

## **SOCIAL SECURITY INSTITUTION PROCEDURES AND PRINCIPLES RELATING TO THE REIMBURSEMENT APPLICATIONS FOR MEDICINES**

### **SECTION ONE Purpose, Scope, Legal Basis and Definitions**

**Purpose and Scope ARTICLE 1-** (1) The purpose of these procedures and principles is to set forth the procedures and principles to be pursued in the applications to be made within the scope of the Regulation Regarding the Reimbursement of Medicines of the Social Security Institution and the Regulation Regarding Alternative Reimbursement of the Universal Health Insurance of the Social Security Institution for the medicines financed by the Social Security Institution and medicines for which request is made for receiving financing.

(2) These Procedures and Principles shall comprise the companies to apply to the reimbursement list and the information and documents to be included into the application dossier.

**Legal Basis ARTICLE 2-** (1) These Procedures and Principles have been prepared on the basis of the provisions of articles 63 and 73 of Law No. 5510 Regarding Social Insurances and Universal Insurance Law, article 79 of the Regulation Regarding the Operation of the Central Organization of the Social Security Institution, the Regulation Regarding the Reimbursement of Medicines of the Social Security Institution and the Regulation Regarding Alternative Reimbursement of the Universal Health Insurance of the Social Security Institution.

**Definitions ARTICLE 3-** (1) The following terms shall apply for the purposes of these procedures and principles; a) Unit price: The price obtained by dividing the public price of a medicine into the package amount, b) Distribution certificate: The certificate indicating that the medicine retrieved from the records of the Drug Tracking System of the Ministry of Health by the relevant company is available on the market, (according to the Guidelines, with regards to the medicines for which it is mandatory to present the Estimated Budgetary Impact in the application dossier; the record of the Drug Tracking System indicating the number corresponding to at least 5% of the number indicated for the specified number of the first year for the number of patients likely to use this medicine on this table) c) Pharmaceutical form: The form of presentation of the medicine/product manufactured with formulations complying with its intended use, ç) Company: Real person or legal entity holding the manufacturing or import authority for medicinal products for human use/medicines for human use, d) Company official: The person authorized to act on behalf and on account of the company based on the authorization certificate received from a notary-public and who holds an authorized signatory list, e) Medicine: Any natural and/or synthetic-derived active substance or combination of substances administered to humans in order to treat and/or prevent a disease, make a diagnosis or restoring, correcting or modifying a physiological function, f) Generic medicine: Medicine which holds the same qualitative and quantitative composition with the original medicine in terms of active substances and the same pharmaceutical form and whose bioequivalence with the original medicinal product is proven with adequate bioavailability studies,

g) Public price: The price obtained upon applying the public institution discount on the retail sale price of a medicine, ğ) SmPCs-PIL: The summary of product characteristics included into the registration dossier of the medicine and the written package insert prepared for the user, h) List: The medicine/product lists published in the annex of the Health Budget Law (SUT) and/or the official website of the Agency, ı) Original medicine: The medicine registered/permitted so as to be introduced into the market for the first time worldwide upon proving that it has a scientifically acceptable efficacy, quality and safety in terms of active substance(s), i) SUT: The Health Budget Law of the Social Security Institution j) TITCK: Medicines and Medical Devices Agency of the Turkish Ministry of Health, k) Product: Products permitted to be sold by the Ministry of Health and the Ministry of Agriculture without receiving a registration, l) Commitment: Document indicating that responsibility has been undertaken for the conduct or delivery of the tasks requested to be made, without or without a contract, within the scope of these procedures and principles with this regulation, on behalf and to the account of the company, towards the Agency, and signed by the

person authorized to represent and bind the company, m) Strength: Amount of active substance in the unit pharmaceutical form, n) Board of Directors: Board of Directors of the Social Security Institution, o) Regulation: Regulation Regarding the Reimbursement of Medicines of the Social Security Institution and the Regulation Regarding Alternative Reimbursement of the Universal Health Insurance of the Social Security Institution.

