

TURKISH MEDICINES AND MEDICAL DEVICES AGENCY
GUIDELINE FOR WORKING PRINCIPLES AND PROCEDURES OF HUMAN
MEDICINAL PRODUCTS PRIORITY ASSESSMENT COMMISSION

SECTION ONE

Objection, Scope, Basis and Definitions

Objection

ARTICLE 1 – (1) This guideline is prepared on the purpose of determining the principles and procedures relating to the working of Human Medicinal Products Priority Assessment Commission, established within the Turkish Medicines and Medical Devices Agency, and prioritization applications.

Scope

ARTICLE 2 - (1) This guideline covers the analysis and finalization of the requests about prioritization of the following applications which are included in the annex of Ministerial Consent dated April 13, 2016 Nr: 2165621 in the Agency’s Assessing Processes;

- a) Applications relating to first generic products or products of which generic is authorized but not on the market,
- b) Applications relating to biosimilar products,
- c) Applications relating to innovative products,
- ç) Applications relating to transferring the production of imported medicines to our country,
- d) Applications for locally manufactured products for exportation purposes ,
- e) Applications relating to products which cause serious public health problems in case they are not ready for use including vaccines or those which are included in the Agency’s foreign medicine procurement list on the date of application,
- f) Applications relating to products of companies which are benefited from the governmental incentives in the fields of R&D, manufacturing and marketing,
- g) Special import permit applications,
- ğ) Applications relating to the Good Manufacturing Practices (GMP) audit,
- h) Applications relating to products which have strategic importance in terms of country policies.

Basis

ARTICLE 3 – (1) This guideline has been prepared on the basis of Article 27 of Decree Law Concerning the Organization and Duties of The Ministry of Health and its Affiliated Institutions Nr:663 and Regulation on the Registration Medicinal Products for Human Use published in the Official Gazette Nr:25705 dated January 19, 2005, referring to the Ministerial Consent Nr: 2165621 dated April 13, 2016.

Definitions

ARTICLE 4 – (1) Following terms used in this Guideline shall have the meaning expressly designated to them below;

- a) Ministerial Consent: Ministerial Consent Nr:2165621 dated April 13, 2016,
- b) Unit: Health Industries Coordination and Tracking Unit within the Department of Economic Assessments and Medicine Procurement Management,
- c) First Generic Product: The product only the original of which is available on the market, namely the generic of it is unavailable,
- ç) Assessment Process: Product analysis procedures, the GMP audit of manufacturing plants, all the phases of marketing authorization application which starts with pre-assessment and ends in placing on the market,
- d) GMP: Good Manufacturing Practices,
- e) Commission: Turkish Medicines and Medical Devices Agency Human Medicinal Products Priority Assessment Commission,
- f) Agency: Turkish Medicines and Medical Devices Agency,
- g) Normal Application: The application for which any prioritization is not requested or of which prioritization request is not approved,
- ğ) Original Product: The product which is authorized in order to be put on the market for the first time in the world by proving that it has scientifically acceptable efficiency, quality and reliance in terms of active substance or substances,
- h) Prioritization: Assessment of applications within the determined criteria and put them forward in the Agency's assessment processes by giving priority to applications about medicines which can contribute to the national economy by decrease in import and increase in export and local production; to public finance by decrease in unit medicine price; to public health, preventive and therapeutical health services by using them in health service delivery,
- ı) Prioritization Process: All the phases of a prioritization request as of it's transmitted to the unit till the end of actions and operations about it in the Agency,
- i) Priority Application: The application determined as a priority in the assessment process by the Agency,
- j) Special import permit: The license given in order to ensure the availability of import licensed medicines in case there is a problem in the supply of them,
- k) Marketing authorization application: Marketing authorization applications carried out within the scope of Regulation on the Registration Medicinal Products for Human Use,
- l) Request Form: Forms included in the Agency website in order to be used in prioritization request,
- m) Innovative Product: The medical product which is the first in or which brings partially or wholly innovation to the diagnosis and treatment of the diseases much faster, much more efficient or with lower costs by aiming at improving the quality of life and health,
- n) High Priority Application: The application determined as high priority by the Agency in the assessment process.

