germany)

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Disclosures

- This workshop was sponsored by Shire
- Annabel Griffiths is an employee of Costello Medical

The Discussion Leaders

Dr Annabel Griffiths
Head of Rare Diseases, Costello Medical, UK

Prof Ming-Chin Yang
Professor, National Taiwan University, Public Health, Taiwan

Prof Shanlian Hu
Professor and Senior Consultant, Fudan University and Shanghai Health Development Research Center, China

Prof Bertram Häussler
Chairman of the Board, IGES Institut GmbH, Germany

Structure of the Workshop

- Each discussion leader will speak for ~10 minutes
- After all discussion leaders have presented there will be a ~20 minute discussion session

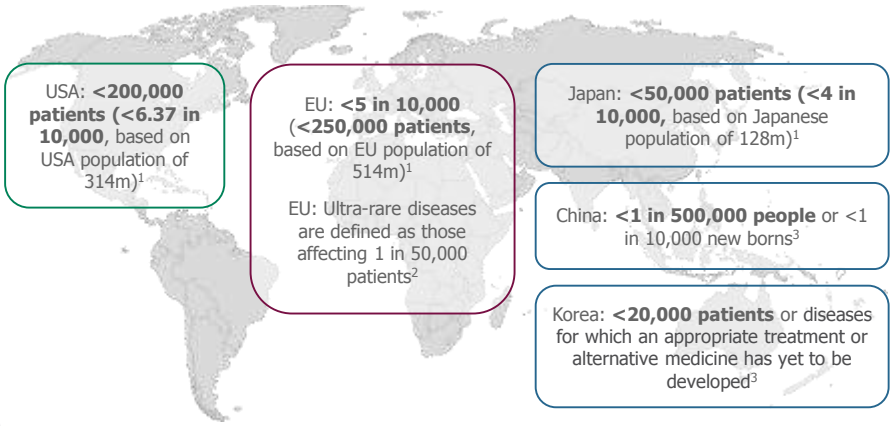
- This symbol indicates an audience vote
- Questions and comments from the audience will be taken during the discussion session

Introduction to Access Challenges for Orphan Drugs in Asia Pacific

Dr Annabel Griffiths

Head of Rare Diseases, Costello Medical, UK

What is a Rare Disease?



EU: European Union; USA: United States of America

1. EvaluatePharma. Orphan drug report 2017. Available at: http://info.evaluategroup.com/rs/607-YGS-364/images/EPOD17.pdf. Last accessed 21st June 2018.
2. European Union. Regulation No 536/2014.2014. Available at: http://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf. Last accessed 21st June 2018.
3. Song P et al. Intractable & rare diseases research. 2012 Feb 29;1(1):3-9.

Examples of Rare Diseases

Fabry Disease

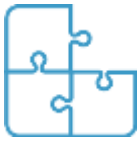
- A progressive, inherited, multisystemic lysosomal storage disease characterised by a range of neurological, cardiovascular and renal symptoms[1,2]
- Prevalence: 1–5 in 10,000[1]
- Available treatments: enzyme replacement therapies[2]

Haemophilia

- Genetic disorder characterised by spontaneous haemorrhage or prolonged bleeding due to factor VIII (haemophilia A) or IX (haemophilia B) deficiency[3]
- Prevalence: 1–9 in 100,000[3]
- Available treatments: recombinant factor VIII and IX[4]

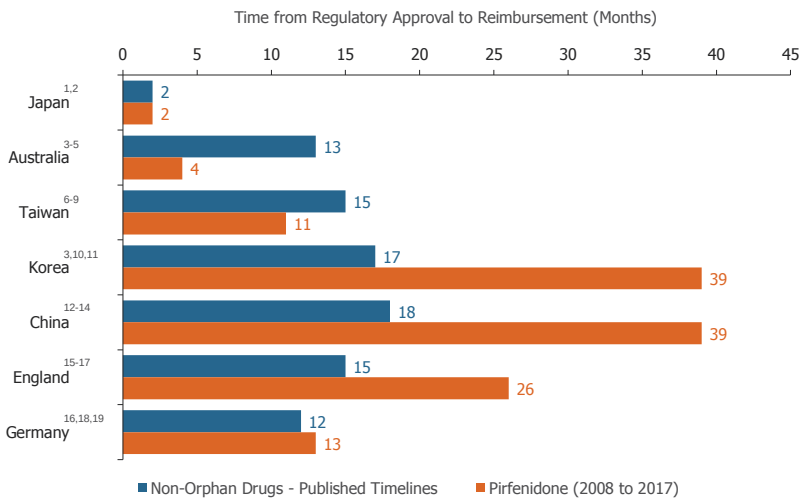
1. Orphanet. Fabry disease. Available at: https://www.orpha.net/consor/cgi-bin/index.php. Last accessed: 29th August 2018; **2.** National Fabry Disease Foundation. Fabry Disease Treatment. Available at: https://www.fabrydisease.org/index.php/about-fabry-disease/fabry-disease-treatment. Last accessed: 29th August 2018; **3.** Orphanet. Hemophilia. Available at: https://www.orpha.net/consor/cgi-bin/index.php. Last accessed: 29th August 2018. **4.** NHS. Treatment Haemophilia. Available at: https://www.nhs.uk/conditions/haemophilia/treatment/. Last accessed 29th August 2018.

What Makes Rare Diseases Different?