## SECTION TWO Preparation of Applications

General matters relating to the applications to be submitted ARTICLE 5- (1) The applications intended for the inclusion of medicines/products into the lists shall be submitted within the framework of one of the 3 (three) categories defined below. a) Applications to be made for original medicines and the new molecules to be included into the lists for the first time, b) Applications to be made for generic medicines, c) Applications to be made for products issued a sale permit without receiving a registration. 2) The applications to be made for the medicines/products included into the lists shall be submitted within the framework of the following 7 (seven) categories defined below. a) Applications to be made for change of company, b) Applications to be made for change of barcode, c) Applications to be made for change in the name of the medicine/product, ç) Applications to be made for change of indication/package insert/SmPCs-PIL/reimbursement rules, d) Applications to be made for change in discount, e) Applications to be made for being delisted, f) Applications to be made again for rejected applications. (3) The application dossiers shall comprise the information, documents and data whose details are stipulated in these procedures and principles. (4) A separate application dossier shall be prepared for each strength or pharmaceutical form for the applications to be made for different strengths and/or pharmaceutical forms of medicines. (5) The application dossiers shall be delivered in folders organized with separators. (6) The name of the medicine/product and the name of the registration holder shall be indicated on the side label of the folder.

(7) All information, documents and data to be delivered in the application dossiers in accordance with these procedures and principles shall be in Turkish. Turkish translation translated by a certified interpreter of the photocopies in the original language of the literature sources to be delivered within the scope of the dossier, all of the studies with an evidence level of Grade I and/or II and the summaries of the other literature references shall be included. (8) The application dossier will be delivered as one original version and one digital version in one 1 (one) CD/DVD and one memory stick. The information presented in digital version should be available in the .pdf format as well as the .docx format. (9) The applicant company shall be responsible for the accuracy of all information and documents and the final nature of the information. Companies shall deliver along with the dossier, the commitment relating to this matter, in all the applications (Annex-3A). With regards to medicines which were previously procured from abroad for personal treatment, which have been registered and for which a request has been made for being included into the list, the applicant companies shall deliver along with the dossier, also the commitment requested to be submitted within the scope of item (b) of clause 5 in article 12 of the Regulation Regarding the Reimbursement of Medicines of the Social Security Institution (Annex-3B).

Content of the dossier to be delivered in applications ARTICLE 6 – (1) The content of the dossier to be delivered in the applications for the inclusion of medicines/products into lists shall be composed of three sections, namely, “Section I-General”, “Section II-Clinical Data” and “Section III-Pharmacoeconomic Evaluation”. The application dossier shall be checked based on the “Form for Application Submitted for the First Time”, in terms of the documents to be contained as per these procedures and principles (Annex-1A) and the commitment will be included into the application dossier (Annex-3A). (2) The information and documents to be included into the dossier content to be delivered in the applications to be made for the medicines/products included into the lists have been defined below; they shall be checked on the basis of the “Application Form for Changes in the Information on Medicines” (Annex-1B) and the commitment will be included into the application dossier (Annex- 3A). a) In the applications for change of company, the relevant petition, colored photocopy of the registration of the medicine, photocopy of the barcode

approval letter, photocopy of the sale permit and the printout of the old and new price list published on the official website of TITCK, indicating also the date of publication, shall be included. b) In the applications for change of barcode; the relevant petition, colored photocopy of the registration of the medicine, photocopy of the barcode approval letter and the printout of the old and new price list published on the official website of TITCK, indicating also the date of publication, shall be included. c) In the applications for change of name of medicine/product; the relevant petition, colored photocopy of the registration of the medicine, photocopy of the name approval letter and the printout of the old and new price list published on the official website of TITCK, indicating also the date of publication, shall be included. ç) In the applications for change of indication/package insert/SmPCs-PIL; the relevant petition, photocopy of the approval letter of the indication change received from TITCK, old and new package insert (SmPCs-PIL, where available), the clinical study relating to the change and the pharmacoeconomic study shall be included.