SECTION TWO

The Organization, Duties and Meetings of the Commission

The Organization of the Commission

ARTICLE 5– (1) The Commission consists of totally 13 people which are President of the Agency, Vice President of Pharmaceuticals and Pharmacy, Vice President of Economical Assessments and Laboratory Services, Head of Drug Registration, Head of Economical Assessments and Medicine Supply Management, Head of Analysis and Controlling Laboratories, Head of Drug Inspections, Head of Pharmaceuticals and Pharmacy Department of Social Security Institution, a Pharmaceutical Technology and a Pharmacology academic member to be determined by the President of the Agency, two clinician members to be determined according to the meeting agenda and a member with academic title to be chosen within the Agency

(2) The duty of Commission Presidency is enforced by the President of the Agency. When the president does not attend the Commission meetings, the duty is enforced by Vice President of Pharmaceuticals and Pharmacy and in case the two do not attend the duty is enforced by Vice President of Economical Assessments and Laboratory Services.

(3) In the event that any one of the Commission members excluding The President, Vice Presidents, academic members and Head of Social Security Institution Pharmaceuticals and Pharmacy, does not attend the meeting, the reserve member determined by the President beforehand attends the meeting in his stead. People apart from members may attend the meetings only when they are invited.

The Duties of the Commission

ARTICLE 6 – (1) Duties of the Commission are stated below:

- a) Assessing and finalizing the prioritization requests,
- b) Following the results of its decisions, reviewing and reassessing them when necessary.

Working Principles and Procedures of the Commission

ARTICLE 7 – (1) The day, place and time of the meeting are determined by the President and are notified to Commission members by the Unit.

(2) The Commission convenes with absolute majority of members.

(3) The decision of high priority application is taken with the affirmative votes of 4/5 members attending the meeting.

(4) The decision of priority application or normal application is taken with the affirmative votes of absolute majority of members attending the meeting.

(5) In the event of equality of votes in the priority or normal product decisions, it is assumed that the majority is constituted in line with the President's vote.

- (6) The decision in the assessments of special import permit is taken with the affirmative votes of absolute majority of members attending the meeting.
- (7) It is not possible to abstain from a vote in the meetings.
- (8) The decisions taken by the Commission are documented and signed by Commission members.
- (9) The correspondence relating to the actions and operations of the Commission is carried out by the Unit.
- (10) The Commission convenes at least bi-weekly.

SECTION THREE

Making and Assessing Applications and Performing the Decisions

Making Applications and Documents Required for Applications

ARTICLE 8 – (1) It is necessary to apply for prioritization in order to prioritize a product. However, Prioritization Commission may put some products on its agenda without prioritization request (application) if deemed necessary.

- (2) Prioritization request is made to the Unit by following the workflows stated below:
 - a) The electronic-based request form on the Agency’s official website is filled.
 - b) Supporting data and documents relating to application group are completed.
 - c) The filled request form and documents are printed.
 - ç) Each page of the stated documents are paraphed and the last page is signed and stamped by the authorized person in behalf of the applicant.
 - d) The list of authorized signatures relating to the one who signed the declarations and commitments is added to application documents.
 - e) The application is made to the Unit through the automation system of the Agency by writing a cover letter with the letterhead of the applicant and documents are given in to the incoming papers unit of the Agency.

Assessment of the Applications

ARTICLE 9 – (1) The Unit follows the ways below while performing the prior review of prioritization requests:

- a) It analyzes the accuracy of statements in the request form on the Agency’s website.
- b) In the event that there are more than one first generic product application, among applications of which 210 days necessary for licensing started, it assesses the suitability of statements about first three applications by application date and about those applications made within two months after the accepted third application.

c) In the biosimilar product applications, the Unit assesses the suitability of declarations of the firm (Annex-2) about the possible Pharmacy Retail Price (TL) and Reimbursement Price (TL) of the product on the market.