Need for accelerated processes	Lack of good quality evidence available	Poor awareness and understanding of the condition	Significant unmet need

Time to Reimbursement



References available in slide notes

Overview of Healthcare Systems

	UK	Taiwan	China	Germany
Subsidised patient access system	National Health Service[1]	National Health Insurance system[2]	Basic Health Insurance Scheme (BHIS)—urban and rural schemes[3]	Statutory Health Insurance system[4]
Public healthcare coverage	Universal healthcare[2]	Universal healthcare[2]	Universal healthcare[5]	Universal healthcare[4]
Healthcare financing	General tax revenue[1]	Insurance premiums (99%), patient out-of-pocket payments[2]	Government funding (for urban non-employed residents and rural residents), payroll taxes (employed urban residents), patient out-of-pocket payments[1]	Statutory Health Insurance (SHI) premiums and private insurance premiums (from high-income holders who opt out of public SHI insurance)[1]
2017 GDP per Capita (% spent on healthcare)	42,514 USD[6] (9.7%[10])	24,318 USD[7] (6.3%[11] [2016 data])	7,329 USD[8] (5.5%[11] [2016 data])	46,747 USD[9] (11.3%[10])
% of total drug spending accounted for by orphan drugs	1.0%[12]	0.5%[13]	<1%*	2.1%[12]
HTA Decisions (National HTA Body)	National (National Institute for Health and Clinical Excellence - NICE)[1]	National (National Health Insurance Administration - NHIA)[14]	Locally-adapted (China National Health Development Research Centre - CNHDRC)[15]	National (Institute for Quality and Efficiency in Health Care – IQWIG)[15]

*Expert opinion

References available in slide notes

Key Considerations for Access to Orphan Drugs Over the Next 10 Years

- How do we ensure fair access for rare disease patients globally?
- Which approaches are most effectively reducing delays to access for rare disease patients?
- How and when could these approaches be used in other healthcare systems?
- How do we ensure the collection of "sufficient" clinical and economic evidence but allow rapid access to treatments?
- How do we manage reimbursement of orphan drugs considering the increasing numbers and development of advanced therapy medicinal products?

Do you think that the current reimbursement system in your own country is able to manage the increasing number of orphan drugs expected in the next 5 years?

Audience Vote – Raise Your Hand for No

Current Status and Challenges of Accessibility to Orphan Drugs in Taiwan

Ming-Chin Yang, Dr.PH
Professor
Institute of Health Policy and Management
National Taiwan University

General Overview of Taiwan

Population, Age, Life expectancy and Economy

TAIWAN FACT SHEET

Population
- Total population: 23.6 million
- 2014-2018 CAGR: 0.15%

Age Distribution
- 0-14 yrs: 13.0%
- 15-64 yrs: 72.8%
- > 65 yrs: 14.2%

Life Expectancy
- Total population: 80.0 years
- Female: 83.4 years
- Male: 76.8 years

Economy
- GDP: USD 565 bn (2017)
- GDP per capita: USD 24,318 (2017)

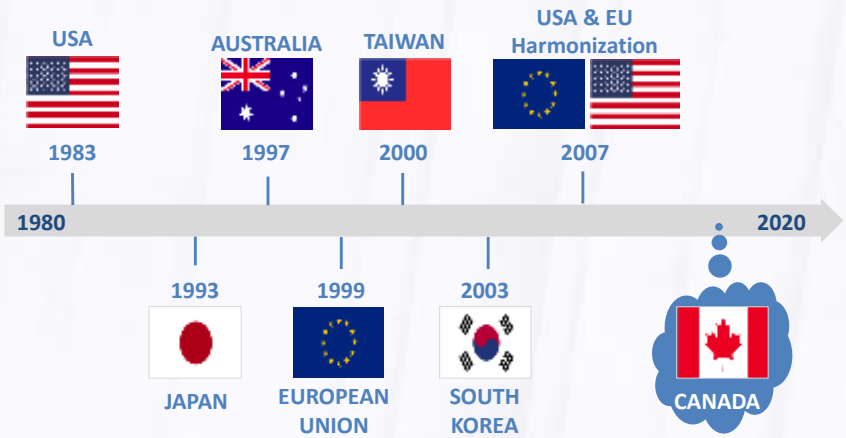
Source: 2014/2018 statistics, Dept. of Household Registration, MOI

Rare Disease Act in Taiwan

Jun, 1999 TFRD started to operate and advocate rare disease patients' rights

Jan, 2000, rare disease act legislation was introduced

Orphan Drug Legislation: Pathway to Rare Disease Action



Definition of Rare Disease in Taiwan

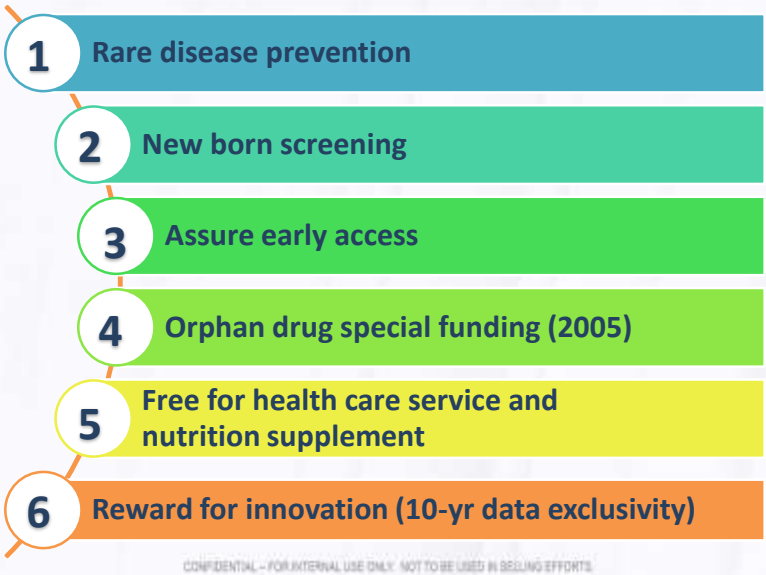
- Prevalent in fewer than 1/10,000 people,
- Has a genetic origin,
- And is difficult to diagnose and treat.