d) In the applications for changes in reimbursement rules; the relevant petition, the new reimbursement proposal, and, where available, the clinical study and the pharmacoeconomic study relating to the proposal, shall be included. e) In the applications for changes in discount; the petition indicating the justification and additional information and documents relating to the justification, if any, shall be included. f) In delisting applications made on the basis of the annulment of registration/annotation at the back of the registration or the annulment of the approval certificate of the import permit; the relevant petition and the annulment of registration received from TITCK/annotation at the back of the registration or the annulment documents of the approval certificate of the import permit, while the relevant petition and the additional information and documents relating to the justifications, if any, shall be included into the delisting applications for cases other than these. (3) In the applications made within the scope of re-application in case of rejection of application; the justifications relating only to the rejection decision without the preparation of the application dossier and additional information and documents relating to these justifications, if any, shall be included in case of first rejection, and the information and documents and the commitment (Annex-3A) defined in these procedures and principles according to the nature of the application shall be included in case of a second rejection. (4) In the applications to be made within the scope of the Regulation Regarding Alternative Reimbursement of the Universal Health Insurance of the Social Security Institution, the information and documents and the commitment (Annex-3A) defined in these procedures and principles according to the nature of the application shall be included. The dossier content to be delivered in the applications for being included into the list of medicines/products ARTICLE 7-(1) The documents included into section one entitled "Section I-General" of the application dossier, have been defined below. a) Table of contents, b) Petition (The request shall be summarized with clear and final statements, the status of the medicine/product subjected to the request (original medicines and new molecules to be included for the first time into the list/generic medicines/products permitted to be sold by the Ministry of Health/Agriculture without receiving a registration), name, pharmaceutical form and strength, discount proposal shall be indicated clearly. The letterhead of the company making the request shall be used for the petition and the contact address of the company, its telephone and fax numbers and e- mail address will be included into the petition. The document indicating that the company authority is authorized to represent and bind the company shall be annexed to the petition), c) Commitment (Annex-3), d) Information card of the medicine (Annex-2), e) Photocopy of the barcode approval letter, f) Photocopy of the sale permit, g) Approved package insert/SmPCs-PIL of the medicine, ğ) Output of the price list published on the official webpage of TITCK, h) Marketing authorization FDA (Food and Drug Administration) marketing authorization and NDA (New Drug Application) number and/or EMA (European Medicines Agency) marketing authorization, where available, and photocopy of the EMA co-marketing certification, where

available, of original medicines and the new molecules to be included into the list for the first time, (These documents shall not be sought for new molecules developed and registered in

Turkey.) i) Registration status in the OECD (Organization for Economic Co-operation and Development) countries of original medicines and new molecules to be included into the list for the first time, whether they are on the reimbursement lists, the countries identified as reference by TITCK as per the Decree Regarding the Pricing of Medicinal Products for Human Use and the "Table on Information on the Status of the Medicine with OECD Countries and Reference and Source Countries" (Annex-4), i) Epidemiology of the disease in which the medicine/product is indicated and a brief summary preferably not exceeding 1 (one) page on the most apparent superiorities and benefits comparing the other medicines/products included into the list for the same indication and/or treatments other than medicines/products shall be included into the application, j) The documents requested for these products in the "Form for Application Submitted for the First Time" (Annex-1A) in the applications of products permitted to be sold without receiving a registration, k) The distribution certificate indicating that the medicine/product is available on the market. (2) The documents included into section two entitled "Section II-Clinical data" in the application dossier have been defined below. The therapeutic class of the medicine and specifically its pharmacological profile will be explained in this section within the framework of the topics listed below. a) The therapeutic class of the medicine shall be identified according to ATC 4 code, and according to the closest ATC code, in case of absence of the ATC 4 code. The main pharmacological effect(s) of the medicine in this class shall be identified. b) Recommended and widely used therapeutic regimes, including the treatment period envisaged, shall be identified. c) If indicated to be used in combination with other medicines, the details of these combinations shall be indicated along with their strengths. ç) The results obtained from the clinical trials relating to the efficacy of the relevant indication(s) of the medicine shall be summarized according to the "Prioritization Table According to the Scientific Reliability of Evidences" and the "Efficacy Table" (Annex-5 and Annex-6). d) The results obtained from the clinical trials on the reliability of the medicine shall be summarized according to the "Prioritization Table According to the Scientific Reliability of Evidences" and the "Efficacy Table" (Annex-5 and Annex-6). e) With regards to alternative therapeutic options; 1) The main existing therapeutic options for the same indication (medicines, surgical interventions, radiotherapy, physical therapy, etc.) and the significant differences compared to these shall be indicated. 2) Comparative clinical trials comparing the medicine recommended with the other therapeutic options used for the same indication shall be used. It is necessary for the data to be tabular format and primarily the clinical trials conducted in Turkey will be preferred.