ç) In the applications about products in the Agency's foreign medicine procurement list on the date of application, the Unit assesses the suitability of declarations of the firm (Annex-2) about the possible Pharmacy Retail Price (TL) and Reimbursement Price(TL) of the product on the market.

d) The Unit assesses the suitability of applications about innovative products to the criteria of ensuring technology transfer to our country, assesses the documents showing the positive contribution of these products to public cost, unmet treatment need, efficiency on society, action time, interaction with other medicines, synergistic-additive action, safety advantage, specific action on some diseases, patient compliance, additional benefit, stepped care, fast effect and action mechanism and also it assesses the suitability of statements of the firm (Annex-2) about the possible Pharmacy Retail Price (TL) and Reimbursement Price(TL) of these products on the market.

e) The Unit assesses the suitability of planned exportation time and size, planned exporting countries, the starting date of exportation and the document stated in Annex-1 for the products which are requested to be assessed within the marketing authorization applications about products having export relation among marketing authorization applications for locally manufactured products.

f) In the applications of firms benefited from the governmental incentives in the fields of R&D, manufacturing and marketing, the Unit assesses the suitability of governmental incentives documents relating to their products.

g) The Unit assesses the suitability of declarations in the applications of medicines including all the vaccines which cause serious public health problems in case they are not ready for use.

ğ) In the applications of products that take part in foreign medicine procurement list of the Agency, the Unit assesses the suitability of documents submitted during application in terms of their effect on public health and public cost.

h) In the applications relating to special import permit, the Unit assesses the reasons why they are not on the market and the suitability of data and documents to be obtained about indication and contribution to treatment.

ı) The Unit assesses the suitability of data and documents which show that at least 10% of total global patient number in the Phase III of the clinical research carried out for the related product is from our country or the bioequivalence study is performed in our country.

(2) The Unit submits applications by date for each assessment topic to the consideration of the Commission.

Scoring and Classification

ARTICLE 10 – (1) The applications made for prioritization are classified as high priority application, priority application and normal application after the assessment to be carried out by the Commission.

(2) The scoring operation of the table in Annex-3 for first generic products is carried out as below:

- a) Scoring is performed as stated in Annex-4 for scoring criteria (1) (Effect on Public cost).
- b) It is scored between 0 and 100 for scoring criteria (1, 2). Scores multiply by the weighted percentage stated in the cell of the related column and the result is written into that cell.
- c) In the Scoring criteria (3) (Market availability), for the product only original of which is available on the market and of which equivalent is not authorized is scored as 100; products one equivalent of which is authorized but is not available on the market are scored as 67; products two equivalent of which are authorized but are not available on the market are scored as 33. In the event that the related firms state by a formal letter that the authorized equivalent(s) are not put on the market; the product for which marketing authorization application is made is scored with the point stated in this paragraph and suitable to its condition. These scores multiply by the weighted percentage stated in the related cell and the result is written into that cell.
- ç) All the weighted scores in the related column are added and the total weighted score is obtained.
- d) Total weighted score obtained in the event that the product is locally manufactured, domestic active substance is used, bioequivalence studies and clinical research are carried out in our country, multiply by coefficients stated in the related part (4, 5, 6). The results obtained are written in to the related cells. The final score about application is obtained by adding the scores in these cells to the total score. In order to prevent the final score to have decimal place, the obtained number is rounding off.
- e) Applications relating to biosimilar products, applications relating to innovative products, applications relating to product including all the vaccines which cause serious public health problems in case they are not ready for use or those which are included in the Agency's foreign medicine procurement list on the date of application, applications relating to products of companies which are benefited from the governmental incentives in the fields of R&D, manufacturing and marketing, about these governmental incentives, applications relating to products which have strategic importance in terms of country policies are assessed by the Commission independently of the scoring criteria in the guideline.
- f) The applications relating to locally manufactured products having export relation among marketing authorization applications are assessed by the Commission according to the criteria of planned exportation time, planned exporting countries, planned exportation size and the starting date of exportation.
- g) The priority matter of applications relating to biosimilar products is assessed by the Commission according to the matters of being produced in our country as of its cell form, providing public cost advantage if it is imported and creating a supply alternative in case it is the first biosimilar product.
- ğ) The priority matter of locally manufactured product applications relating to the transferring of production of imported medicines to our country is assessed by the Commission.

