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8. Pharmaceutical Market Access in Denmark, Sweden, and The Netherlands: an Overview

Amir Sharaf [1]
[1] *CarthaGenetics, Carthage, Tunisia*

8.1 Denmark

General Outlook of Healthcare System and Health Policies

Denmark has a public decentralized healthcare system that slightly varies among its regions. The healthcare legal framework and services are managed by each region, which owns the corresponding hospitals and employs and pays the healthcare personnel.

Healthcare expenditure – that in 2014 peaked at 102,569 billion DKK – is mainly funded through taxes, with a specific tax for healthcare [1]. Each region covers more or less totally its expenditure, in accordance with the overall national policy regulated by the Danish National Health Act, which covers all the citizens of the country. While the healthcare system appears to be strongly decentralized, the government still keeps control of the definition of the general directions of healthcare with minor choices of specific target health projects.

Private health practices are equally reimbursed by the regions, provided that they have set a prior agreement with the corresponding region, based on the number of physician per 1000 inhabitants [2].

On a more global scale, Denmark takes into consideration the European directives, not least for the pharmaceutical products' authorization. However, pricing and reimbursement, in addition to distribution, are rather assessed and discussed at national level [3].

Stakeholders

In addition to the Ministry of Health and the Danish Parliament, the Danish Health and Medicines Authority has a pivotal role in the healthcare system, with specific regard to pharmaceuticals' assessment, pricing and reimbursement. In 2015 this authority was divided into three independent yet complementary bodies: The Danish Health Authority, The Danish Medicines Agency, and the Danish Patient Safety Authority. These divisions are rather central and directly under the control of the Danish Ministry of Health (MoH). They are responsible for implementing the MoH directives, but also for reporting on the overall healthcare and pharmaceutical industry and consumption activities from the regions, with

the elaboration of corresponding advisory opinions for the MoH. Once a year, the latter establishes the limits for the reimbursement of the approved pharmaceuticals [4].

The Danish Medicines Agency

The Danish Medicines Agency has responsibilities that are more targeted to the approval, reimbursement and distribution of medicinal products in the country. Specifically, it follows the EU regulations and monitors EU central and local decisions for pharmaceuticals, before dealing with them at national level. The Agency decides then which pharmaceuticals to approve, license and reimburse within the Danish market, then closely follows up their consumption and adverse events. The agency is also responsible for the pharmacy structure and operations, and supervises sales and retailers. It also authorizes clinical trials and monitors their operations. The agency performs similar activities for medical devices [5].

Reimbursement Committee

For the reimbursement of pharmaceuticals occurring at local level, the Danish Medicines Agency takes its primary decisions with respect to the regional landscape for the global and/or individual reimbursement of pharmaceuticals. For this, the Danish Medicines Agency receives continual advice from the Reimbursement Committee on the applications for reimbursement by the pharmaceutical companies, as well as reimbursement decision criteria, reimbursement schemes (single reimbursement, terminally ill, etc.) and final expert-based decisions, taken by the committee's expert groups [6].

Payer Stakeholders

Pharmaceuticals in Denmark are paid by the patient and the region the patient belongs to; such co-payment varies, but is always partially reimbursed by the region, as long as the drug is approved for reimbursement at central level [7].

Health Insurance

There are two categories of national health insurance in Denmark, called "Group 1" and "Group 2". The former – the main choice of Danish citizens – covers up to 97% of Danes. Members of this group visit general practitioners (GPs) and specialists for free, provided that the visit with the latter is subject to a referral from the former. Otherwise, patients join "Group 2", if they prefer to freely choose a GP and/or a specialist, without the need for a referral from the GP. While "Group 1" costs are fully covered by the state, those for "Group 2" are only partially covered by the regions [4].

Pathways of Market Access

Regulatory Process

Denmark closely follows the EU directives for the marketing authorization of medicinal products. The decisions regarding the pricing and reimbursement of pharmaceuticals remain rather an internal concern. As for manufacturers, they need to inform the Dan-

ish Medicines Agency of their Pharmacy Purchasing Price (PPP) as a first step to enter the market. Health Technology Assessment (HTA) follows later, to determine the eligibility for reimbursement from the national perspective [4].

