To:

Ms Ch. Papanicolaou, Secretary-General of Public Health;
Ms Z. Dede, Chair of the Pharmaceutical Pricing Committee;
Mr. N. Karapanos, Head of the Medicines and Pharmacies Directorate

Cc.: Mr A. Lykourentzos, Minister of Health;
Mr M. Salmas, Alternate Minister of Health;
Mr I. Tountas, President of EOF;
Ms M. Skouroliakou, 1st Vice President of EOF;
Mr P. Vassilakis, 2nd Vice President of EOF

Halandri, 6 September 2012

Subject: Accelerated pricing procedure for specific medicinal products and immediate inclusion in the upcoming Pharmaceutical Price Bulletin of September 2012 - Immediate reimbursement by social security funds

Dear Madams and Sirs,

We would like to draw your attention to specific pharmaceutical products warranting urgent pricing and inclusion in the upcoming Price Bulletin of September 2012, as well as immediate reimbursement by the social security funds, in order to ensure patient access to important and innovative medicines which are necessary for the treatment of rare and life-threatening diseases.

The pricing applications for these pharmaceutical products have been pending for a long time (more than one year now), and there have been repeated calls by the medical community, patients' associations and sponsor companies on the Ministry of Health and Social Welfare to proceed to pricing as soon as possible. The pharmaceutical products in question fulfil **two** clear and objective criteria:

1. Accelerated assessment procedure by the European Medicines Agency (EMEA). A fast track review and approval procedure is envisaged by the EMEA for medicinal products which are of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation[1]; the purpose of this procedure is to ensure the fastest possible availability of the relevant products on the market. The National Organisation for Medicines (EOF) has already issued a certificate verifying this accelerated procedure.

2. Orphan drug status. Orphan drugs are those intended for rare, serious and chronic, debilitating or life-threatening conditions (rarity is defined in the European Union as a prevalence of no more than five in 10,000 people). In the European Union, orphan medicine designation is subject to the requirements of Regulation 141/2000 of the European Parliament and of the Council and

[1] Guideline on procedures for the granting of a marketing authorization under exceptional circumstances, pursuant to Article 14(9) of Regulation (EC) No 726/2004..

Commission Regulation 847/2000. All orphan drugs are entered in the Community Register of Orphan Medicinal Products, which is established and updated by the EMEA. For the relevant categories of patients, orphan drugs improve survival rates and are the only hope for a decent quality of life.

Pharmaceutical products that meet the above criteria are the following:

No.	Pharmaceutical product	Active substance	Condition	Criterion	Estimated number of patients (annually)
1	Victrelis	Boceprevir	Hepatitis C	Accelerated EMEA assessment	120
2	Incivo	Telaprevir	Hepatitis C	Accelerated EMEA assessmen	120
3	Zytiga	Abiraterone acetate	Prostate cancer in adult men whose disease has progressed during or after treatment with chemotherapy containing docetaxel	Accelerated EMEA assessmen	280
4	VPRIV	Velaglucerase alfa	Gaucher Disease	Orphan/Accelerated EMEA assessmen	10
5	Tasigna	Nilotinib	Chronic Myelogenous Leukemia	Orphan	Νέα περιεκτικότητα
6	Signifor	Pasireotide	Cushing disease	Orphan	20
7	Votubia	Everolimus	Tuberous sclerosis	Orphan	30
8	Tobi Podhaler	Tobramycin	Cystic Fibrosis	Orphan	New pharmaceutical form
9	Sprycel	Dasatinib	Treatment of cancer	Orphan	New strength
10	Revatio IV	Sildenafil	Pulmonary Arterial Hypertension	Orphan	20
11	Vindapel	Tafamidis	Amyloidosis	Orphan	12
12	Tepadina	Thiotepa	Conditioning (preparative) treatment before transplantation of haematopoietic progenitor cells	Orphan	-

No.	Pharmaceutical product	Active substance	Condition	Criterion	Estimated number of patients (annually)

It is obvious that the potential higher cost from the introduction of these pharmaceuticals is negligible, as they are intended for **a small number of patients** (about **600 annually**), and any such cost largely outweighs the cost of inappropriate treatments and secondary care (e.g. hospitalisation, diagnostic tests, medical care, etc.). Moreover, only two thirds of the above products are cases of new active substances, while the remainder refers to enhanced or new pharmaceutical forms (e.g. Tobi Podhaler, Revatio IV) or higher strength (e.g. Sprycel 100 mg, Tasigna 150 mg) in order to better address patients' needs.

