Research Office
Legislative Council Secretariat

Fact Sheet

Supplementary information on rare disease policies in selected places

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1. Introduction

1.1 Rare diseases are a large group of diseases that are characterized by a low prevalence in the population.[1] While individually rare, there are more than 7 000 rare diseases collectively affecting 1 in 15 persons worldwide.[2] While nearly all genetic diseases are rare diseases, not all rare diseases have a genetic origin since they also cover very rare forms of infectious diseases, auto-immune diseases and rare cancers.[3]

1.2 Rare diseases are serious chronic diseases and are often life-threatening. They pose challenges to the medical sector in view of the diverse types of rare disease conditions that exist, insufficient knowledge or training on the diseases, and the high costs and risks of research and development of drugs (commonly referred to as "orphan drugs") for treating the diseases given the small and dispersed patient base for each disease. As a result, medical care for patients suffering from rare diseases may be hampered by delayed diagnosis, unavailability of treatments, and/or limited access to costly drugs and treatments. These patients and their families face immense physical, psychological and economic burdens.

1.3 This fact sheet is an update on the one published under the same title by the Research Office on 12 May 2017,[4] with additional information on the rare disease policy framework of Hong Kong, the United States ("the US"), the European Union ("the EU"), Australia, Japan, Taiwan and South Korea.

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1 Rare diseases are often referred to as orphan diseases due to the lack of financial incentives for pharmaceutical companies to develop drugs that would treat a small target patient population.

2 See De Vrueh, R. et al (2013), Shafie, A. et al (2016) and Song, P. et al (2012).

3 See De Vrueh, R. et al (2013).

4 On 12 May 2017, the Research Office issued a fact sheet entitled "Supplementary information on rare disease policies in selected places" which studied the United States, the European Union, Australia, Japan, Taiwan and South Korea in terms of their policies over the years to address issues faced by rare disease patients.

This includes: (a) the background leading to legislation on orphan drugs; (b) the mechanism for determining and controlling the prices of orphan drugs reimbursed under the respective healthcare systems; (c) the number of rare disease patients receiving subsidy on medical costs and the amount of costs incurred; and (d) the recent developments on rare disease policy. The paragraphs below give an overview of the rare disease policies in Hong Kong and the overseas places studied, and the salient features of their policies are compared in the **Table**.

2. Rare disease policy in Hong Kong

2.1 In Hong Kong, the Clinical Genetic Service of the Department of Health provides clinical diagnosis, counselling and prevention services for families possibly affected by genetic related diseases. Meanwhile, the Hospital Authority provides medical services for patients suffering from genetic diseases. Added to this, the Department of Health and the Hospital Authority started the Pilot Study of Newborn Screening for Inborn Errors of Metabolism in October 2015, in an effort to prevent and reduce severe problems arising from inborn errors of metabolism. The number of inborn errors of metabolism covered under the Pilot Study increased from 21 to 24 in April 2016.

2.2 Since 2008-2009, the Government has also subsidized patients who suffer from six specified types of lysosomal storage disorder[5] and meet the specific clinical criteria to obtain enzyme replacement therapy. As a new initiative, eligible patients suffering from Paroxysmal Nocturnal Haemoglobinuria will be provided with drug subsidies under an assistance programme of the Community Care Fund from August 2017 onwards.

2.3 Notwithstanding the above-mentioned medical services provided, the Government has not established any official definition of rare diseases, nor has it set out any specific policy on provision of support for rare disease patients. Indeed, some key stakeholders (particularly patient groups) have criticized the Government for being unable to provide adequate support to rare disease patients, as evidenced by (a) the delay in the time to diagnose rare diseases; (b) limited number of patients receiving subsidies to help cover the

[5] The six types of lysosomal storage disorder are Gaucher disease, Pompe disease, Mucopolysaccharidosis Type I/Type II/Type VI and Fabry disease. Up to December 2016, the Hospital Authority had provided enzyme replacement therapy to 27 patients with lysosomal storage disorders.

high-cost medication; (c) the lack of a comprehensive patient registry to facilitate the provision of evidence-based treatments to patients; and (d) insufficient provision of social care services to patients and their carers.[6]

3. Rare disease policies in the overseas places studied

3.1 The US, the EU, Australia, Japan, Taiwan and South Korea have devised policies over the years to address issues faced by rare disease patients. These places have set out their definition for rare diseases and put in place an orphan drug designation system to encourage the development of orphan drugs for treating rare diseases. They have also implemented other measures to support the medical and/or social care of rare disease patients under their respective rare disease policy framework.