Pricing

Pricing in Denmark is free and the Danish Medicines Agency has no influence in determining the manufacturer's price. Prices are fixed for 14-day period and the companies must report changes in price to the Danish Medicines Agency every two weeks. Any change is reported to pharmacies and patients through the "medicinpriser.dk" portal. A given drug has then the same price across all pharmacies.

It being free, pricing can drive the pharmaceuticals' costs to high levels. Furthermore, some medicines may not be exposed to a great competition and the original drugs are protected against competition from generics. These situations would further raise the prices. The Danish Medicines Agency decided to issue requirements about the number of medicine packages that each manufacturer could provide prior to entering the market. This requirement is based on the cheapest reimbursable drug, since this is the most demanded. Thanks to this measure, Denmark is able to offer the lowest-priced generic drugs in Europe [8]. Denmark shifted its reference pricing policy from external (EU) to internal (domestic) in 2005. Since then, retail prices have been falling (-26%) along with patient and government expenditures (reduction of 3.0% and 5.6%, respectively). On the other hand, revenues for pharmaceutical companies decreased by 5% [3].

Reimbursement

The Reimbursement Committee, part of the Danish Medicines Agency, along with the pharmacies, oversees the applications that companies submit to the Danish Medicines Agency for the reimbursement of their drug. They take into account different criteria, among which the drug's efficacy, safety, and additional value compared to what exists on the market and/or the standard of care for a given indication. Health economic evaluation also contributes to the decision of reimbursement, and price comparison with other alternatives is a key information. For this, the Danish Medicines Agency provides a pharmacoeconomic analysis guideline, which allows the companies to understand the key information required and to thus provide it accordingly, even though this is not mandatory [9]. Once a drug is approved for reimbursement in a given Danish region, the reimbursement is automatically deducted from the drug's price on retail, at pharmacy level. Some special rules are available for specific cases of prescription-only medicines that are still not yet approved in the country [10].

Health Technology Assessment

Health technology assessment (HTA) is applied to all levels of healthcare services, with the objective to have a rationale-(evidence)-based decision. HTA begins among all the healthcare providers who identify and seek national decision-making projects. Despite this high interest in evaluating healthcare interventions, there still are no HTA regulating policies or administrative procedures in Denmark, and often the outcomes of HTA

studies are ignored, because of political or healthcare priorities. One main reason behind this is the time-consuming HTA process, which therefore cannot be adapted to the political processes offering and/or discussing short-term decisions for more or less immediate interventions [4].

Nordic Collaboration

The Nordic Council of Ministers oversees various healthcare issues for the Nordic Countries. In 2015, the Danish Minister of Health proposed a plan to gather all regulatory and pricing policies, as a first step to increase the sharing of information for a better management of healthcare costs. This step is among the first to harmonize decisions and ensure a comparative healthcare standard across the Nordic region.

8.2 Sweden

General Outlook of Healthcare System and Health Policies

The Swedish national healthcare system offers health services to all citizens and operates thanks to the funding from taxes collected at regional levels and from municipalities, along with state subsidies [11].

The system has three levels: central, regional (county councils) and local (municipalities). The county councils and regions are the main responsible for ensuring healthcare and pharmaceutical treatment coverage to the relevant citizens. Patients bear co-payment charges when using healthcare services, with a maximum of 2200 SEK (€ 232) per year for pharmaceuticals consumption in outpatient settings. Cost for pharmaceuticals in the benefits scheme are covered by a national grant [12].