f) The original version and the Turkish translations translated by a certified interpreter of the studies with a scientific reliability degrees of the (evidence level) of I and/or II of each clinical trial and evidences summarized in the "Efficacy Table" and "Reliability Table shall be added to this section. The Turkish translations translated by a certified interpreter only of the summary section of the other literature sources added shall be presented at the beginning of each literature. g) Regarding its epidemiology; 1) The status of the disease(s) in which the medicine is indicated (pathophysiology and clinical course) and the tiered therapeutic regime, where available, will be summarized. 2) The estimated prevalence of the diagnosis where the medicine regarding the epidemiology of the disease(s) and, where available, the prevalence data in the other countries shall be added (Annex-9, Table 9.4 and Annex-10, Table 10.4). ğ) The document indicating the position in the international diagnostic-therapeutic guidelines on applications, where available, shall be included. h) The information requested in this section shall also be included into the dossiers to be prepared for the applications for changes of indication/package insert/SmPCs-PIL and in reimbursement rules. 3) The documents requested to reveal the cost of the medicine and the economic outcomes arising with their implementation via analytical methods in section three entitled "Section III- Pharmacoeconomic evaluation" of the application dossier have been defined below. The applications within this scope shall be evaluated under three categories. a) For generic medicines; no pharmacodynamics study will be requested for medicines which contain the same active substance at the same strength and the same pharmaceutical form for the same indication if

the original medicine is on the list. However, it is necessary to make a comparative unit price calculation with the original medicine included into the list and, where available, the other generics, for the generic medicines requested to be included into the lists. The calculations shall be made on the public prices upon preparing the “Comparative Table for Generic Medicines” (Annex-8). The evaluations in the generic medicines not included into this group shall be made within the scope of item (b) of this clause. b) In relation with original medicines, new molecules to be included into the list for the first time, changes of indication/package insert/SmPCs-PIL and changes in reimbursement rules; 1) The clinical trial(s) used in pharmacoeconomic evaluation shall be conducted with the clinical trials published as original article (except for letter to the editor, abstract, compilation, short communication and book critique), starting with the journals within the scope of SCI/SCI-Expanded or which have been planned for registration application. Although it is preferred for clinical trials to be conducted as meta-analyses or randomized double-blind controlled studies, also other studies may be used according to the scientific reliability degrees of the evidences. The therapeutic cost information, other relevant information and the sources of this information shall be listed. 2) The purpose of the pharmacoeconomic analysis made shall be clearly indicated. If the pharmacoeconomic analysis has been conducted with the data of other countries, also the countries from which such data have been used and the details of adaptations upon making relevant adaptations specific to Turkey (hospital services, cost of medicines, consultation, administration fees, etc.) shall