Indicatively, the total cost for social security funds from the reimbursement of the above medicines is estimated at about **€12 million** annually, after taking account of reimbursement costs (9%), rebates to public hospitals / social security funds, etc. Also, according to estimates from the Panhellenic Union of Pharmaceutical Industries, the simultaneous pricing of about 20 new generics of products that were so far without a generic equivalent can lead to savings in public pharmaceutical expenditure of about 70-80 million **(given the increasingly widespread use of prescribing by active substance)**. For instance, the introduction of just one generic in the category of gastrointestinal medicines could result in savings of €30 million.

The reasons justifying the **urgent pricing and reimbursement** of the above pharmaceutical products reflect the need to **protect public health and fill a therapeutic void regarding the treatment of rare and life-threatening diseases. It should be stressed that Greek patients have been without access to these innovative treatments for more than one year now.**

Moreover, the above medicines are characterised as **necessary for addressing risks to life and are covered by international clinical protocols** (thus qualifying for the exception from the reimbursement regime under Article 21 of Law 4052/2012). They are therefore innovative medicinal products which should be included in the list of serious diseases under Article 12(2) of Law 3816/2010 and be classified under an ATC 5 level group within the positive reimbursement list.

Against this background, we call for the immediate pricing of the above medicines with the Price Bulletin of this month of September and for their immediate reimbursement by the social security funds, in order to ensure he access of Greek patients to new innovative treatments in the field of rare and life-threatening diseases.

Sincerely,

Nicholas Kefalas
Vice President

Konstantinos M. Frouzis
President

ANNEX

This annex contains excerpts from a communication by the EMEA [2] explaining the reasons for the **accelerated assessment of these medicinal products.** Here are some relevant points of the communication:

- ***INCIVO (telaprevir):*** *·The Committee for Medicinal Products for Human Use (CHMP) assessed this application under an accelerated timetable, because it considered that, as 70% of hepatitis C virus infections in the Western world are genotype 1*, ***there would be an important public health gain in making this medicine available to patients as a treatment option.***

- ***ZYTIGA (abiraterone acetate):*** *The Committee for Medicinal Products for Human Use (CHMP) assessed this* application under an accelerated timetable, because it considered that the poor prognosis of the target patient population ***represents a high unmet medical need while the novel mechanism of action of abiraterone has the potential to offer an alternative therapeutic option for these patients.***

- ***VICTRELIS (boceprevir):*** *The Committee carried out an accelerated assessment of this medicine, because it found that boceprevir could answer the unmet medical need to provide improved treatment options for chronic hepatitis-C genotype-1 naïve as well as pretreated patients. Boceprevir is the first of a new class of medicines for the treatment of chronic hepatitis that directly inhibit the replication of the hepatitis-C virus in hepatitis-C-virus-infected host cells.*

- ***VPRIV (velaglucerase alfa):*** *The Committee for Medicinal Products for Human Use (CHMP) carried out* an accelerated assessment of this medicine, due to a major public health interest. In the light of the ongoing shortage of the authorised medicine for the treatment of Gaucher disease, the CHMP found that Vpriv might constitute an alternative treatment option for this condition.

ORPHAN DRUGS (excerpt from the European Medicines Agency authorisation)

Tasigna *is used to treat patients with chronic myelogenous leukemia (CML), a type of cancer of the white blood cells.*

It is used when the patient is 'Philadelphia chromosome positive' (Ph+), which means that some of the patient's genes have re-arranged themselves to form a special chromosome called the Philadelphia chromosome. This chromosome produces an enzyme, called Bcr-Abl kinase, that leads to the development of leukaemia.

[2] Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP), 18-21 July 2011.

Tasigna is used to treat the 'chronic' and 'accelerated' phases of CML, in patients who cannot tolerate other treatments including imatinib (another anticancer medicine), or when their disease is not responding to them. There is no information available on its effectiveness in patients whose disease is in 'blast crisis' (another phase of CML).

Tasigna is also used in newly diagnosed patients with CML in the chronic phase.

Because the number of patients with CML is low, the disease is considered 'rare', and Tasigna was designated an 'orphan medicine' (a medicine used in rare diseases) on 22 May 2006.

***Signifor** is used to treat adults with Cushing's disease when surgery has failed or is not an option.*

Cushing's disease is caused by a tumour of the pituitary gland (a gland located at the base of the brain) releasing too much of a hormone called ACTH that stimulates the production of too much cortisol (a hormone also known as the 'stress hormone' because it is released in response to stress).

Because the number of patients with Cushing's disease is low, the disease is considered 'rare', and Signifor was designated an 'orphan medicine' (a medicine used in rare diseases) on 8 October 2009.