Rare Disease Act

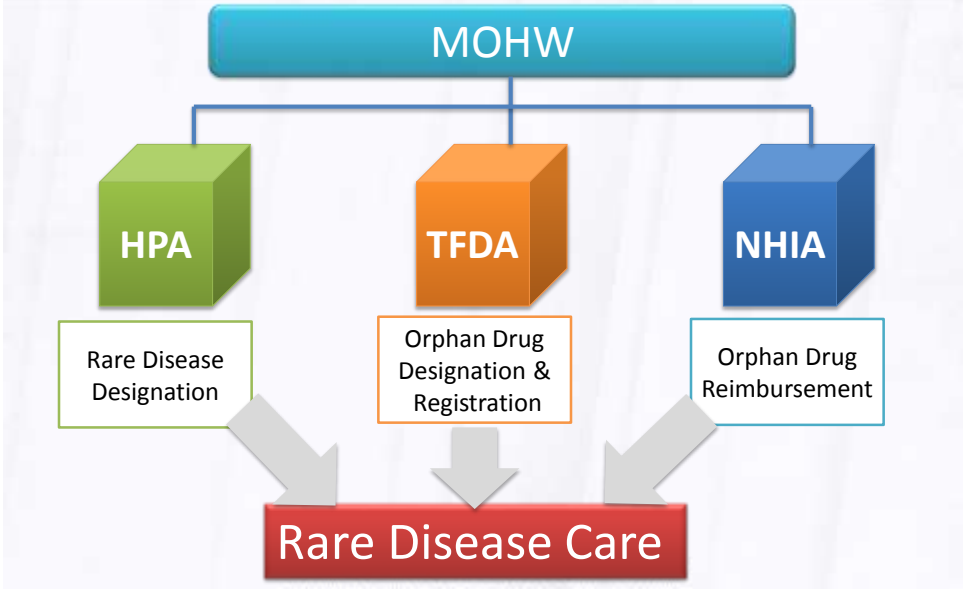
The Rare Disease and Orphan Drug Act was enacted for:

- preventing the occurrence of rare diseases;
- early diagnosis of rare diseases;
- intensive care of rare disease patients;
- assisting patients in gaining access to specific drugs and special nutritional foods essential for the maintenance of life; and for promoting and ensuring the supply, manufacturing, research and development of such drugs and foods.