Definition of rare diseases

3.2 All the above overseas places have defined rare diseases in terms of a prevalence rate measured by the total number of rare disease patients (less than 200 000 in the US and 20 000 or less in South Korea), the number of rare disease patients in 10 000 persons (fewer than five persons in the EU and Australia, and fewer than one in Taiwan), or the proportion of rare disease patients in the total population (less than 0.1% of the total population in Japan). Japan and Taiwan have also considered other criteria in their definition of rare diseases such as diseases that are difficult to diagnose and treat, or no appropriate treatment is available.

Orphan drug designation system

3.3 The US was the first to pass specific legislation (the Orphan Drug Act) designed to promote development of treatments for rare diseases. The Act contains provisions governing the designation of orphan drugs and granting of incentives and assistance in the regulatory process to encourage pharmaceutical companies to develop orphan drugs. Following the US, Japan, Australia, the EU, Taiwan and South Korea have also passed legislation

[6] See Minutes of Meeting of the Panel on Health Services of the Legislative Council (2014) and Hong Kong Alliance for Rare Diseases (2016).

to establish a similar orphan drug designation system. The orphan drug designation systems of the above overseas places cover all of the seven uncommon disorders which have been or will be covered under the drug subsidization schemes of the Hong Kong Government.[7]

3.4 The above overseas places have also provided incentives to pharmaceutical companies to address the issue about the limited availability of drugs and treatments for rare diseases. The incentives granted by them generally include financial subsidies and tax relief on research expenses, fast-track marketing approval process, reduced or waived application fees, and marketing exclusivity for a certain number of years after obtaining marketing authorization/approval of an orphan drug.

3.5 The introduction of the orphan drug designation system has resulted in increased orphan drug development activities and greater availability of authorized/approved orphan drugs for treating rare diseases. For example, between 2000 and 2016, the EU has designated 1 805 orphan drugs and granted marketing authorizations to 128 orphan drugs for treating 101 conditions. Likewise in the US, the number of designated orphan drugs totalled 4 171 as at June 2017. The orphan drug designation system has also successfully enabled the development and marketing of over 600 drugs and biologic products for rare diseases since 1983. In contrast, fewer than 10 such products supported by industry came to market between 1973 and 1983.

Mechanism for determining and controlling the prices of orphan drugs

3.6 Japan, Taiwan, South Korea, Australia and some EU member states have established their respective mechanisms for pricing orphan drugs, thereby facilitating the calculation of patients' drug costs to be reimbursed under their national health insurance or public healthcare systems. Factors that are considered in determining the price of a newly listed orphan drug include: (a) availability and prices of alternative products in the market; (b) degree of innovation of the product or efficacy/usefulness over existing comparable products; and (c) prices of the product in reference overseas countries.

[7] Comparison made is based on the latest information available on the orphan drug designation systems of the respective places.

3.7 For example, in Taiwan, the price of an orphan drug listed by the National Health Insurance Administration is determined with reference to the median of drug prices of 10 reference countries, and a 10% premium is added to a breakthrough innovative product that has undergone efficacy and safety clinical trial in Taiwan. In Japan, the reimbursement price of a new orphan drug is determined with reference to the prices of existing drugs in the same category and a premium of 10% to 20% will be added to the price if the new drug is considered to be more useful than the existing drugs. If no similar product is available in the market, the reimbursement price is determined based on cost accounting method. In both cases, the price calculated will be adjusted in case there is a big discrepancy compared against the prices of the drug in four reference countries.

3.8 In contrast, the prices of orphan drugs in the US are set by the respective pharmaceutical companies. However, the federal and state governments have implemented measures to control the prices of prescription drugs reimbursed under Medicaid, the social healthcare scheme.[8] These price controlling measures include (a) requiring the pharmaceutical companies to offer rebate on prices of prescription drugs; and (b) setting a limit on the reimbursement price for specified multiple-source prescription drugs.

Other support measures for rare disease patients

3.9 All the overseas places studied have also adopted one or more of the following common measures to enhance the awareness, early identification, prevention and treatments of rare diseases: (a) providing relevant information on rare diseases through an online information centre; (b) implementing a newborn screening programme; (c) establishing a patient registry or a repository of registries to facilitate information sharing for patient care and research purposes;[9] and (d) committing resources on research and development on rare diseases. It is noteworthy that Japan and Taiwan have specifically incorporated the need for social care services among rare disease patients into their rare disease policy framework. In particular, they have expanded the

[8] Medicaid is a means-tested welfare programme to assist individuals and families with low incomes and relatively few assets with paying for their health care. The programme is administered by the state governments and is funded jointly by the federal and state governments.

[9] In Australia, there have been calls for the federal government to formulate a comprehensive national plan on rare diseases covering the establishment of a national registry and provision of coordinated care to rare disease patients. At present, some research institutions are collecting rare disease patients' information but none of them is reportedly resourced adequately.

definition of persons with disabilities to cover patients suffering from designated rare diseases and provided them with social care services that are stipulated in the relevant legislation.

