**Access to the market of medicines: three years' experience of the Sicilian Regional Drug Formulary**

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**Background:** The approval of drugs for hospital use in Italy, both at the national and regional level, is a long and complex process. As a member state of the EU, Italy automatically accepts drug marketing authorizations centrally released by the European Medicine Agency (EMA). In Italy, drugs are initially granted a marketing authorization by the Italian Drug Agency (AIFA) at national level; subsequently, in most Italian Regions, a Drug Formulary Committee has to further evaluate the drug before granting the approval for Regional hospital use. Objective: To describe the outcomes of the Sicilian Regional Committee drug approval process by quantifying: a) the number and types of drugs being approved in the region; b) lag time between EMA, AIFA and Regional Committee drug approvals; c) the estimated economic impact on the Regional Healthcare System (RHS) after one year from drug approval at regional level. Methods: All the drugs for which a dossier was submitted from the 1st January 2013 to 1th April 2016 to the Sicilian Regional Drug Formulary Committee by a marketing authorization holder (MAH) were classified according to the presence of monitoring registry, prescription restriction to specialist centres and innovative status, and stratified by ATC (Anatomical Therapeutic Chemical Classification System). The lag time in days between the EMA approval date and the AIFA/Regional Committee approval dates was calculated by subtracting the three dates. The one-year budget impact analysis (BIA) was performed by taking into account the yearly mean cost of treatment for individual patients and the estimated number of all potentially eligible patients in Sicily.

**Results:** During the study years, the Regional Committee evaluated 170 drugs' dossiers: 117(68.8%) drugs were newly approved on the Regional market, 29 (17.1%) had an extension of already approved therapeutic indications and 24 (14.1%) were rejected. Of these 12 drugs (50.0%) were in class A, 6 in class C (25.0%) and 6 H (25.0%).

Of the 117 approved drugs, antineoplastic and immunomodulating agents (ATC: L*) were the largest group (n=37; 31.6%), followed by alimentary tract and metabolism drugs (ATC: A*; n=17; 14.5%), anti-infective agents for systemic use (ATC: J*; n=14; 12.0%) and nervous system drugs (ATC N*; n= 12; 10.2%). Median (IQR) lag time between EMA and AIFA approval and between AIFA and Regional Drug Formulary Committee approval was respectively equal to 447.5 days (IQR: 313-606) and Drug Formulary Committee 112 days (IQR: 53-231). Of the 117 approved drugs, n= 18 (15.4%) were judged by AIFA as being innovative (24.3% of all drugs belonging to ATC L*, 57.1% for ATC J* and 50.0% for ATC M*). A monitoring registry was not available for drugs belonging to ATC D* and G*, while antineoplastic and immunomodulating agents had the largest number of drugs requiring a monitoring registry (30/37; 81.1%) upon AIFA request. Restriction in the use to selected specialist centers was reported for all drug classes except for ATC M*, D*, G*, with antineoplastic and immunomodulating agents showing the highest frequency of restriction in the use (25/37, 67.6%). Payment by Results, Cost Sharing and Success Fee were the most commonly

reported managed entry agreements (MEAs) for reimbursement of approved drugs for ATC L* (n=10, 5 and 1, respectively). The BIA for one year of therapy showed that approved drugs in the years 2013-2016 accounted for a total estimated cost of € 500.9 million euro to the RHS. The total cost attributable to the first year of therapy with newly approved drugs ranged from € 968,801 for drugs belonging to ATC S* to € 215 million for drugs belonging ATC R*. Conclusion: In the last three years the Regional Committee approved a large number of high-cost drugs which was estimated to account for around € 500 million euro only during the first year of treatment. The presence of drug registries and prescribing restrictions to specialist centres for most newly approved drugs offers opportunity for post-marketing monitoring which is essential to optimize use of high-cost drugs in routine care.