(3) The products scored as 75 and over after the scoring operation carried out for first generic product applications are assessed as high priority; the scores below 75 are assessed as priority.

(4) Documents relating to importation of products of which special import permit request is approved by the Commission are prepared by the related department.

(5) In the event that prioritization requests are not approved by the Commission, operations relating to the product are carried out by the related department in the normal application status by date.

(6) It is necessary to make prioritization application again at the beginning of marketing authorization process for the products of which GMP audit prioritization are made previously. However, application relating to both GMP audit prioritization and marketing authorization prioritization can be made at the same time. The Commission can assess those two applications together or separately.

(7) The GMP assessments of products of which GMP priority is determined as category 1 in the assessments carried out before the publication of this guideline are accepted as high priority application, the GMP assessments of products of which GMP priority is determined as category 2 are accepted as priority application, the GMP assessments of which GMP priority is determined as category 3 and 4 are accepted as normal application.

Implementation of Decisions

ARTICLE 11 – (1) The prioritization decision taken by the Commission is implemented in all phases of processes stated through the decision.

(2) The applications defined as high priority and priority are put into process by sorting according to their contribution to treatment, effect on public cost and manufacturing condition unless otherwise specified by the Commission.

(3) Among the products of which marketing authorization applications are made after this guideline enters into force, it is aimed to complete the registration process of high priority products in 150 days and of priority products in 180 days, if any deficiency is stated, the clock is stopped. Processes about products of which applications are made to the Agency before and operations of which are still continuing are reassessed by the Commission within the scope of this guideline if the related firm applies to the Agency.

(4) On the grounds that equivalent products authorized before are not put on the market, the situation of these products is followed by the Unit monthly during the registration process of first generic products for which prioritization decision is taken. If it is determined that the product is put on the market before, it is assessed by the Commission whether the prioritization decision will be revoked or not.

(5) The validity of GMP prioritization decisions which are taken by the Commission recently or before the publication of this guideline is three years. GMP audit prioritization application can be made again for those which require re-inspection or are not concluded at the end of three year.

Notification and Opposition

ARTICLE 12 – (1) The result of prioritization request is notified to the related firm through a formal letter by the Unit.

(2) If the prioritization request is not approved and it is decided to evaluate the dossier in the normal application status;

a) The applicant has the right of opposition to the decision in writing with justifications within 20 days as of the date of formal letter which declares the refusal decision. The applicant is given the right of verbal explanation and self-defense during the assessment of opposition if deemed necessary.

b) The opposition is assessed by the Commission and the result is notified to the applicant. One cannot oppose to the decision taken after the assessment of opposition unless any data and documents which may change the decision are submitted.

SECTION FOUR

Various and Final Provisions

Secretariat

ARTICLE 13 – (1) The secretariat of the Commission is enforced by the Unit.

(2) If deemed necessary by the Unit, one permanent and one reserve Agency personal determined by the Commission beforehand among departments relating to assessment processes can study together in coordination.

The duties of the Unit about prioritization

ARTICLE 14 – (1) The duties of the Unit are stated below:

a) To present the applications made in order to be put on the Commission's agenda, to the Commission together with the comparative data and documents by subjecting them to prior review in terms of suitability to the assessment criteria.

b) To inform the related units about the decisions taken by the Commission,

c) To present the data as chart which is transmitted to the Unit biweekly by the related departments, relating to the following of Commission decisions to the Commission,

ç) To follow the products for which the prioritization decision is taken providing that they are reassessed and to put them on the Commission's agenda in due course,

d) To follow once a year during five (5) calendar years, the data about the previous calendar year of products authorized by taking prioritization in terms of suitability to the prioritization criteria and to submit them to the Commission as chart every year till the end of March.