Stakeholder	Abbreviation	Description
Medical Products Agency	MPA	National authority responsible for pharmaceuticals from regulation to development, manufacturing and sale
Dental and Pharmaceutical Benefits Agency	TLV	National authority responsible for pricing and reimbursement decisions
County councils	-	Self-governing local authorities responsible for financing and delivering health services
The Council on Technology Assessment in Healthcare	SBU	Organization responsible for Health Technology Assessment

Table I. Main stakeholders for the Swedish pharmaceutical market access

The Swedish healthcare system underwent a gradual shift from the responsibility on the part of physicians in choosing the best available treatment for their patients to a choice that is made more by county councils, thereby adding a politicized note to the decision-making process [13]. This process features independent budgets from one county to another, and led to gaps in the equality of healthcare service delivery across the country [14].

Stakeholders

Table I reports the main stakeholders for the Swedish pharmaceutical market access.

The Medical Products Agency (MPA)

The Medical Products Agency (*Läkemedelsverket* – MPA) is the national body that issues regulations and monitors the development of pharmaceuticals from manufacturing to sales. In addition, MPA issues drug monographs, reporting about safety and effectiveness. MPA is not involved in the pricing and reimbursement decision-making, nor the prescription and use of medicinal products [15].

The Dental and Pharmaceutical Benefits Agency (TLV)

The Dental and Pharmaceutical Benefits Agency (*Tandvårds-och läkemedelsförmånsverket* – TLV) is the main body responsible for the pricing and reimbursement process and decides which products and/or interventions should be covered by the pharmaceutical benefits scheme [16]. Final decision for new medicines is taken by the Pharmaceutical Benefits Boards, a separate expert board within the agency which consists of seven members from county councils, health economic centers and patients organizations [12].

While TLV decides on the reimbursement, it only validates the price which should be proposed by the manufacturer. TLV has, in fact, no involvement in price negotiations, but rather deals with the decision for reimbursement. TLV's decisions are binding at both national and local level (county councils). However, given the variability of the counties' budget, not all counties strictly follow the TLV's recommendations. For this, budget studies and cost-effectiveness modelling are having a growing importance, and pharmaceutical companies are more aware of their importance in applying for reimbursement at local levels, since this is another possibility which runs in parallel with TLV applications. Still, to ensure the reimbursement at national level, the TLV must approve the drug and recommends its reimbursement.

The Council on Technology Assessment in Healthcare (SBU)

The Council on Technology Assessment in Healthcare *(Statens beredning för medicinsk utvärdering* – SBU) looks for evidence to assess healthcare technologies on different levels, not least including medical and economic perspectives, in addition to ethical considerations and social impact. SBU issues guidelines and spreads data on new healthcare interventions without any intention to influence the pricing of pharmaceuticals, the reimbursement decisions nor the prescription or consumption of drugs.

Pathways of Market Access

Regulatory Process

To access the Swedish market, a drug has first to gain approval either at European level or from the MPA, according to the Medicinal Products Act (*Läkemedelslag* 2015:315) [12]. Manufacturers can first apply to the European Medicines Agency (EMA) and gain approval at EU level. It is possible to begin the national assessment in parallel to the European processes, which would allow early considerations and discussions about the pricing and reimbursement issues at national level. Pharmaceuticals are characterized by two sub-pathways at national level, depending on their primary target (in- or outpatient settings), even though there is no clear distinction between the two subgroups and the processes are quite similar.

Pricing and reimbursement

The pharmaceutical company submits an application for including a medicine in the reimbursement system.

According to the Act on Pharmaceutical Benefits (SFS 2002:160) pricing and reimbursement decisions must take into account three fundamental principles: the human principle (equity), the need and solidarity principle – prioritizing more severe conditions over mild ones, and the cost-effective principle (the requested price is reasonable from a medical, humanitarian and social-economic perspective) [12].

Generally, the TLV delivers its decisions within 180 days from the submission. If a drug is denied reimbursement, it is still possible for a company to reapply and submit new data and/or a new price and the process starts all over. Even if the TLV rejects a drug, it is still possible to have it reimbursed at local level, provided that some conditions are fulfilled, like unmet needs, number of patients who would benefit from the drug and – above all – cost-effectiveness [12].