Observations

3.10 Among the overseas places studied, Japan and Taiwan have put in place a comprehensive policy framework which incorporates the medical and social care needs of the rare disease patients. In the US, the EU and South Korea, the rare disease policy focuses on addressing the medical care needs of patients and promoting research and development on rare diseases. In contrast, Australia has set out its rare disease policy targeting at promoting the research and development of orphan drugs. As such, there have been calls for the Australian federal government to formulate a comprehensive national plan on rare diseases.

3.11 While the scope and focus of the rare disease policy differ among the overseas places studied, their rare disease patients have benefitted from the increased availability of orphan drugs consequential to the introduction of the orphan drug designation system. Japan, Taiwan, South Korea and Australia have also implemented measures to subsidize the medicine and/or medical costs of patients, particularly those with low income. This has helped improve the accessibility of rare disease patients to expensive drugs and treatments.

Table – Rare disease policies in selected places

	Hong Kong	Japan	Taiwan	South Korea
Definition and prevalence of rare diseases				
Definition of rare diseases in terms of prevalence criterion	• No official definition of rare diseases.	• Less than 0.1% of the total population.	• Fewer than one in 10 000 persons (i.e. less than 0.01%).	• 20 000 or less.
Other criteria considered for designation of rare diseases	• Not applicable.	• Other criteria include: (a) causes of diseases not identified; (b) lacking effective treatments; (c) requiring long-term treatments; and (d) existence of objective diagnostic criteria.	• Other criteria include: (a) having a genetic origin; and/or (b) being difficult to diagnose and treat.	• Not specified.
Number of rare diseases/ designated rare diseases affecting the population	• Information not available.	• 330 designated intractable/rare diseases.	• 216 designated rare diseases.	• Over 133 rare diseases.
Prevalence of rare diseases	• Information not available.	• 943 460 patients suffering from designated intractable/rare diseases as at end-2015.	• 7 625 patients suffering from designated rare diseases in 2015.	• An estimated 500 000 persons suffering from rare diseases in 2013.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Definition and prevalence of rare diseases (cont'd)			
Definition of rare diseases in terms of prevalence criterion	• Less than 200 000 patients.	• Fewer than five in 10 000 persons.	• Fewer than five in 10 000 persons.[10]
Other criteria considered for designation of rare diseases	• Not specified.	• Not specified.	• Not specified.
Number of rare diseases/ designated rare diseases affecting the population	• About 7 000 rare diseases.	• About 5 000 to 8 000 rare diseases.	• Information not available.
Prevalence of rare diseases	• Between 25-30 million persons suffering from rare diseases.	• About 30 million persons suffering from rare diseases.	• An estimated 1.2 million persons suffering from rare diseases in 2015.

[10] The Australian Government Department of Health has changed the orphan disease prevalence threshold under its orphan drug designation system in July 2017, potentially allowing additional conditions to be classified as orphan conditions. Previously, the threshold was set at "not more than 2 000 individuals at any time".

Table – Rare disease policies in selected places (cont'd)

	Hong Kong	Japan	Taiwan	South Korea
Policy framework				
Responsible authorities	• Food and Health Bureau.	• Ministry of Health, Labour and Welfare ("MHLW").	• Ministry of Health and Welfare ("MOHW").	• Ministry of Health and Welfare and Ministry of Food and Drug Safety.
Relevant legislation	• No dedicated legislation on rare diseases/ uncommon disorders.	• The amended Pharmaceutical Affairs Act, and the 2014 Act on Medical Care and Social Supports for Patients with Intractable/Rare Diseases.	• Rare Disease and Orphan Drug Act《罕見疾病防治及藥物法》 implemented in 2000.	• The amended Pharmaceutical Affairs Act, and the Rare Disease Control Act 2015.
Background leading to the legislation	• Not applicable.	• The Pharmaceutical Affairs Act was amended in 1993 to address the issues of (a) meagre orphan drug related research and development activities; and (b) limited availability of orphan drugs. • The Act on Medical Care and Social Supports for Patients with Intractable/Rare Diseases was enacted in 2014, after a policy review conducted in 2011 to assess the provision of comprehensive and equitable support to patients with intractable/rare diseases.	• The implementation of the Rare Disease and Orphan Drug Act was in response to the earlier calls from key stakeholders for the government to enhance the support provided to rare disease patients amid their limited access to costly orphan drugs and treatments. At that time, the drug and treatment costs incurred by rare disease patients were not covered under the National Health Insurance programme[11] unless the rare diseases had been defined as major illnesses.	• The Pharmaceutical Affairs Act was amended in 2001 to provide for the legal basis for the operations of the Korea Orphan Drug Center, including the authorization to sell medications needed for diagnosis and treatment to the patients suffering from rare diseases to ensure they have access to the best treatment possible. • The Rare Disease Control Act was enacted in 2015 to enhance the policy on supporting rare disease patients.