also be indicated. In case of absence of data specific to Turkey, estimated data may be used upon indicating the justifications and sources. 3) Pharmacoeconomic analysis is made in a manner so as to comprise directly healthcare expenditures. The studies considering the overall cost may be presented as a supplementary study. 4) In case of market placement of the new medicine being compared, the medicine(s) to be replaced shall be selected and the reasons for this selection shall be explained along with the selection criteria. 5) If the medicine belongs to an existing pharmacotherapeutic group, it shall be compared with the medicine most widely used among the other alternative medicines in this group and the alternative medicines used for direct comparative purposes in literature. 6) If the medicine is the first member of a new pharmacotherapeutic group, it shall be compared with the most widely used medicine for the same indication(s) in the other pharmacotherapeutic groups and the medicines used for direct comparative purposes in literature. 7) In case of presence of non-pharmacological therapeutic options for the same indication (such as surgical interventions, radiotherapy, physical therapy, etc.), it shall be compared also with this. 8) If the widest administration is non-therapeutic follow-up, it shall be compared with this. 9) The doses and periods used for pharmacoeconomic analysis, shall be compliant with the studies in which the inputs of the analysis have been included for the medicines subjected to the analysis and the medicines compared. 10) Pharmacoeconomic analysis shall be conducted with cost minimization or one of the cost effectiveness methods and will comprise the adequate sensitivity analysis in its annex. The analyses conducted with the cost utility method, may be submitted in addition to the cost efficacy analysis. 11) The “New Treatment Balance Tables” shall be completed for original medicines, the new molecules to be included into the list for the first time, changes of indication/package leaflet/SmPCs- PIL and changes of reimbursement rules. (Annex-9). c) The “Comparative Table for Generic Medicines” and the “Table of Products Permitted to be Sold with the Control Certificate Without Receiving Registration for the applications of products permitted to be sold by the Ministry of Health/Agriculture without receiving a registration (Annex-8 and Annex- 10). Execution ARTICLE 8 – (1) These Procedures and Principles have been regarded suitable with the decision dated 11/02/2016, with No. 2016/56 of the Board of Directors and will become effective on the date of their publication.

Enforcement ARTICLE 9 – (1) These Procedures and Principles shall be enforced by the President of the Social Security Institution.

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REGISTRATION

ANNEX-1 APPLICATION FORMS ANNEX-1A Form for Applications Submitted for the First  
Time

Name, pharmaceutical form, strength of medicine: Name of company

For original medicines and new molecules to be included into the list for the first time For  
generic medicines Application for products permitted to be sold without receiving a registration  
Section I Section I Section I 1) Product permitted by the Ministry of Health ☐ Petition and its  
annexes ☐ Petition and its annexes ☐ Petition and its annexes ☐ Commitment ☐ Commitment ☐  
Commitment ☐ Information Card of the Medicine (Annex-2) ☐ Information Card of the Medicine  
(Annex-2) ☐ Information Card of the Medicine (Annex-2) ☐ Colored photocopy of the registration  
of the medicine ☐ Colored photocopy of the registration of the medicines ☐ Photocopy of the  
permit ☐ Photocopy of the barcode approval letter ☐ Photocopy of the barcode approval letter ☐  
Label sample ☐ Photocopy of the sale permit ☐ Photocopy of the sale permit ☐ Sale permit ☐  
Approved package insert (where available, approved SmPCs and PIL) ☐ Approved package insert  
(where available, approved SmPCs-PIL) ☐ Barcode information ☐ Printout of the price list (Official  
website of TITCK) ☐ Output of price list (official website of TITCK) ☐ Table on Information Relating  
to the Status of the Medicine in OECD Countries and Reference and Source Countries (Annex-4) ☐  
FDA marketing authorization/NDA number, EMA marketing authorization/photocopy of  
co-marketing certificate ☐ Brief summary ☐ Output of price list (official website of TITCK) ☐ Table  
on Information Relating to the Status of the Medicine in OECD Countries and Reference and Source  
Countries (Annex-4) ☐ Distribution certificate ☐ Brief summary ☐ Brief summary ☐ Distribution  
certificate ☐ Distribution certificate 2) Product permitted by the Ministry of Agriculture ☐ Petition  
☐ Commitment ☐ Information Card of the Medicine (Annex-2) ☐ Photocopy of the permit ☐  
Export/Import approval certificate ☐ Label sample ☐ Photocopy of proforma invoice ☐ Barcode  
information ☐ CE certificate ☐ Table on Information Relating to the Status of the Medicine in OECD  
Countries and Reference and Source Countries (Annex-4) ☐ Brief summary ☐ Distribution  
certificate Section II

