30 May 2016

Ministry of Health, Welfare and Sport
Rijnstraat 50
2515XP The Hague
c/o Minister Mrs. E. Schippers

Subject: Position Paper Affordable Drugs

Dear Mrs. Schippers, dear Edith,

Introduction.
It is clear to you and many others that the price of new drugs, especially anti-cancer drugs, has to be lowered drastically. The model of the industry “ask what the fool will pay for it”, or in other words “what is bearable on the basis of gross national product” has to be got rid of. The profits that are made are much higher than in other industries. The pharmaceutical industry has profit margins up to 30% (1). On an average twice as much is spent on marketing than on innovative research and development. Added to that it is estimated that 85% of basic research into new (anti-cancer) drugs is paid for by the taxpayer (public funding) and not by the industry. In order to force the industry to decrease prices and act “service driven” instead of “finance driven” a central and international approach is the route to be taken in Europe. You and your colleagues can do this and that is why we ask you this in the interest of the patient. Individual and non-transparent negotiations between the industry and the individual ministers of health, hospital boards, pharmacists or health care insurers in the EU take too long and do not lead to the result desired. The parties are played off against each other. For if in one country the industry does not succeed in reaching a maximum pricing which is attractive for its shareholders, it will be in the next country. This is an undesirable development where the availability of new and effective drugs for all the inhabitants of the EU is in danger.

Recently you took steps to mobilize your colleagues of the other member states to negotiate with the industry about drug prices together. A good initiative, but difficult to execute. That is why on April 15th 2016, in the presence of your managing director drugs, Mr. Van Raaij, patient advocates, clinicians, pharmacists, health economists, experts in Health Technology Assessment, lawyers, CEO University Medical Center, representatives of Health Insurance Companies and others came together in Amsterdam at De Nederlandsche Bank and discussed the question what measures have to be taken to bring down the prices of drugs to an acceptable level. We offer you three initiatives.

Initiative 1: Central role of EMA (European Drugs Agency) in negotiating the price of drugs with the pharmaceutical industry.
Central in this initiative is linking the registration of a new drug in Europe to determining a maximum price also - in this proposal - by EMA. EMA’s mission is among other things “to facilitate development and (early) access to drugs”. The PRIME scheme, recently developed by EMA, is meant “to enhance support for the development of drugs that target unmet medical needs”. And that is what it is all about here. Besides the responsibility of registering new drugs for the European market the proposal is establishing a socially acceptable price under the umbrella of EMA, which has representatives of all EU member states. If this cannot be reached: no registration. The price has to be determined with maximum transparency, based on:

- How much was spent on research to develop a specific drug? The industry will have to open its books.
- How much has been spent on “abandoned drugs” which have led to the development of the new drug?

- What are the actual costs to make the drug? Here the industry will have to cross the threshold of "corporate confidentiality" keeping a realistic profit margin, certainly in case of "personalized drugs" in smaller markets (2).

Price negotiations must be realistic, fair and transparent, with the patient in the center of attention.

A new department will have to be added to EMA, consisting of patient advocates, experts in the field of health economics and Health Technology Assessment (HTA) and lawyers. In contact with the existing EMA department, which gives advice on the registration of new drugs on clinical-scientific grounds this group will have to reach realistic pricing linked to that in respectful consultation with the industry. This new, promising initiative has to be started by the powerful organization that EMA is. It is our conviction that this model will have a great chance of success at short notice, also because of the urgency of this European problem. If the will is there, this can be realized fast. That is why we request you to introduce and defend this proposal in the regular international consultation with your EU colleagues and further it to Brussels.

Initiative 2: Importing generic drugs and ingredients from China/India.
It is certainly possible to buy the ingredients of expensive drugs abroad (think of India and China). After that the pharmacist can produce the drugs with the correct quality and the oncologist / hematologist is able to prescribe the drug to the patient. We, Cinderella Therapeutics and Inspire2Live, once followed this procedure for a breast cancer patient with a BRCA-mutation who needed Olaparib and did not get it via the official route. The ingredients of the drug were bought in China and were less than 10% of the official catalogue price of the industry (AstraZeneca). This procedure was completely within legal bounds. However, we are aware of the fact that buying ingredients abroad and preparing the drug in the Netherlands will encounter legal questions. The drugs are patented and in principle it is not allowed to buy them for daily care (although most researchers and doctors do not know this, it is allowed for setting up studies). But it can be justified on the basis of the essential drug exemption, because medically and morally it is not sound to keep life-saving drugs away from patients. These patients will die and we have a moral obligation to help them. Moreover, the larger part of the research is financed with public money that is given to the universities. Why should we pay twice and why shouldn't we save the lives of patients?

A second and legal initiative is buying "off patent" drugs and biosimilars in India or China. Cinderella Therapeutics and Inspire2Live already worked at the Glivec case (a drug for patients with chronic myeloid leukemia). If Glivec is bought in India, the price might decrease to less than 10% of the catalogue price. It is estimated that in the Netherlands we can save 50 million euros every year, if we import Glivec from India. Health care insurers can easily organize this route. If they only will reimburse the price of generic drugs from India and China, hospital pharmacies and doctors are forced to buy these drugs there.

