ONCOINDEX Methodology, September 2021

BACKGROUND:

1. Oncoindex (OI) is a study evaluating the scope of reimbursement of cancer medicines registered in EMA (*European Medicines Agency*) in the past 15 years and recommended by ESMO (*European Society for Medical Oncology*).
2. OI value may range from 0 to 100. Value 0 means that patients have no access to any of the recommended medicines. Value 100 means that every patient may be treated in accordance with current medical knowledge.
3. Evaluation involves therapeutic areas - solid tumours and haemato-oncological diseases that are the most common causes of deaths of cancer patients in Europe.
4. The procedure of OI value evaluation includes the following stages:
    a. Selection of therapeutic areas (WOT).
    b. Selection of active substances registered by EMA for particular therapeutic areas (WEMA).
    c. Selection of ESMO concerning particular therapeutic areas (WESMO), and as a consequence, the list of recommended molecules.
    d. Evaluation of the scope of reimbursement of the active substances obtained in the previous stages of the procedure (OREF).
    e. Estimation of suboncoindices (SOI) and OI (WOI) in the analysed country.

    Detailed description of the stages is presented in the following subchapters. WEMA and WESMO stages are performed parallelly.
5. Rate of OI value calculation for individual countries is presented in Table A.
6. Data sources are shown in Table B. Also, their characteristics are presented that concerns: usage at analysis stage, frequency of updating and values of maximal time divergence from the date of OI value determination.

THERAPEUTIC AREAS/DATA SOURCES - Selection of therapeutic areas (stage WOT):

1. The analysis involves maximum: 10 solid tumours and 10 haemato-oncological diseases characterised by the highest cancer-related mortality in Europe.
2. The data related to the number of deaths and thus, the selection of therapeutic areas is performed based on reports published by GHDx (http://ghdx.healthdata.org/gbd-results-tool). Oncoindex calculations are performed for therapeutic areas in accordance with the ones determined by GHDx.
3. The analysis omits cumulative categories of the therapeutic areas defined in GHDx as they only complement the set of recommendations unconsidered in other therapeutic areas, encompassing a vast number of various indications of minor share in the total number of deaths due to cancer diseases.

4. Therapeutic areas presented by GHDx might be combined into one area for OI calculation if the found ESMO recommendations (at WESMO stage) concern such a combined therapeutic area.
5. The data is updated once a year. Updating process is performed when processing the first OI calculation in a given year.
6. Updating process involves:
    a. Obtaining the data concerning the number of deaths due to cancer diseases in Europe from the source presented in item 2.
    b. Determination, based on the above data, of the list of maximum 10 therapeutic cancer groups of solid tumours and the list of maximum 10 therapeutic groups of haemato-oncological cancers.

EMA - SELECTION OF ACTIVE SUBSTANCES (stage WEMA):

1. Selection of registered active substances in EMA requires the fulfilment of all of the following conditions:
    a. Analysed active substances have ATC code starting with letter "L" (Anticancer drugs and immunomodulators) and are indicated for cancer treatment.
    b. Analysed active substances are registered in EMA and their first registration for a given analysed OI therapeutic area (determined by therapeutic categories of GHDx data concerning cancer-related death) was performed within the past 15 years. The data is updated once a year. Updating process takes place when the first OI calculation in a given year (n) takes place as of 1 January of this year (n-15).
    c. Updating of active substances selection was performed in accordance with time restrictions presented in Table B.
2. The obtained list of active substances must consider collection of data of names referring to the active substances, information of registered OI indications (or their lack) including dates of their first EMA registration, EMA status recommendation, information whether the particle concerns orphan drug therapy or it is a biosimilar drug, ATC code values and URL addresses for Summary of Product Characteristics - SPC (all data in the following language versions: English and the country for which OI analysis is being prepared).

ESMO - SELECTION OF RECOMMENDATIONS AND ACTIVE SUBSTANCES (stage WESMO):

1. Selection of recommendations published by ESMO requires the fulfilment of all of the following conditions:
    a. The analysed ESMO clinical indications concerned the selected therapeutic areas obtained within WOT.
    b. The analysed ESMO clinical indications concerned the European population.
    c. Updating of ESMO indications was performed in accordance with time restrictions presented in Table B.