☐ Clinical data ☐ Prioritization Table According to the Scientific Reliability of Evidences  
(Annex-5)

☐ Efficacy table (Annex-6) ☐ Reliability table (Annex-7) ☐ Literature sources, list, photocopies  
and translations

Section III Section III Section III ☐ Pharmacoeconomic evaluation ☐ Comparative Table for  
Generic Medicines (Annex-8) ☐ Comparative Table for Generic Medicines (Annex-8) ☐ Tables on  
New Treatment Balance (Annex-9) ☐ Table of Products Permitted to be Sold with a Control  
Certificate Without Receiving a Registration (Annex-10)

ANNEX-1B Application Form for Changes in the Information on Medicines

Name of Medicine, pharmaceutical form, strength: Name of Company

Change of company Change of barcode Change of name of medicine Change of  
indication/package insert/SmPCs-PIL Change of reimbursement rules Change of discount ☐  
Petition ☐ Petition ☐ Petition ☐ Petition ☐ Petition ☐ Petition ☐ Commitment ☐ Commitment ☐  
Commitment ☐ Commitment ☐ Commitment ☐ Commitment ☐ Colored photocopy of the  
registration of the medicine ☐ Colored photocopy of the registration of the medicine ☐ Colored  
photocopy of the registration of the medicine ☐ Photocopy of the approval letter for the change of  
indication, received from TITCK ☐ Clinical data on the new rule

☐ Photocopy of barcode approval letter ☐ Photocopy of barcode approval letter ☐ Printout  
of the price list and its publication date (along with the old and new price published on the official

website of TITCK) □ Old and new package insert (where available, SmPCs and PIL)\* □ Prioritization Table According to the Scientific Reliability of Evidences (Annex-5)

□ Photocopy of sale permit □ Printout of the price list and its publication date (along with the old and new price published on the official website of TITCK) □ Photocopy of the approval letter for the name received from TITCK □ Clinical trial related with the change □ Efficacy table (Annex-6)

□ Printout of the price list and its publication date (along with the old and new price published on the official website of TITCK) □ Prioritization Table According to the Scientific Reliability of Evidences (Annex-5) □ Reliability table (Annex-7)

□ Efficacy table (Annex-6) □ Pharmacoeconomic study

□ Reliability table (Annex-7) □ Tables on the New Treatment Balance (Annex-9)

□ Pharmacoeconomic study □ Tables on the New Treatment Balance (Annex-9)

\*Changes of indication/package insert/SmPCs-PIL should be marked on the text.

ANNEX-1C Delisting Application □ Petition □ Annulment of registration/annotation at the back of the registration or letter for the annulment of the import permit approval certificate □ Commitment

ANNEX-2 INFORMATION CARD ON THE MEDICINE\* Name of Medicine: Barcode: Name of Company: Registration/Permit Date/No: Sale permit Approval Date/No: Barcode Approval Date/No: Site of Manufacture and/or Import: FDA/EMA Approval Dates (where available): Additional Information (including additional discount proposal, where available) Name of medicine Price Information Active substance of the medicines (Pharmaceutical form, strength, package amount) Sale Price to Wholesalers Retail Sale Price Public Discount (%) Public Price and its amount

The Usual Dose Used Maximum Dose (According to ICD-10 codes)

Indication With ICD-10 Codes The closest ATC Classification if ATC4 is not available

\*Printout will be taken on A4 cardboard

ANNEX-3 COMMITMENT ANNEX-3A Commitment

As the undersigned authorized to act for and on behalf of the company, I/we hereby declare and undertake that our company is responsible for the accuracy of any information included into the dossier delivered in relation with the application we have made to your Agency and the finalized nature of such information, that our company holds all financial and legal responsibility relating to the loss of the Agency to arise due to the decisions based on information and documents submitted erroneously, that the loss will be collected and compensated by our company in line with general provisions. .../.../