[11] The National Health Insurance programme is a mandatory social insurance programme to cover the medical and medication costs of the Taiwanese people. The programme is financed by premiums contributed by the insured, employers and the government.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Policy framework (cont'd)			
Responsible authorities	• The United States Department of Health and Human Services, the United States Food and Drug Administration, and relevant state authorities.	• European Medicines Agency and relevant authorities of individual member states.	• The Australian Government Department of Health and the Australian Government Department of Human Services.
Relevant legislation	• The Orphan Drug Act of 1983 and the Rare Diseases Act of 2002.	• The European Union Regulation on Orphan Medicinal Products.	• The amended Therapeutic Goods Regulations.
Background leading to the legislation	• The Orphan Drug Act was passed in 1983 to address the little incentive on the part of pharmaceutical companies to invest in the development of orphan drugs, leading to limited availability of treatments for rare disease patients. • The enactment of the Rare Disease Act of 2002 was to empower the Office of Rare Diseases Research under the National Institutes of Health ("NIH[12]") to promote research and development on rare diseases, and provide for NIH to set up an information centre to provide stakeholders with information on rare diseases.	• The European Union Regulation on Orphan Medicinal Products was adopted in 1999 to stimulate the development of orphan drugs at the Community level and individual member state level.	• The Therapeutic Goods Regulations was amended in 2001 to provide for the establishment of an orphan drug designation system in Australia. The objective of the system is to improve the Australian community's access to orphan drugs by providing incentives for pharmaceutical companies to register such products and removing barriers which may discourage registration.

[12] NIH is an agency under the Department of Health and Human Services responsible for providing leadership and direction to research programmes to improve the health of the public. NIH comprises 27 institutes and centres with each having its own specific research agenda.

Table – Rare disease policies in selected places (cont'd)

	Hong Kong	Japan	Taiwan	South Korea
Policy framework (cont'd)				
Policy scope identified	• Preventing and reducing severe health problems arising from inborn errors of metabolism. • Providing drug subsidies to eligible patients suffering from specified rare diseases/uncommon disorders.	• Developing effective treatments, and enhancing medical and social care services for rare disease patients. • Establishing a fair and consistent subsidization mechanism. • Enhancing public understanding of rare diseases.	• Improving the awareness, prevention, diagnosis, and treatment of rare diseases. • Enhancing medical and social care services for rare disease patients.	• Promoting development of orphan drugs. • Improving quality of life of patients with rare diseases. • Promoting research and development on rare diseases.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Policy framework (cont'd)			
Policy scope identified	• Promoting development of orphan drugs. • Supporting research and development on rare diseases.	• Promoting development of orphan drugs. • Supporting member states to ensure their effective and efficient recognition, prevention, diagnosis and treatments of, and research on, rare diseases.	• Promoting development and marketing of orphan drugs.

Table – Rare disease policies in selected places (cont'd)

	Hong Kong	Japan	Taiwan	South Korea
Orphan drug designation system				
Criteria of defining an orphan drug	• Not applicable for the lack of an orphan drug designation system in Hong Kong.	• The drug must meet three criteria: (a) to be used by less than 50 000 patients in Japan; (b) indicated for the treatment of serious diseases and no alternatives are available; and (c) with a scientific rationale to support the need for the drug.	• The drug should have major indications for the prevention, diagnosis and treatment of designated rare diseases.	• The drug must meet the following criteria: (a) treating a disease which affects 20 000 or less patients in South Korea; and (b) there is no appropriate therapies and drugs available to treat the disease, or the drug demonstrating a significant improvement in safety or efficacy over the existing alternative drugs.
Provision of financial incentives and assistance in regulatory process to facilitate research and development activities	• Not applicable.	• Including financial subsidies/tax relief, a 10-year period of marketing exclusivity and fast-track marketing authorization.	• Including a 10-year period of marketing exclusivity, and allowance for special application for usage reimbursement of designated orphan drugs prior to market approval.	• Including reduced application fees and expedited review process for the marketing authorization of orphan drugs.
Number of designated orphan drugs	• Not applicable.	• 318 as at May 2015.	• 98 as at January 2017.	• Information not available.
Number of designated orphan drugs granted with marketing authorization or approval	• Not applicable.	• 238 as at May 2015.	• Information not available.	• 341 as at 2016.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Orphan drug designation system (cont'd)			
Criteria of defining an orphan drug	• The drug is to treat a disease which (a) affects less than 200 000 persons in the United States ("the US"); or (b) affects more than 200 000 persons in the US but cost of developing the drug is not recoverable from sales in the country.	• The drug is intended for treating a life-threatening disease that meets the prevalence criterion and no satisfactory treatment is available.	• The criteria include that: (a) the drug is intended to treat, prevent or diagnose a life-threatening or seriously debilitating condition; (b) the condition affects less than five in 10 000 individuals, or not commercially viable to supply the drug unless the relevant fees are waived; and (c) no similar drug has been registered, or the drug provides significant benefit over registered drugs.
Provision of financial incentives and assistance in regulatory process to facilitate research and development activities	• Including financial subsidies/tax credit, fast-track marketing authorization and a seven-year period of marketing exclusivity.	• Including a 10-year period of marketing exclusivity and reduced fees for marketing authorization applications.	• Including waiver of fees for the application, evaluation and registration of drugs.
Number of designated orphan drugs	• 4 171 as at June 2017.	• 1 805 between 2000 and 2016.	• 287 between 1998 and 2013.
Number of designated orphan drugs granted with marketing authorization or approval	• 625 since 1983.	• 128 between 2000 and 2016.	• 144 between 1998 and 2013.