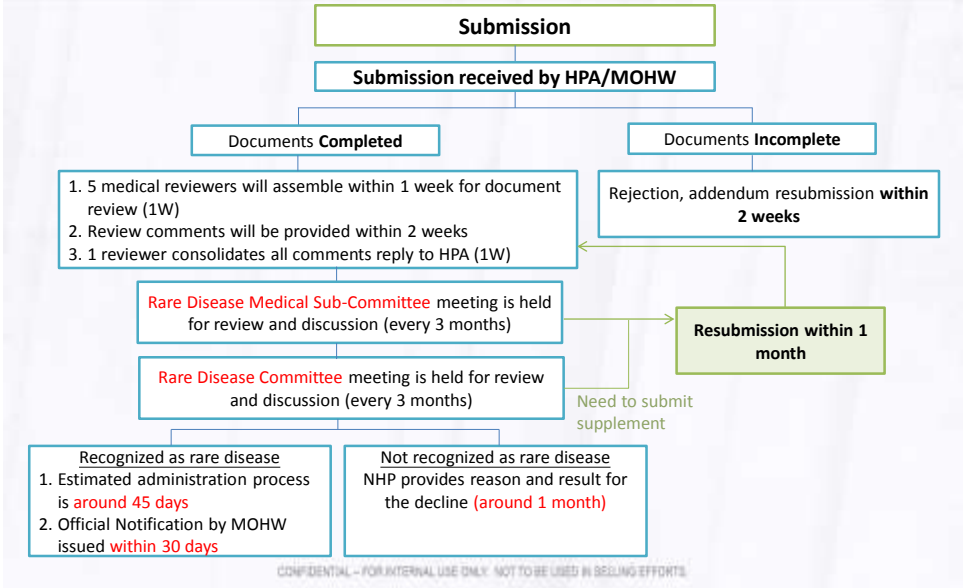
Taiwan Rare Disease Act Key Highlights

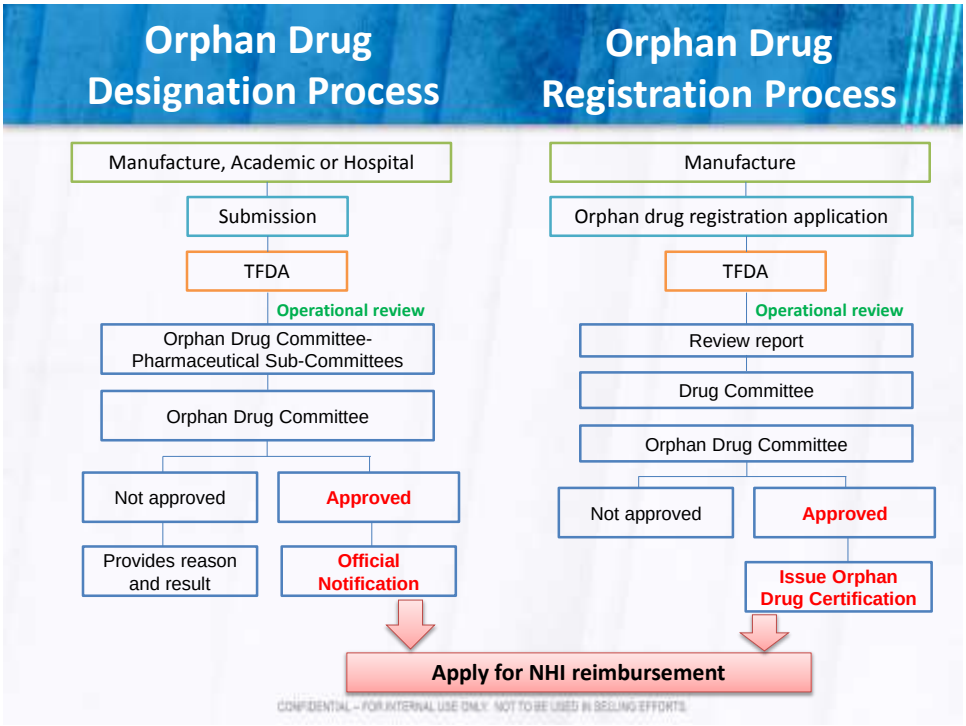


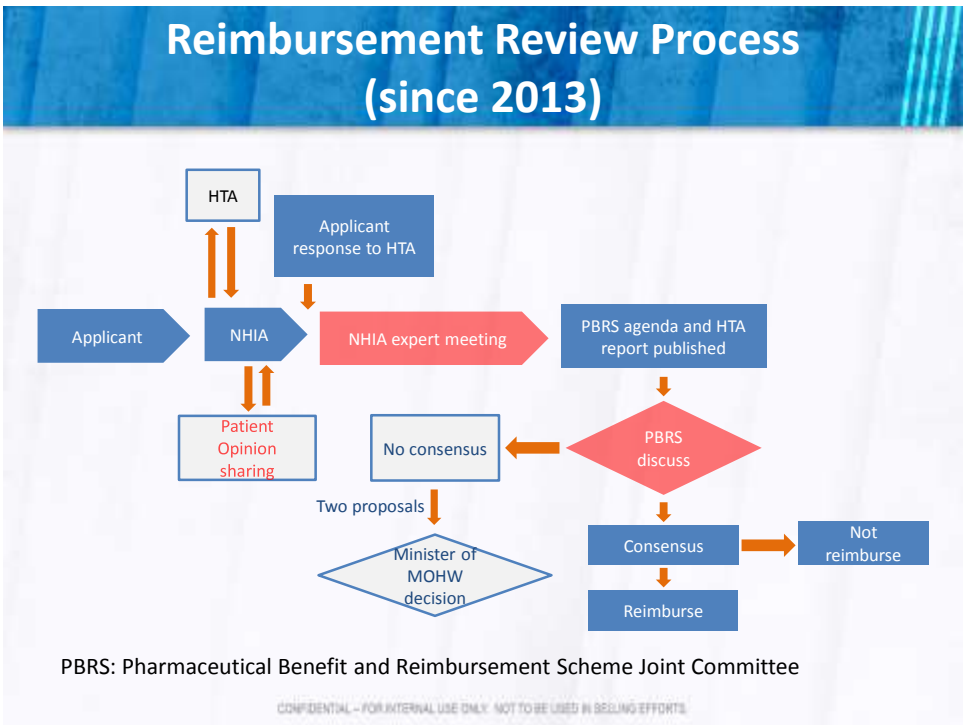
Rare Disease Care Network within the Government



Rare Disease Designation Process







PBRS: Pharmaceutical Benefit and Reimbursement Scheme Joint Committee

Reimbursement Challenges

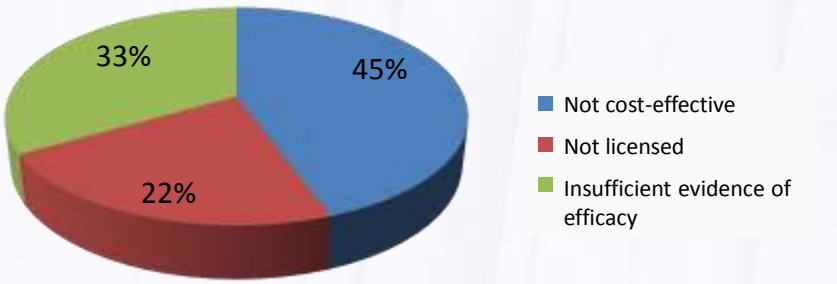
- **Prompt access to orphan drug became harder after the new review process started in 2013**

  98 ODD granted items only 57 items received reimbursement approval **(58%)**

From 1995-2012 NHI		Since 2013 NHI	
ODD granted	Reimbursement approval	ODD granted	Reimbursement approval
80	52	18	5

Reasons for PBRS Reject to Reimburse -Since 2013 NHI

- Major reasons for PBRS reject to reimburse：



Resource: PBRS meeting minutes (2013-2017)

Orphan Drug Pricing Methodology

NHIA article 35, reference A-10 Medium price / Cost-plus pricing

NHIA new drug pricing methodology (A-10 lowest)

International reference pricing (IRP), A-10 country pricing

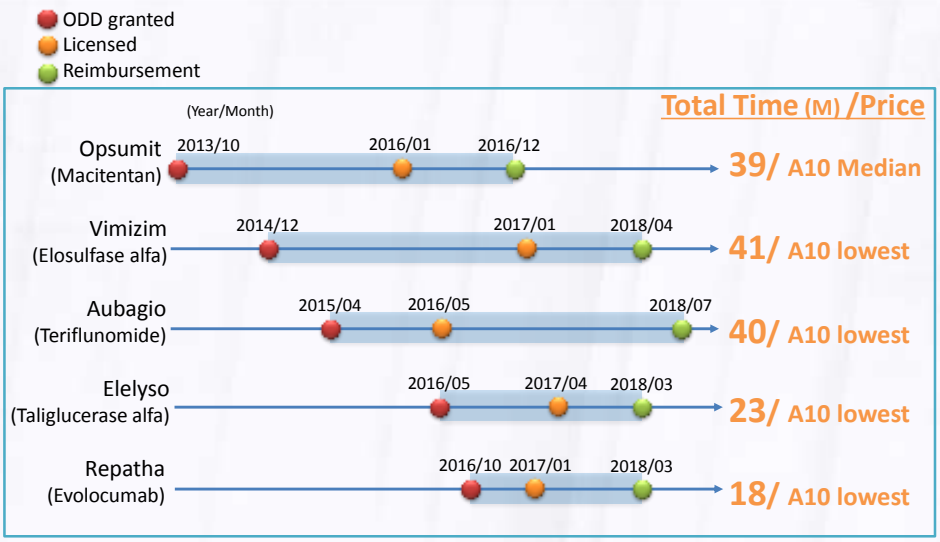
- Annual sales ≤ €0.17m, upper limited: A10-median mark-up 20%
- €0.17m < annual sales ≤ € 0.34m, upper limited: A10-median mark-up 10%
- € 0.34 < annual sales, upper limited: A10-median

Cost-plus pricing

- Imported products: Import cost (including shipment, insurance, storage etc..) mark-up 30% management and marketing expense
- Domestically manufactured products: manufacturing cost (excluding R&D) mark-up 30% management and marketing expense