Name-Surname of the Company Official (Signature and Stamp)

ANNEX-3B Commitment As the undersigned authorized to act for and on behalf of the company, I/we hereby declare and undertake our medicine for which we have applied to your Agency for its inclusion into the scope of reimbursement, is a medicine/are medicines containing the same amount of the same active substance previously procured from abroad for personal treatment and registered in Turkey, that we are authorized and responsible for the market placement in Turkey of the medicine(s) if it is/they are included into the reimbursement list, that I/we will present to the Agency the distribution certificate relating to our medicine latest 1 (one) month as of the date on which it is included into the list, that in case the medicine(s) are procured personally by the parties authorized by the Ministry of health and paid by the Agency if the submission of the distribution certificate exceeds the deadline of 1 (one) month, the financial responsibility of the difference to arise between the procurement prices of the medicine(s) and the Public price of the medicine belongs to our company, that the damage to arise will be collected and compensated by our company in line with general provisions. .../.../

Name-Surname of the Company Official (Signature and Stamp)

ANNEX-4 TABLE OF INFORMATION RELATING TO THE STATUS OF THE MEDICINE IN OECD COUNTRIES AND THE REFERENCE AND SOURCE COUNTRIES \*

ANNEX-4A OECD countries

Name of country Registration status (present/absent) Reimbursement status provided by health insurance institutions (present/absent/not accessible Australia Austria Belgium Canada Chile Czech Republic Denmark Estonia Finland France Germany Greece Hungary Iceland Ireland Israel Italy Japan Luxembourg Mexico Netherlands New Zealand Norway Poland Portugal Slovak Republic Slovenia South Korea Spain Sweden Switzerland UK USA

#### ANNEX-4B Reference and source countries

Countries designated as reference by TITCK as per the Decree Regarding the Pricing of Medicines for Human Use and countries of manufacture and/or import Registration status (present/absent) Reimbursement information and restrictions on prescription, where available

\*Information will be provided at the end of the tables on the dates on which the information provided on the tables could be accessed.

#### ANNEX-5 PRIORITIZATION TABLE ACCORDING TO THE SCIENTIFIC RELIABILITY OF EVIDENCES

Scientific Reliability Degrees of Evidences Type of Research I Evidences obtained from systematic reviews and meta-analyses comprising randomized controlled clinical studies II Evidences obtained from at least one randomized controlled clinical study III Observational studies; cross-sectional, case-control studies IV Evidences obtained from case reports, expert views

The evidences obtained from systematic reviews and meta-analyses comprising randomized controlled researches shall be at level I and the evidences based on at least one randomized clinical experiment shall be at level II. The other levels are non-randomized researches.

#### ANNEX-6 EFFICACY TABLE Summary Table Relating to the Published and Reported Clinical Research Data Comparative Efficacy Analyses

Title, Source and Date of the Source Publication/Report Purpose Type of Research Evidence Level Method Result [1] [2] [3] [4] [5] [6]

[1] Source: Author, title, name of journal, year, volume, page [2] Purpose: Purpose of the study [3] Type of research: Randomized controlled, blinded (masked) study, cohort, case control, etc. [4] Evidence level: To be made according to the ranking indicated in Annrx-5 Table 1. [5] Number of patients: Number of patients included into the research, characteristics of patients: Age, gender, level of disease, other diseases, inclusion and exclusion criteria, duration of treatment, comparative group(s), monitoring period [6] Outcome: primary and secondary outcome criteria.