Responsibility of the Applicant

ARTICLE 15 – (1) As part of the prioritization application, the prioritization applications of firms which do not send the data and documents requested by the Agency on time or do not meet the commitments are rejected. The other prioritization applications to be made by the product owner within a year after this decision is declared to the applicant by the Commission are not assessed. The applications of which prioritization processes are already continuing of licensees who have such products are reassessed by the Commission.

(2) It is obligatory to put a product prioritized by the Commission on the state market within six month after the product registered. The licensee is obliged to notify to the Commission the justification about why he does not put the product on the market at the fifth month of this period at the latest. The new prioritization applications to be made within a year after the due date of six month period stated in this paragraph by the licensee whose justifications is not approved by the Commission are not assessed. The applications of which prioritization processes are already continuing of licensees who is in such a matter are reassessed by the Commission. The locally manufactured products for which marketing authorization is issued for exportation are not assessed within this context.

Transition Process

PROVISIONAL ARTICLE 1 – (1) All the prioritization applications to be made to the Agency before the publication of this guideline should be renewed through the electronic application system and the automation system of the Agency. The applications made by this way are assessed by date. The special import permit are exempt from this situation.

Entry Into Force

ARTICLE 16 – (1) This guideline enters into force by the approval of the President of the Agency.

Enforcement

ARTICLE 17 - (1) The provisions of this guideline are enforced by the President of the Agency.

ANNEX-1:

Declaration and Commitment for locally manufactured products for exportation

DECLARATION AND COMMITMENT

We declare, agree and commit that the marketing authorization taken from the exporting country about the product with _____ active substance and named _____ which takes part within the scope of marketing authorization applications of locally manufactured products for exportation will be submitted to the Commission secretariat, at least 99% of first three full scale production series will be exported, the exportation data relating to the product will be reported to the Unit once every six months, if otherwise specified, the sanction within the scope of the prioritization will be imposed.

Company Seal

Name/Surname of the Authority

Date

Signature

ANNEX-2:

Possible Pharmacy Retail Price and Reimbursement Price

DECLARATION

We agree and declare without force major that the possible Pharmacy Retail Price will be ____ TL and the possible Reimbursement Price will be ____ TL of the product named _____ and with _____ active substance, which is the matter of the application within the scope of products that have strategical importance in terms of state policies/products included in the Agency's foreign medicine procurement list on the date of application/innovative products/biosimilar products/first generic products or products of which equivalent is authorized but is not on the market.

Company Seal

Name/Surname of Authority

Date

Signature

ANNEX-3:

Prioritization Assessment Criteria and Scoring Chart

	Coefficient Criteria					
Application Type	1.Positive Effect on Public Cost	2.Negative Effect on Public Cost	3.Availability on the market	4.Local Production	5.Local active substance	6.Performing Bioequivalence studies in Turkey*
Applications relating to first generic products or products of which equivalent is authorized but is not on the market	70%	-70%	30%	x 0,15	x 0,15	x 0,3

*It is assessed according to the data and documents which indicates that the bioequivalence studies about the related product are carried out in our country.

ANNEX-4: Criteria 1: Possible effect on public cost

Possible Public Cost Advantage (TL)	Score
100.000- 200.000	1
200.000- 300.000	2
300.000- 400.000	3
400.000- 500.000	4
500.000- 600.000	5
600.000- 700.000	6
700.000- 800.000	7
800.000- 900.000	8
900.000- 1.000.000	9
1.000.000- 2.000.000	10
2.000.000- 3.000.000	20
3.000.000- 4.000.000	30
4.000.000- 5.000.000	40
5.000.000- 6.000.000	50
6.000.000- 7.000.000	60
7.000.000- 8.000.000	70

8.000.000- 10.000.000	80
10.000.000- 20.000.000	90
20.000.000- 30.000.000	95
30.000.000 ≤	100