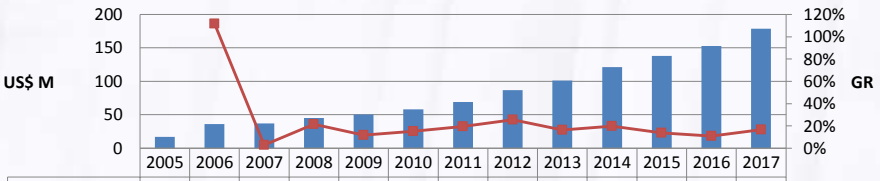
A-10 lowest price is the norm, yet the orphan drug pricing rule is much more generous than the rest

Delayed Access to Orphan Drugs -Since 2013 NHI



Orphan Drug Special Funding From 2005

- High growth rate in the past decade from 11% to 25%. In 2017, the total orphan drug expenditure was around USD 179M.
- Multiple stakeholders are challenging the spending and asking for appropriate adjustment in orphan drug pricing



	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Orphan drug expenditure	17	36	37	45	50	58	69	87	101	121	138	153	179
growth rate		112%	3%	22%	12%	15%	20%	25%	16%	20%	14%	11%	17%

Exchange rate: 1 USD = 30 TWD

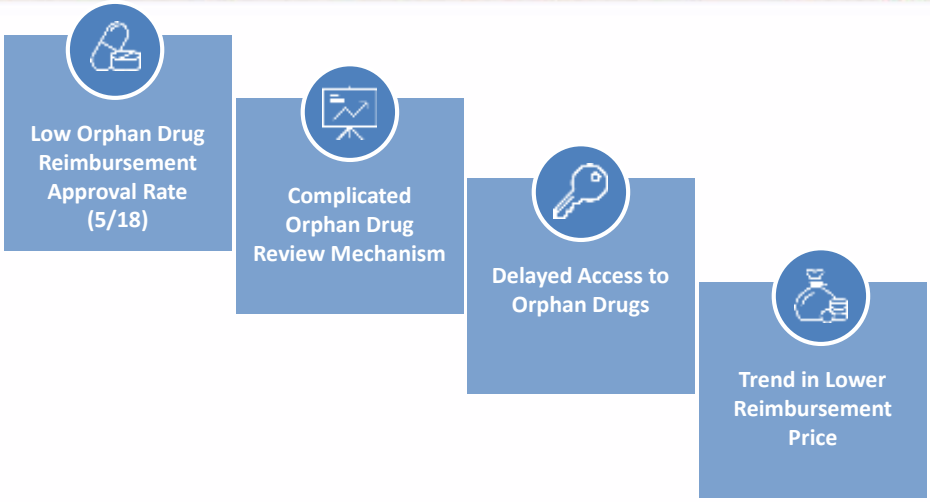
Hemophilia Drug Special Funding From 2005

- Hemophilia is classified as a catastrophic illness by the NHI, exempting patients from a co-payment and assuring them to obtain sufficient clotting factor concentrates for suitable replacement therapy.
- NHIA introduced new reimbursement guideline in 2014 for patients with hemophilia to get prophylaxis therapy.

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Hemophilia drug expenditure	45	54	63	74	77	88	99	106	115	118	118	116	114
growth rate		18.4%	16.8%	18.6%	3.1%	14.8%	12.1%	7.8%	8.2%	2.9%	-0.3%	-1.7%	-1.7%

Exchange rate: 1 USD = 30 TWD

Reimbursement Challenges



Conclusions

1. Policy decisions and legitimization of the Rare Disease Act provides clear authorization to various government agencies to implement the Act.
2. Transparency in TFDA, NHIA, and HPA improves the control, monitoring and management in related domains.
3. Well-organized patient advocate group (TFRD) provides public scrutiny and support.
4. New approval process introduced by NHIA in 2013 making orphan drugs reimbursement more challenging.

Audience Vote

Taiwan NHI allows ODs to apply for reimbursement before receiving TwFDA license, do you think this is feasible in your country or region?

Audience Vote – Raise Your Hand for Yes

The Recognition of Rare Disease Importance in China

Shanlian Hu. MD. MSc. Professor

W14. Delayed Access for Patients with Rare Diseases in Asia Pacific: Finding to Solution that Works

ISPOR Asia Pacific, Sept. 10, 2018, Tokyo Japan

The Definition of Rare Disease Prevalence Rate in Mainland China

- In May 2010, the Medical Genetics of the Chinese Medical Association proposed the definition of rare diseases to be <1/500,000 population or <1/10,000 newborns
- It is estimated that the number of patients with each rare disease in China is about 2,800. The total number of rare diseases in China is about 16.8 million
- Mainland China has a 1.34 billion population, and there is a large number of rare diseases with low prevalence

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The Publication of a List of Rare Diseases in China

- In 2016, 56 rare diseases were published in Shanghai, which can be prevented and cured
- In May 2018, five Ministries, including the National Health Committee, jointly formulated the first national list of rare diseases and published 121 rare diseases, which will be on the Chinese national registry

- However, only 44 diseases (36.4%) have orphan drugs globally, while less than half of them have been launched in the Chinese market

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Pattern of Rare Diseases in Beijing

- An eMR study conducted in tertiary hospitals in Beijing for five years (2015)
- 1,423 rare disease cases were found in 400,000 medical records
- The top 6 diseases were congenital malformations, diseases of the nervous system, endocrine and metabolic disorders, and diseases of the circulatory system, skeletal muscle and connective tissue

- Another eMR study of 405,000 medical records in 93 tertiary hospitals in 7 provinces
- 2.27% cases suffered from 952 rare diseases
- More than half of the rare diseases were congenital diseases

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A Synergistic Study of RD in China

RD Epidemiological Survey

- Hemophilia
- Kawasaki disease
- Down's syndrome
- Paroxysmal nocturnal hemoglobinuria
- Hepatolenticular degeneration
- Myasthenia gravis
- Chronic thromboembolic pulmonary hypertension (CTEPH)
- Hereditary cerebellar atonic attune (SCA)