#### ANNEX-7 RELIABILITY TABLE Summary Table Relating to the Published and Reported Clinical Research Data Comparative Reliability Analyses

Title, Source and Date of the Source Publication/Report Type of Research Evidence Level Adverse Effects Treatment Group Comparative Group Monitoring Period [1] [2] [3] [4] [5] [6] [7]

[1] Source: Author, title, name of journal, volume, year page. [2] Type of research: Randomized controlled, blinded (masked) study, cohort, case control, etc. [3] Evidence Level: To be made according to the ranking indicated in Annex-5 Table 1. [4] The adverse effects relating to the medicine shall be listed separately as serious and non-serious one (the definition of serious adverse effect should be perceived as stipulated in the current Pharmacovigilance Guidelines for Registration Holders of Medicinal Products for Human Use). [5] and [6] Number of persons and percentage where adverse effects have occurred in the treatment and comparative groups, the p value and confidence interval, if indicated. [7] Monitoring period: Period for monitoring patients.

#### ANNEX-8 COMPARATIVE TABLE FOR GENERIC MEDICINES Name of Medicine Pharmaceutical Form, Strength Package Amount Retail Sale Price Public Discount (%) Public Price Unit Price New medicine Medicine A Medicine B Medicine C

#### ANNEX-9 TABLES ON THE NEW TREATMENT BALANCE

9.1. Information on the medicine Name of medicine Name of active substance(s) Pharmaceutical form, strength and unit price Therapeutic group Relevant alternatives (including non-pharmacological ones) Proposal on the prescription, use and reimbursement rules of the medicine

9.2. Indication and dosage information Indication(s) included into the package insert and summary of product characteristics (SmPCs) The therapeutic dose and duration recommended for this indication/these indications

9.3. Information on cost of medicine/patient/month\* Indication(s) Total cost of medicine/patient/month for the public\*

\*Treatments lasting shorter than one month should be indicated and the cost should be calculated accordingly.

9.4. Estimated prevalence in Turkey for the indication(s) of the medicine and estimated number of patients Estimated number of patients Population Estimated prevalence of the diagnosis in which it is used Estimated number of patients Diagnosis 1 in which it is used Diagnosis 2 in which it is used

9.5. Regarding the medicine; 9.5.1. Estimated budgetary impact Estimated Budgetary Impact Year 1 Year 2 Year 3 Rate of patients likely to use the medicine (%) Number of patients likely to use the medicine Annual number of packs per patient Annual total number of packs of the patient Public cost of the medicines Budgetary impact \*The term “year” stated in the table refers to a period of 12 (twelve) months and the current calendar year.

#### **9.5.2. Market balance Public Cost per Unit Current Status**

Year 1 Year 2 Year 3 Medicine A Medicine B Medicine C New Medicine

Market Distribution – Unit – Excluding New Medicines Current Status

Year 1 Year 2 Year 3 Total Market: Medicine A Medicine B Medicine C

Market Balance Excluding New Medicines - □ Current Status

Year 2 Year 1 Year 3 Total Market: Medicine A Medicine B Medicine C

Market Distribution – Unit – Including new Medicines Current Status

Year 1 Year 2 Year 3 Total Market: Medicine A Medicine B Medicine C New medicine

Market Balance Including New Medicines - □ Current Status

Year 1 Year 2 Year 3 Total Market: Medicine A Medicine B Medicine C New medicine

### **ANNEX-10 TABLES OF PRODUCTS PERMITTED TO BE SOLD WITHOUT RECEIVING A REGISTRATION**

10.1. Product information: Name of product Content Unit price Relevant alternatives (where available) Proposal of the applicant on prescription, use and reimbursement conditions

10.2. Field of use and daily use amount: Diagnosis where it is used Recommended amount and duration of use

10.3. Information on cost/patient/information: Diagnosis where it is used Total cost/patient/month for the public

10.4. Estimated prevalence of the diseases where it used/number of patients in Turkey Estimated number of patients Population Estimated prevalence of the diagnosis where it is used Estimated number of patients Diagnosis 1 where it is used Diagnosis 2 where it is used

10.5. Market distribution estimations Number of patients to be used in Turkey

Diagnosis where it is used Year 1 Year 2 Year 3

Market distribution in the group in which the product is included in Turkey Diagnosis where it is used Year 1 Year 2 Year 3

10.6. Direct cost Total cost for the public Diagnosis where it is used Year 1 Year 2 Year 3