The patent system is abused by the industry via re-patenting old drugs. In June 2006 FDA announced a new safety initiative, which had as its purpose the removal from the market of non-approved "old" generic drugs on the basis of criteria of safety and effectiveness. The program has had unintentional consequences. If a drug is not approved, FDA may require a New Drug Application to determine if the drug meets with FDA-standards. Cheap and generic drugs are studied again. Exclusive patent rights to be allowed to sell a drug are given to the manufacturer that complies with the new FDA-standards. In that case the manufacturer can calculate a new price.

<u>What are the barriers?</u>

- Doctors are not likely to welcome the idea, for the industry invests much money in their laboratories for the trials. These laboratories may lose part of their income.

- The judge will have to weigh the legal obstacles of the patent against the moral obligation to save lives. With the help of independent lawyers this is a problem that can be overcome.
- A small part of the patients does not like a change in the administered generic drugs. If the doctor explains that this new generic drug does not influence the result of the treatment, there is no problem. If doctors do have problems with it, a public campaign must be started for doctor and patient to increase pressure on the industry as well. This calls for media attention. Patients, doctors and researchers have a key role in this and they will have to co-operate constructively, independent of the industry. For all three groups independence is a challenge.

Initiative 3: Public Funding Trials (PFT)

We all know that patents and research to get them bring along high costs. Moreover, marketing, lawsuits and lobbying are expensive as well. Patients and governments have to accommodate these costs, together with the expenses of development and production of drugs. Besides, the patent system encourages secrecy in research. The terms (think of registration, reimbursement and access) for the introduction of the drugs can be made shorter than they are now.

In our opinion it makes sense to set up trials initiated and financed by the government (PFT). The most important motive for these PFTs is that as soon as a drug has been approved, it can be sold at production cost price. The patent could be owned by the government or be placed into the public domain. Moreover, doctors and researchers could benefit from direct access to the results of clinical trials. Doctors can make better informed decisions about a treatment when they know that a drug works better for women than for men or may have a bad interaction with other drugs. Other researchers may look for patterns in trial results that the original researchers might have missed. Executing clinical trials can be done in a more inexpensive way. However, the compensation per patient in the trial that hospitals get for participation will have to be equal to the compensation from the industry. If not, doctors and hospitals will be encouraged to participate in the trials of the industry. Mind you, most activities with regard to trials are carried out by doctors and hospitals, not by the industry. Another advantage of PFT is that prices of bio-similars will be lowered. On top of that, results (both positive and negative) of the trials will be publicly available. This system has advantages for all stakeholders, in as much as the profit of the industry will be lowered.

Outside the health care sector open-source technology has already been used in the car industry. Think of car manufacturer Tesla and its electric engine. They gave the patent away and see what is happening: more electric cars and a lower price of electric cars and fuel. If this is applied to the pharmaceutical sector, this will also lead to cost reduction. The Centre for Economic and Policy Research in Washington estimates that without patent only $40 billion per year will be spent on drugs. With trials financed by the industry and privatized patents this is $420 billion at the moment. So a reduction of $380 billion of tax money per year is possible. The center mentioned above indicates that among other things the results of PFT are better and more efficient research, cheaper drugs and availability of public data. This is no wishful thinking, this is reality.

<u>What are the barriers?</u>

- It is time-consuming because of regulations, because the present system was set up around and by the industry.
- The government asks the industry to organize a PFT, but does not give them the patent. This will lead to obstruction. However, if the industry is not willing to co-operate, this could be considered cartel behavior and that is not permitted.
- The industry will block PFT before government money is available. The lobby is powerful. That is why it can only be successful if the (larger part of the) EU participates.

Finally, there is a moral obligation to set up PFTs, because a lot of (fundamental) research with regard to the development of new drugs is carried out with public money. A well-known example is the researcher who

developed the Hepatitis C drug Sovaldi®. Much of the research into this was done with public money. It is simply wrong to estimate a price for society that financed that itself and that has as a consequence that patients have no access to life-saving drugs.

Finally, our request to you.
Of course the aforementioned proposals deserve both an explanation and further elaboration, but it is essential that in your role as EU chairwoman for Public Health you introduce them to your colleagues at short notice. We have decided to present them to you in this way and we would like to elaborate on them in a conversation. We are looking forward to this, as during the congress it became clear how hopeful and feasible these possibilities are. There was international, interdisciplinary consensus and those present had certainly not been selected for their self-evident unanimity. Good will is required, but undoubtedly the goal to be realized justifies this.

We are looking forward to the appointment.

With kind regards,

Prof. dr. Carin Uyl-de Groot (health economist) en Prof. dr. Ton Hagenbeek (hematologist) on behalf of Cinderella Therapeutics

and

Dr. h.c. Peter Kapitein (patient advocate) on behalf of Inspire2Live.

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