Table – Rare disease policies in selected places (cont'd)

	Hong Kong	Japan	Taiwan	South Korea
Orphan drug designation system (cont'd)				
Reimbursement of drug costs incurred by rare disease patients	• Not applicable. Nonetheless, the Hong Kong Government provides drug subsidies to eligible patients suffering from six specified types of lysosomal storage disorder ("LSD").[13] Eligible patients suffering from Paroxysmal Nocturnal Haemoglobinuria ("PNH") will be provided with drug subsidy under the Community Care Fund from August 2017 onwards.	• Costs of using orphan drugs granted with marketing approval can be reimbursed under the national health insurance system.	• Reimbursement of drug costs can be arranged for those drugs which are approved to be on the list of drugs covered by the National Health Insurance Administration ("NHIA"). • Reimbursement of the costs of using unlisted drugs is allowed if approval is sought prior to drug usage.	• Costs of orphan drugs approved to be on the reimbursement drug list of the Korean National Health Insurance Service ("NHIS")[14] can be partially reimbursed.
Seven uncommon disorders that have been or will be covered under the drug subsidization schemes of the Hong Kong Government	• The drug subsidization schemes cover the above seven uncommon disorders.	• Japan, Taiwan and South Korea have covered these seven uncommon disorders under their respective orphan drug designation systems.		

[13] The six specified types of LSD are Gaucher disease, Pompe disease, Mucopolysaccharidosis Type I/Type II/Type VI and Fabry disease.

[14] NHIS is a quasi-public organization under the Ministry of Health and Welfare responsible for operating and managing the national health insurance system in the country.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Orphan drug designation system (cont'd)			
Reimbursement of drug costs incurred by rare disease patients	• Drug costs are covered by (a) the public or private insurance schemes that the patients enrolled in; and (b) co-payments by patients.	• Reimbursement of drug costs is made in accordance with the healthcare financing systems and reimbursement arrangements put in place by individual member states.	• Patients who meet specific clinical criteria for using orphan drugs listed in the Pharmaceutical Benefits Scheme ("PBS") Schedule can recover part of the drug costs under the government-funded PBS.
Seven uncommon disorders that have been or will be covered under the drug subsidization schemes of the Hong Kong Government	• The US, the European Union (the "EU") and Australia have covered these seven uncommon disorders under their respective orphan drug designation systems.		

Table – Rare disease policies in selected places (cont'd)

	Hong Kong	Japan	Taiwan	South Korea
Mechanism for pricing orphan drugs				
Pricing mechanism	• The Hospital Authority follows the prevailing guidelines set out in its Procurement and Materials Management Manual, whereby it procures drug items through competitive tenders where appropriate and selects offers having the best value for money. • In situations where negotiation is justified, the Hospital Authority would initiate the negotiation process with the prospective tenderers/suppliers on the price, terms and conditions, after sales support and other value added services.	• Under the national health insurance system, the reimbursement price of a new drug is determined with reference to the prices of existing drugs in the same category. A premium of 10% to 20% will be added to the price if the new drug is considered to be more useful than the existing ones. • If no similar product is available in the market, the reimbursement price is determined based on cost accounting method. • Whatever the method adopted for pricing orphan drugs, the drug prices calculated will be adjusted if there is a big discrepancy when compared against the prices of the drug in four reference countries.[15]	• For new drugs listed by NHIA which are categorized as breakthrough innovative products, the price is set as the median of drug prices of 10 reference countries.[16, 17] A 10% premium will be added for products that have undergone efficacy and safety clinical trial in Taiwan. • For new products that have moderate improvement on or similar therapeutic value of comparable products, the ceiling price of the products is set as the median of drug prices of 10 reference countries.[18] • If the drug price set according to the above mechanism is below the costs of the supplier, up to 20% premium will be added on the median of drug prices of 10 reference countries depending on the total amount of reimbursement per month.	• For a new drug listed by NHIS, the price is set at the weighted average price of alternative drugs in the country. • If no alternative drugs are available in the country, the drug price is based on the negotiation between NHIS and the pharmaceutical company supplying the new drug with reference to (a) the lowest price or average price of comparable drugs among seven reference countries;[19] or (b) a risk sharing agreement signed between them.[20]

[15] The reference countries are the US, the United Kingdom, Germany and France.