Establishing Registry System

- Establishing National and regional registry system platform registered >50 RD
- Establishing national RD research network
- In 2016, National Health and Family Planning established a National Advisory Committee of RD diagnosis & treatment

Research Report on Rare Diseases in China 2018

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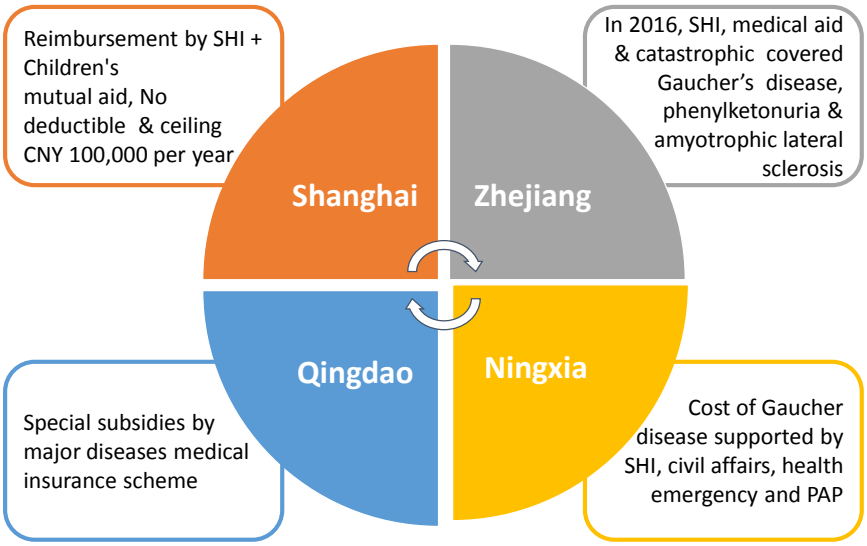
Medical Security System for RD in China



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Potential Models to Accelerate Patient Access of Orphan Drugs

- Doctor training, and prescribing orphan drugs by designated medical institutions and experts, & fixed distributors to supply
- Priority setting on some rare diseases that are expected to significantly improve patients' access to care
- Listing some orphan drugs in the basic insurance reimbursement drug formulary through price negotiations
- Drug companies & Red Cross jointly conducted PAP for charitable donations
- Multi-party fund-raising, including civil affairs' medical assistance

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The Legislation Environment for Rare Disease is Getting Better

Key Market Events

1. NHC released first batch of rare disease in China
2. CDE Granted expedited approval to urgently-needed orphan drugs marketed overseas
3. CNDA issued the Technical Guidelines for Acceptance of Foreign drug clinical trial data
4. Chinese government waived import tariffs on import oncology drugs
5. SMIA intended to regularly hold nationwide price negotiation for high cost drugs in China

Implications

1. China may start to legislate on rare disease related field
2. The launch time of pipeline orphan drug will be significantly brought forward
3. It is possible that OD may also enjoy 0 tariffs in the near future due to similarity in high cost
4. The reimbursement review cycle can be significantly shortened, and in future, BMI inclusion may be quicker

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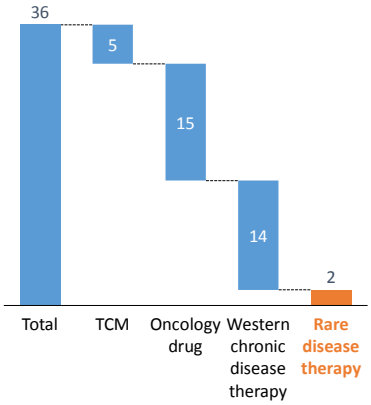
In Line with the Recent Acceleration in Rare Disease Legislation, Rare Disease in China is Gaining Awareness

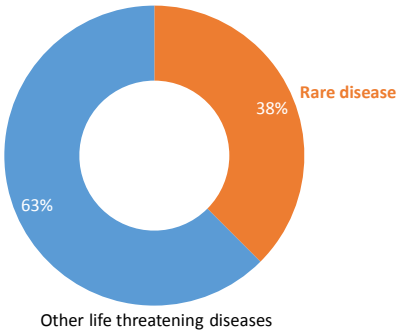
2016

Type distribution of 36 NRDL listing negotiation high-cost drug (2017)



2017

Type distribution of 48 list of urgently-needed new drugs marketed overseas published by CDE (2018)



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Policy Recommendations

- Formulating master plan
- Promoting government role & social security
- Strengthening register & monitoring system
- Establishing rare disease clinical center & referral
- Clinical pathway & guidelines
- Integrating social forces

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Audience Vote

Do you agree that the most practical and fastest way to achieve national reimbursement coverage for rare disease therapy is through national price negotiation?

Audience Vote – Raise Your Hand for Yes

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| **Gesundheit** | Mobilität | Bildung |

IGES

The German Solution: Immediate Access and Data Collection

Bertram Häussler, IGES Institut

ISPOR Asia Pacific 2018 – Workshop W14
Tokyo, September 11th, 2018

Overview

Every new drug (including OD) can be marketed after

- EU marketing authorization &
- German licencing

Immediate market access for OD

- no further delay by decision process

Reimbursement for new drugs subject to demonstration of additional benefit

For Ods „additional clinical benefit" is automatically demonstrated

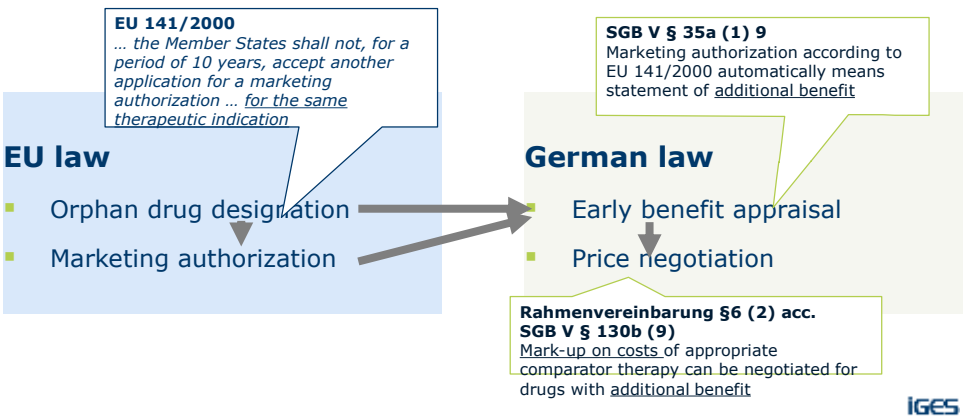
- if expenditure < 50 €m p.a.
- > 50 m → full clinical assessment