TLV sets the pharmacy retail margin (difference between pharmacy purchasing price and pharmacy retail price) and regulates the substitution of medicines at the pharmacies, knowing that generic substitution is mandatory, unless the patients request the original brand, and therefore are ready to pay the difference out of their pocket. As for the drugs for hospital use, they are directly funded by counties' hospitals, with discounts [11].

Health Technology Assessment

A TLV assessment of a new drug is a closed process, and only its conclusions are made available to the public. TLV issues guidelines helping the manufacturers to submit their application and comply with the TLV's assessment criteria. The cost-effectiveness rationale is a key piece of information and should be supported by a health economic model. TLV seriously consider all cost aspects, including direct and indirect costs to patients and society [11]. The importance of cost-effectiveness has increased so much that all drugs previously reimbursed before 2002 are being closely re-examined by the TLV.

Challenges and Catalyzers for Market Access

Sweden's healthcare system features many challenges caused by the decentralized healthcare system across the country, which makes it difficult to coordinate between healthcare centers and local authorities [17]. The system remains fragmented, with many gaps in the funding, and therefore in the quality of the delivered services. For the pharmaceutical industry, the regionalized landscape makes it challenging to gain access to the whole country, which is not guaranteed by TLV approval but still requires efforts to secure reimbursement at each county level. Sweden is currently undertaking new measures for having the TLV decision making more transparent and to reduce market access gaps between regions, by focusing more on health economics and cost-effectiveness criteria in addition to managed and early access programs for the patients in need. Sweden has created a special commission of inquiry (SOU) to review the current system of financing, pricing and reimbursement of pharmaceuticals, with a final report to be made public in December 2018 [12].

8.3 The Netherlands

General Outlook of Healthcare System and Health Policies

The Dutch healthcare system is based on a social health insurance system. Since 2006, a mandatory health insurance is required for every person who lives or works in the Netherlands. Adults pay a monthly premium, plus an income-related contribution, for the basic insurance covers most healthcare services, as care provided by GP, hospital treatment, prescription drugs, etc.

Although the Dutch health system is among the most expensive in Europe, in the last years it has enjoyed a prestigious position among the 35 European healthcare systems, according to the Euro Health Consumer Index (EHCI). This is not surprising, since the Netherlands' healthcare has continually searched for innovation and reforms, in partnership with the industry, with the aim of reaching and implementing a sustainable system, in order to promote translational medicine and public-private partnership [18].

Stakeholders

Medicines Evaluation Board (CBG)

The Medicines Evaluation Board (*College ter Beoordeling van Geneesmiddelen* – CBG) is an independent body that is responsible for marketing authorization. It also assesses and monitors the efficacy, risks and quality of medicines [19]

The Ministry of Health, Welfare and Sports (VWS)

The Ministry of Health, Welfare and Sports (VWS) is responsible for including drugs and healthcare services in the benefit package, negotiating lower drug prices with phar-

maceutical companies, and setting maximum allowable prices for medicines in accordance with the Medicine Prices Act (*Wet geneesmiddelenprijzen* – WGP) [20].

The National Health Care Institute (ZIN)

The National Health Care Institute (*Zorginstituut Nederland* – ZIN; formerly *College voor Zorgverzekeringen* – CVZ) is an independent body that oversees and ensures the quality, accessibility and affordability of healthcare services across the country. It is responsible for advising the VWS on the content of the basic health insurance package, improving healthcare services' quality, and managing contribution funds distributing them over the health insurers

Within the National Health Care Institute, the Scientific Advisory Board (*Wetenschappelijke Adviesraad* – WAR; formerly *Commissie Farmaceutische Hulp* – CFH) and the Appraisal Committee (*Adviescommissie Pakket* – ACP) are involved in the assessment of pharmaceuticals for the inclusion in the Medicines Reimbursement System (GVS) and thus for reimbursement [21].