[16] The 10 reference countries are: the United Kingdom, Germany, Japan, Switzerland, the US, Belgium, Australia, France, Sweden and Canada.

[17] If Taiwan is the first market for introducing the new drug, the drug price will be determined based on the market price, the cost accounting method, or prices of similar products in 10 reference countries.

[18] The methods adopted for determining the drug price include the lowest of the drug prices in 10 reference countries and drug price in the country of origin.

[19] The seven reference countries are: the US, Japan, the United Kingdom, Germany, France, Switzerland and Italy.

[20] For example, NHIS allows a pharmaceutical company to be exempted from undertaking the cost-effectiveness test before marketing its new drug. Yet the pharmaceutical company has to share the responsibilities if the new drug proves to be ineffective to the rare disease patients, such as refunding NHIS for the cost it incurs on the drug.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Mechanism for pricing orphan drugs (cont'd)			
Pricing mechanism	• The prices of the drugs are determined by the pharmaceutical companies. • Nonetheless, the federal and state governments have implemented measures to control the costs of prescription drugs reimbursed under the Medicaid Programme. For example, rebate on prices of prescription drugs is offered by pharmaceutical companies[21] under the Medicaid Drug Rebate Programme. Besides, a limit is set on the reimbursement price for specified multiple-source drugs dispensed to Medicaid patients under the Federal Upper Limit Programme.[22]	• The mechanism for determining and controlling the reimbursed pricing of orphan drugs varies among the member states. In general, the drug price may be set by the pharmaceutical companies or fixed after negotiation between the responsible authorities and the pharmaceutical companies in the respective member state. • Factors taken into account by the responsible authorities in determining the price for an orphan drug may include: (a) its clinical performance and cost-effectiveness; (b) availability and prices of existing alternative treatments; (c) prices of the drug in other countries; and (d) degree of innovation of the drug.	• The price of an orphan drug listed in the PBS Schedule comprises the following components: (a) the costs to the pharmacist of procuring the drug which is calculated as the approved ex-manufacturer price[23] plus a wholesale mark-up; (b) a specified level of pharmacy mark-up; (c) specified levels of dispensing fees; and (d) other fees the pharmacist is entitled to.

[21] The level of rebate varies depending on the drug category. For example, for innovator drugs, the rebate level for each unit of a drug is the greater of 23.1% of the average manufacturer price ("AMP") per unit or the difference between AMP and the best price per unit, and adjusted by the consumer price index. See Medicaid.gov (2017).

[22] The federal upper limit is set at no less than 175% of the weighted average of the most recently reported monthly AMP of multiple-source drug products that are available for purchase at retail community pharmacies on a nationwide basis.

[23] The ex-manufacturer price of a drug is negotiated between the pharmaceutical company and the responsible authority. The pricing method adopted may vary by the types of drug to be listed in the PBS Schedule. For example, the "cost plus method" is commonly used for stand-alone products if no specific comparable product exists in the market. Alternatively, reference pricing is adopted for drugs having similar safety and efficacy levels as other listed drugs.

Table – Rare disease policies in selected places (cont'd)

	Hong Kong	Japan	Taiwan	South Korea
Other support measures for diagnosis and treatment of rare disease patients				
Information provided to enhance key stakeholders' awareness and knowledge of rare diseases	• Not specified under the existing policy.	• Information provided through an online resource centre (i.e. the Japan Intractable Diseases Information Center).	• Information provided by MOHW through a specific portal and public education programmes.	• Information provided through a nationwide portal (i.e. the Helpline).
Facilitation measure for early identification of rare diseases	• Pilot Study of Newborn Screening for Inborn Errors of Metabolism covering 24 inborn errors of metabolism.	• Not specified under the government's policy framework.	• Newborn screening programme covering 11 metabolism disorders.	• Newborn screening programme is implemented.
Facilitation measures for accessing medical care services	• Seven uncommon disorders have been identified by the Hong Kong Government and covered under its drug subsidization scheme.[24]	• Patients only have to bear 20% of the medical costs as co-payment, capped at a monthly limit set by MHLW.	• Patients of designated rare diseases are provided with 80% reimbursement for medical and medication costs under the National Health Insurance programme. Low-income patients can receive 100% reimbursement. • Patients are subsidized to access overseas diagnostic services in case these services are not available locally.	• The government subsidizes medical expenses for low-income patients suffering from 133 specified rare diseases. • The government funds a regional hospital network dedicated to providing effective patient care and enhancing counselling services for genetic and rare diseases in four provinces.