No patient-specific second opinion needed

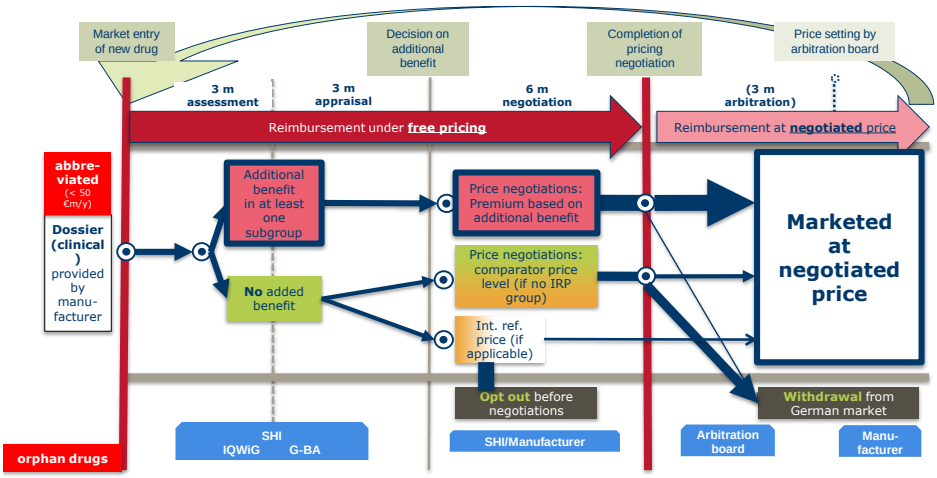
Speciality drugs (including OD) may be

- restricted to specialized physicians or centers
- charged with requirements for data collection

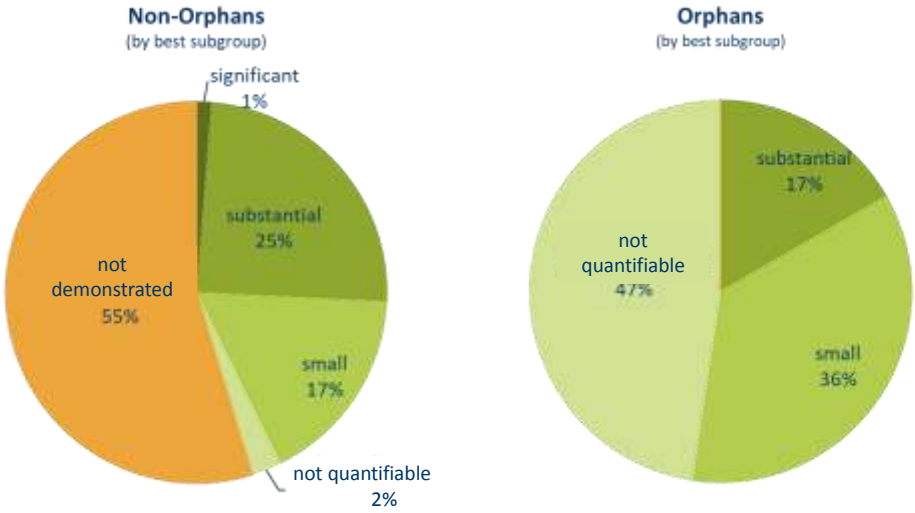
Legal situation: Germany complies with EU regulation



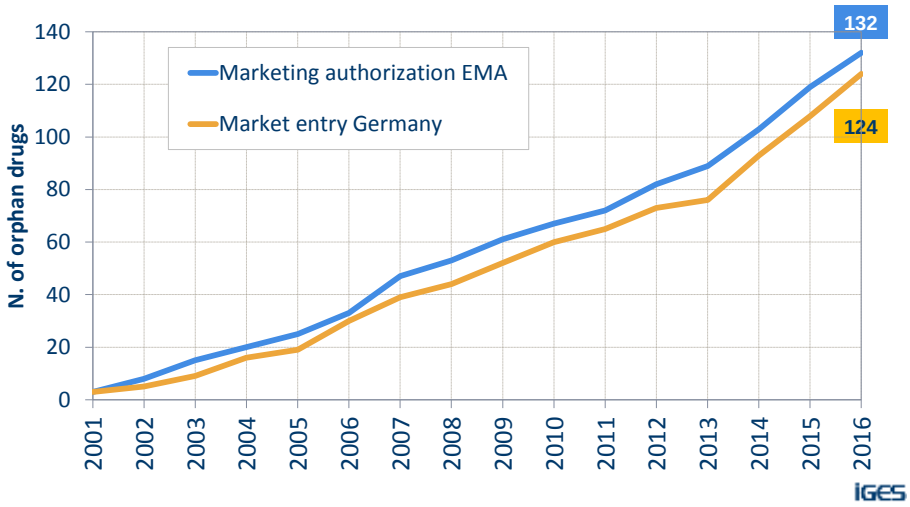
Assessment / appraisal in detail



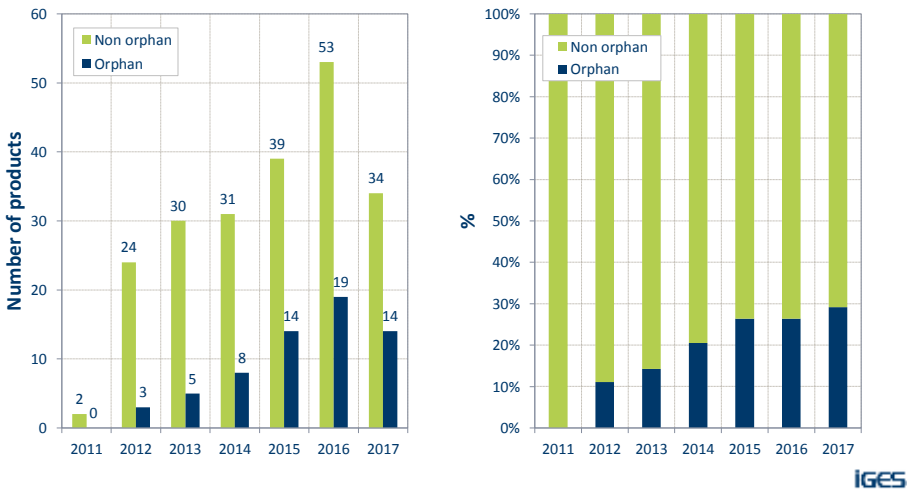
Appraisals all positive for orphan drugs