***Votubia** is used to treat a type of brain tumour called 'subependymal giant cell astrocytoma' (SEGA) in patients with tuberous sclerosis. Tuberous sclerosis is a genetic disease that causes growth of benign (non-cancerous) tumours in different organs of the body, including the brain.*

Votubia is used in adults and children aged three years and above whose brain tumour cannot be surgically removed.

Because the number of patients with tuberous sclerosis is low, the disease is considered 'rare', and Votubia was designated an 'orphan medicine' (a medicine used in rare diseases) on 4 August 2010.

***Tobi Podhaler** is used to suppress chronic lung infection caused by bacteria called Pseudomonas aeruginosa in adults and children aged six years and over who have cystic fibrosis.*

Cystic fibrosis is an inherited disease that affects the cells in the lungs and the glands in the gut and pancreas which secrete fluids such as mucus and digestive juices. The accumulation of mucus in the lungs allows bacteria to grow more easily causing infections, lung damage and breathing problems. Bacterial lung infection with P. aeruginosa is frequent in cystic fibrosis patients.

Because the number of patients with cystic fibrosis and P. aeruginosa bacterial lung infection is low, the disease is considered 'rare' and Tobi Podhaler was designated an 'orphan medicine' (a medicine used in rare diseases) on 17 March 2003.

***Sprycel** is an anticancer medicine. It is used to treat adults with the following types of leukaemia (cancer of the white blood cells):*

- *chronic myeloid leukaemia (CML) in the 'chronic' phase in newly diagnosed patients who are 'Philadelphia chromosome positive' (Ph+). CML is a leukaemia where granulocytes (a type of white blood cell) start growing out of control. Ph+ means that some of the patient's genes have rearranged themselves to form a special chromosome called the Philadelphia chromosome which produces an enzyme, Bcr-Abl kinase, that leads to the development of leukaemia.*
- *CML in 'chronic', 'accelerated' and 'blast' phases. Sprycel is used when patients cannot tolerate, or when their disease is not responding to, other treatments including imatinib (another anticancer medicine);*
- *Ph+ acute lymphoblastic leukaemia (ALL), where lymphocytes (another type of white blood cell) multiply too quickly, or in 'lymphoid blast' CML. Sprycel is used when patients cannot tolerate, or when their disease is not responding to, other treatments.*

Because the number of patients with CML and ALL is low, the diseases are considered 'rare', and Sprycel was designated an 'orphan medicine' (a medicine used in rare diseases) on 23 December 2005.

Revatio *is used to treat adults and children aged one to 17 with pulmonary arterial hypertension (PAH, abnormally high blood pressure in the arteries of the lungs). In adults, Revatio is used in patients with class II (slight limitation of physical activity) or class III (marked limitation of physical activity) PAH.*

Revatio has been shown to be effective in PAH with no identified cause in adults and in children, in PAH caused by connective tissue disease in adults, and in PAH caused by congenital (inborn) heart disease in children.

The solution for injection is for adults who cannot take Revatio tablets or oral suspension for a short period, but whose condition is stable.

Because the number of patients with PAH is low, the disease is considered 'rare', and Revatio was designated an 'orphan medicine' (a medicine used in rare diseases) on 12 December 2003.

Vyndaqel *is used to delay nerve damage caused by transthyretin amyloidosis, a hereditary disease in which fibres called amyloid build up in tissues around the body including around the nerves. Vyndaqel is used in adult patients with the early stage of nerve disease (stage 1).*

Because the number of patients with transthyretin amyloidosis is low, the disease is considered 'rare', and Vyndaqel was designated an 'orphan medicine' (a medicine used in rare diseases) on 28 August 2006.

Tepadina *is used in combination with chemotherapy (medicines to treat cancer) in two ways:*

- *as a 'conditioning' (preparative) treatment before transplantation of haematopoietic progenitor cells (the cells that make blood cells). This type of transplant is used in patients who need to replace their blood-making cells because they have a blood disease such as a cancer of the blood (including leukaemia) or diseases causing low red blood cell counts (including thalassaemia or sickle-cell anaemia);*

- *during the treatment of solid tumours when high-dose chemotherapy followed by transplantation of haematopoietic progenitor cells is needed.*

Tepadina can be used for transplantation of cells from a donor and for transplantation of cells derived from the patient's own body.

Because the number of patients in the European Union (EU) that undergo this type of conditioning and transplant is low, Tepadina was designated an 'orphan medicine' (a medicine used in rare diseases) on 29 January 2007.

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