2. Selection of active substances recommended by ESMO requires:
    a. The analysed list of active substances to be obtained based on indications obtained at the stage of selection of the published ESMO recommendations.
    b. The list of recommendations considered in the analysis to include the ones that have recommendation strength evaluation (GOR) at the level of A, B or C (values ranging from strong recommendation, through general recommendation to optional one).
    c. Every update of recommendation selection also has an adequate update of particle selection recommended by ESMO.

EVALUATION OF REIMBURSEMENT SCOPE IN A COUNTRY (stage OREF):

1. Evaluation of reimbursement scope requires:
    a. Collection of appropriate data concerning reimbursement of medicines used in treatment of selected therapeutic areas designated in the first stage of analysis (WOT).
    b. Analysis of available data concerning assignment of inclusion and exclusion criteria for individual therapeutic areas and active substances obtained in WEMA and WESMO stages allowing for evaluation of compatibility of the criteria with relevant recommendations published in ESMO clinical guidelines.
    c. Update time of the data concerning the scope of reimbursement ensuring its currentness in relation to the predicted date of OI value publication, in particular, the time limitations presented in Table B must be met.
2. The obtained ordered set of data allowing for performance of OI value calculation.

ONCOINDEX CALCULATION - OI VALUE DETERMINATION (stage WOI):

1. OI value determination is performed in the following stages:
    a. We determine whether the medicine registered for a particular indication by EMA is reimbursed in this case in accordance with the guidelines published by ESMO.
        i. **Full reimbursement**: therapy with a particular medicine for a particular indication may be financed with public means for all patients in total accordance with ESMO guidelines - with no limitations, 1 point.
        ii. **Partial reimbursement**: therapy with a particular medicine for a particular indication may be financed with public means, however, there are certain population, territory, procedural, formal and time limitations associated with the onset or continuation of this therapy, 0.5 point.
        iii. **No reimbursement**: therapy with a particular medicine for a particular indication may not be financed with public means or such financing involves a marginally narrow group of patients out of the ones qualified for this treatment in accordance with ESMO guidelines, 0 point.

   b. For every type of disease we summarize the points resulting from provided access to medicines and we divide them by the maximum number of possible points (e.g. for cancer 'x' it is 6/18). We multiply the result 100 times (6/18x100=33.33).
   c. Having calculated SOI for all therapeutic areas we calculate major OI, that is SOI weighted mean, where the weights are the numbers of deaths in particular therapeutic areas for the analysed country based on the reports published by GHDx. OI value is obtained and this can be seen on the website.
2. On the website we publish the following values:
   a. Main OI,
   b. SOI for individual therapeutic areas,
   c. Remaining data

Table A

Country	**Institutions responsible for medicine reimbursement out of public means**	**Frequency of update of reimbursement conditions**	**Frequency of determination of Oncoindex value**
Poland	*Ministry of Health of the Republic of Poland*	*Every 2 months since 01 January 2020*	*Every 4 months since 01 January 2020*
Spain	*Ministry of Health and Consumer Affairs of Spain*		*Every 4 months since 01 September 2021*

Table B

No.	Name	Notes	Source of data - name of the Institution	Stage	Maximal distance from the date of predicted OI publication
1	*The number of deaths due to cancer diseases*	*Evaluated together with calculations of the first OI in a given calendar year*	*GDHx*	*WOT*	*Updated on 1 November of the preceding year, once updated and continuously used for the whole subsequent year (i.e. update on 1 November 2019 is used throughout 2020)*
2	*Data on registered in EMA active substances whose ATC code begins with letter "L"*		*EMA*	*WEMA*	*12 months*
3	*Data on published in ESMO European recommendations for selected therapeutic areas*		*ESMO*	*WESMO*	*1 month*
4	*Reimbursement data for the analysed country*		*Table A*	*OREF*	*0 days (current as of the day of predicted OI publication)*