Germany market is attractive and permissive as well

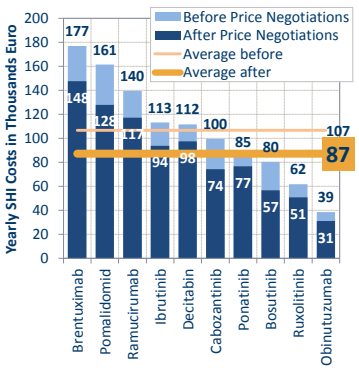


Orphan drugs account for appr. 30% of all new drugs in the German market

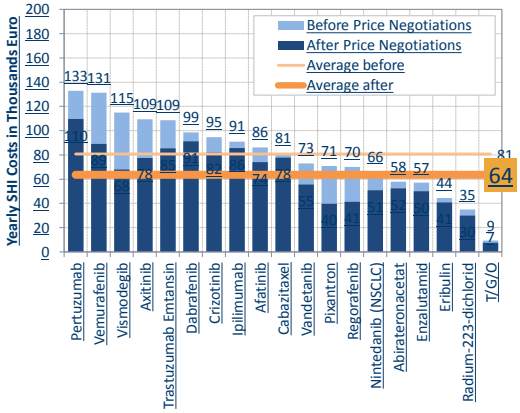


Prices higher for orphan drugs (within oncology indication)

Orphans (oncology)



Non-Orphans (oncology)



T/GO = Tegafur/ Gimeracil/ Ote
Source: IGES calculations based on Lauer-Taxe® and (

Only 1 "opt out" since 2011

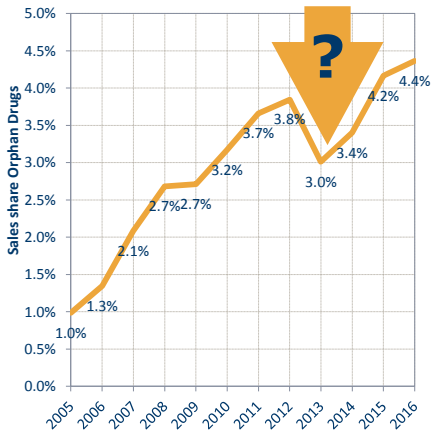
Re-assessment for exceeding 50 €m p.a. threshold

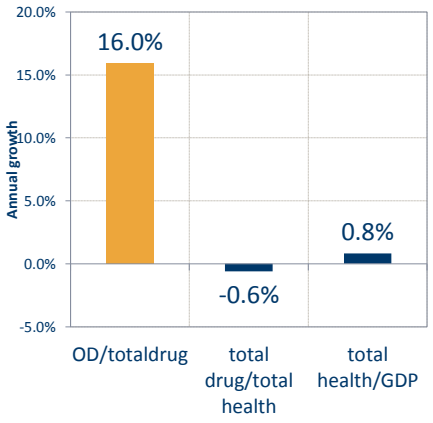
- → Full assessment against comoarator

4 / > 120

Drug	Initial Assess-ment	Reass-essment
Ruxolitinib	Small ↑	Substantial +21%
Pomali-domid	Substantial ↓	Substantial/ not dem. -7%
Ibrutinib	Not quant. ↓	Not quant. / not dem. -3%
Macitentan	Small ↓	Not dem. -17%

Budget impact of Orphan Drugs growing relatively - „explosion" of health expenditures did not occur





Annual growth 2016 / 2005

Audience Vote

Do you believe that the expiration of the OD status does substantially contribute to contain the OD budget?

Audience Vote – Raise Your Hand for Yes

| **Gesundheit** | Mobilität | Bildung |

IGES Institut
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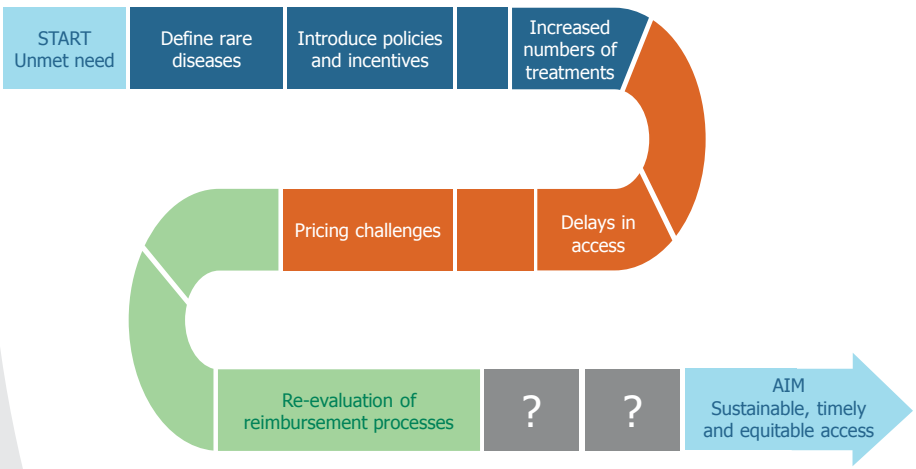
Discussion

Summary and Close

Dr Annabel Griffiths

Head of Rare Diseases, Costello Medical, UK

Summary



Acknowledgements

Thank you for your attention

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