[24] As mentioned above, these seven uncommon disorders are Gaucher disease, Pompe disease, Mucopolysaccharidosis Type I/Type II/Type VI, Fabry disease and PNH.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Other support measures for diagnosis and treatment of rare disease patients (cont'd)			
Information provided to enhance key stakeholders' awareness and knowledge of rare diseases	• Current and easy-to-understand information provided through the Genetic and Rare Diseases Information Center.	• Comprehensive and updated information provided through the Orphanet portal.	• Not specified under the national policy framework.
Facilitation measure for early identification of rare diseases	• Newborn screening programmes implemented by individual states.	• Newborn screening programmes implemented by individual member states.	• Newborn screening programmes implemented by individual states/territories.
Facilitation measures for accessing medical care services	• Passage of the Patient Protection and Affordable Care Act in 2010 to remove various discriminatory insurance practices against rare disease patients.[25]	• Subject to the policy framework of individual member states.	• Under the Life Saving Drugs Programme, eligible rare disease patients are fully subsidized on the costs of 12 expensive and life-saving drugs that are not available through PBS due to failure to meet the cost-effectiveness criterion. These patients must be those who suffer from eight specified types of rare diseases and meet specified eligibility criteria and conditions.

[25] The Patient Protection and Affordable Care Act has been opposed by some stakeholders as it has brought about issues such as increase in insurance costs from better insurance coverage. Currently, the federal government has been reviewing the health insurance system with a view to repealing the Act.

Table – Rare disease policies in selected places (cont'd)

	Hong Kong	Japan	Taiwan	South Korea
Other support measures for diagnosis and treatment of rare disease patients (cont'd)				
Facilitation measures for accessing social care services	• Not specified under the existing policy.	• Provision of social care services through the intractable/rare diseases consultation and support centres. • Expanding the definition of persons with disabilities to cover persons suffering from most designated intractable/ rare diseases and providing them with relevant social care services.	• Expanding the definition of persons with disabilities to cover persons suffering from designated rare diseases and providing them with relevant social care services.	• Not specified under the government's policy framework.
Establishment of a patient registry/ reporting system	• Not specified under the existing policy.	• Yes.	• Yes.	• Yes.
Committing resources on research and development ("R&D") on rare diseases	• Not specified under the existing policy.	• MHLW commits resources on R&D projects related to rare diseases.	• MOHW provides incentives to encourage institutions to engage in R&D on rare diseases.	• The Ministry of Health and Welfare promotes research on rare diseases through (a) providing the infrastructures (e.g. establishing the Korean Mutation Database and organizing the clinical study networks); and (b) leading basic research.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Other support measures for diagnosis and treatment of rare disease patients (cont'd)			
Facilitation measures for accessing social care services	• Not specified under the government's policy framework.	• Not specified under the policy framework of the EU.	• Not specified under the national policy framework.
Establishment of a patient registry/reporting system	• Yes, through the Global Rare Diseases Patient Registry Data Repository to store patient information from different registries set up by patient advocacy groups or researchers.	• Yes, member states develop their own patient registries.	• The federal government has not established a comprehensive rare disease registry.
Committing resources on research and development ("R&D") on rare diseases	• The Office of Rare Diseases Research under NIH is tasked to promote R&D on rare diseases.	• The European Commission funds collaborative R&D projects conducted by institutions across Europe and other countries.	• The federal government sponsors the Australian Paediatric Surveillance Unit to conduct research for facilitating national surveillance of rare childhood conditions. • There have been calls for a coordinated research strategy and targeted research funding on R&D on rare diseases.

Table – Rare disease policies in selected places (cont'd)

	Hong Kong	Japan	Taiwan	South Korea
Number of patients receiving subsidy on medical costs and the costs incurred				
Number of patients receiving subsidy on medical costs	• As at December 2016, 27 patients with LSD received subsidy to undergo enzyme replacement therapy.	• As at end-2015, about 943 460 patients with designated intractable/rare diseases were receiving subsidy on their medical costs.	• In 2015, 7 625 rare disease patients were provided with subsidies on drug costs.	• In 2015, 27 761 low-income patients suffering from 133 specified rare diseases were provided with subsidies on drug costs.
Costs incurred by the government	• An additional annual recurrent funding of about HK$75 million has been allocated in recent years to provide drug treatment for patients with uncommon disorders.	• The costs of the subsidization scheme were estimated to be ¥222 billion (HK$14.2 billion) in 2015.	• Amount of drug costs incurred totalled NT$4.1 billion (HK$1.0 billion) or averaged at NT$542,000 (HK$136,000) per patient in 2015.	• Scanty information is available on the amount of drug costs incurred under the drug subsidy programme.[26]