Health Insurers

Every person who resides or works in the Netherlands is insured under the Health Insurance Act (*Zorgverzekeringswet* – ZVW), which covers basic medical expenses, and the Long-term Care Act (*Wet Langdurige Zorg* – Wlz), which covers long-term nursing and care treatment (i.e. patients with dementia or other severe mental, physical and sensory impairments) [20]. The health insurance is compulsory and is funded by a monthly premium set by each insurer (people on a low-income may be eligible for a government contribution), an income-related contribution, and a government grant for children under 18. The content of the benefit package is defined by The Ministry of Health, Welfare and Sports (VWS) and includes basic medical care, hospital treatment, dental age up to 18 years, maternity care, prescription drugs, etc. Health insurers must offer the same insurance package to each insured and must accept all applicants, regardless of age or state of health.

In addition to this compulsory scheme, voluntary health insurance allows to cover for other benefits that do not figure in the mandatory insurance, as dental care for adults, physiotherapy, glasses and contact lenses, and homeopathic or other alternative medical products.

Pathways of Market Access

Pricing and reimbursement

Manufacturers who seek the reimbursement approval submit a request to the Ministry of Health, Welfare and Sports (VWS). The ZIN prepares an assessment report based on four criteria: necessity, effectiveness, cost-effectiveness, and feasibility. Finally, the ZIN incorporates the advices of the WAR and the ACP and forward the final advice to Ministry of Health, Welfare and Sports (VWS) who makes the reimbursement decision [20,21]. Figure 1 shows the procedure for reimbursement application in the Netherlands.

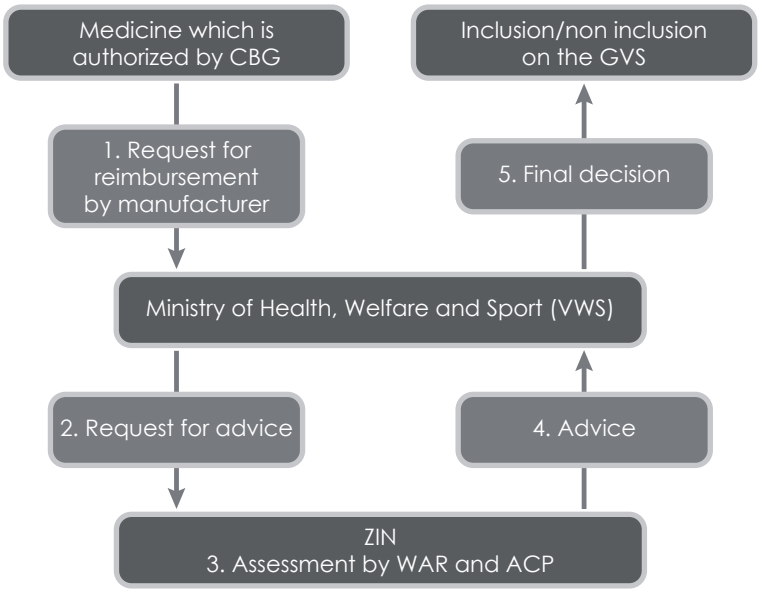

Figure 1. Dutch procedure for the reimbursement application
ACP = Appraisal Committee; CBG = Medicines Evaluation Board; GVS = Medicines Reimbursement System; WAR = Scientific Advisory Board; ZIN = National Health Care Institute

Once a medicine is included on the GVS it is eligible for reimbursement and belongs either to List 1A, which collects therapeutically interchangeable drugs reimbursed according to the reference price system (reimbursement limit), or List 1B, which collects drugs with added therapeutic value that can not be reimbursed according to the reference price system (no reimbursement limit). Finally, List 2 includes specialist drugs that are only reimbursed under specific circumstances. A health economic evaluation is only required for application for List 1B and List 2.

The Medicine Prices Act (*Wet Geneesmiddelenprijzen* – WGP) is the legal framework regulating the pricing of pharmaceuticals in the Netherlands. According to this Act, the Ministry of Health, Welfare and Sport sets maximum prices for specific medicines and pharmacies are not allow to purchase medicines exceeding these prices. These prices are subject to revision every six months, according to the drug prices in reference countries and to exchange rates. The countries of reference are Belgium, France, the UK and Germany [20].

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