[26] According to Park (undated), it was reported that the expenditure on orphan drugs incurred under the national health insurance system in South Korea amounted to KRW160.5 billion (HK$1.14 billion) in 2013.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Number of patients receiving subsidy on medical costs and the costs incurred (cont'd)			
Number of patients receiving subsidy on medical costs	• Information not available.	• Information not available.	• In 2014-2015, 260 patients with specified rare diseases were fully subsidized to obtain orphan drugs under the Life Saving Drugs Programme.
Costs incurred by the government	• Information not available.[27]	• Information not available.	• A total of AUS$155.3 million (HK$1,087 million) was spent on the Life Saving Drugs Programme in 2014-2015.

[27] According to America's Health Insurance Plans (2016), a 2013 estimate put the total expenditure on brand-name orphan drugs approved in the US during 1983-2013 at US$30 billion (HK$232.7 billion) or 8.9% of the total drug expenditure during the period. However, distribution of the expenditure by sources of funding is not available.

Table – Rare disease policies in selected places (cont'd)

	Hong Kong	Japan	Taiwan	South Korea
Recent developments				
Review conducted and initiatives considered/taken	• The Hospital Authority will select suitable drugs according to the existing evaluation mechanism for the consideration of the Commission on Poverty for inclusion under the assistance programme of the Community Care Fund, and study the feasibility of including ultra-expensive drugs into the safety net of the Samaritan Fund or other funds.	• The Japanese government has been introducing improvement measures pursuant to the Act on Medical Care and Social Supports for Patients with Intractable/Rare Diseases since 2015. These measures include reducing patients' co-payment of medical fees[28] and strengthening the provision of coordinated medical and social care for patients at the community level.	• According to MOHW, implementation of the measures prescribed under the Rare Disease and Orphan Drug Act since 2000 has helped rare disease patients relieve their economic and psychological burdens. • Nonetheless, there have been concerns about the practice of allowing reimbursement of costs of orphan drugs before the completion of the relevant registration and market approval process. As such, some drug suppliers are unwilling to go through the process, leading to incomplete information about the therapeutic and adverse effects of the drugs.	• The South Korean government has recently reviewed its rare disease policy and implemented the Rare Disease Control Act enacted in 2015 in order to strengthen the prevention and treatment of, and research on rare diseases. • The Rare Disease Control Act provides for, among others: (a) accelerating the approval process of orphan drugs; and (b) committing resources on initiatives such as research and development, professional training and public education related to rare diseases.

[28] Patients with intractable/rare diseases are only required to bear 20% of the medical costs as co-payment, capped at a monthly limit set by MHLW. This figure is lower than the 30% co-payment rate applicable to general patients covered under the national health insurance system in Japan.

Table – Rare disease policies in selected places (cont'd)

	The United States	The European Union	Australia
Recent developments (cont'd)			
Review conducted and initiatives considered/taken	• The implementation of the Orphan Drug Act has been considered a success in facilitating the development of over 600 drugs for treating rare diseases. Nonetheless, stakeholders are concerned about the high prices of some orphan drugs, and rising drug prices and cost-sharing of patients which limit patients' access to the drugs.[29] • There have also been concerns about pharmaceutical companies taking advantage of the provisions of the Orphan Drug Act to repurpose inexpensive drugs for rare diseases and charging high prices for these drugs.	• According to the European Commission, the implementation of the overall Community strategy on rare diseases has fostered cooperation and exchange in experiences among the EU member states and other stakeholders. The strategy has also supported the EU member states to develop their national plans for rare diseases. • However, there has been disparity in patients' access to authorized orphan drugs among the EU members with different pricing and reimbursement mechanisms.	• The Australian Government Department of Health has recently reformed its orphan drug designation system with a view to aligning more closely with international criteria for designation[30] without impeding the availability of orphan drugs. • Nonetheless, there have been calls for the federal government to formulate a comprehensive national plan on rare diseases to provide clear national guidance on rare disease management and research, and to guide the development of efficient diagnosis, treatment and care for rare disease patients.

[29] See Harvard Business Review (2017), and Hyde, R. and Dobrovolny, D. (2010).

[30] Changes in the orphan drug designation criteria include requiring: (a) the proposed orphan condition to be life threatening or seriously debilitating; and (b) the product to treat conditions for which no therapeutic goods are registered, or provide significant benefit over registered products.

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