

APPENDIX 2

EAP in Italy, including Compassionate use

| EAP | | Compassionate use | 648 List | 5% Fund |
|--------------------------------|----------------------------|---|--|---|
| General Label | | Accesso precoce e uso off label | | |
| Regulatory Reference | | DM 8/5/2013 - DM 7/9/2017 | Legge 648/96, Legge 79/2014, Decreto 2/8/2019 | Legge 326/03 |
| Named / Cohort | | Named / Cohort (expanded access) | Cohort | Named |
| Coverage | | Before MA / Till the medicine is 'available' | Before MA (but expanded for new drug till the completion of P&R process) | Before MA (after MA for orphan drugs) |
| Process | Applicant | Clinicians | Patient Associations, Scientific Societies, Health Care Organisations, IRCCS, University, Clinicians, AIFA (CTS) | Reference / Specialised Centres (online form till July 2022) |
| | Approval | Ethics Committee (Notification to Aifa for cohort-based) | Aifa (CTS): simplified price negotiation (Decreto 2/8/2019) | Aifa (CTS) |
| | Payers of medicines | Industry | Regions | AIFA through 5% Fund fed by the industry |
| Selection criteria | Target diseases | Severe diseases or rare life-threatening diseases | - | Rare diseases / Particular and severe diseases |
| | Medicines | No valid alternatives Medicines / Indication under clinical development Medicines / Indications with MA but not available yet | No valid alternatives Cheaper than valid alternatives | Orphan drugs / Drugs in development not approved yet "which represent a hope of therapy" |
| | Evidence | Phase II (Phase I per rare diseases and rare tumours) | Phase II / Data that may support to their use (pure 'off label') | Clinical report |
| Data collection | | Adverse reactions (to notify to AIFA) | In principle data on efficacy and safety profile (from the Regions to AIFA) (data are not available) | No |
| Data on economic impact | | -* | In principle data on efficacy and safety profile (from the Regions to AIFA) (data are not available) | Till 2017 dedicated fund and consolidated data on applications. 2020 only dedicated fund. From 2020 data on each single application |
| Dedicated budget | | - | No | Yes (funded by the industry) |
| MEA | | No | Rarely applied | No |
| Impact on P&R | | ? | Yes (medicines in 648 as comparators / revenue from 648 considered in P&R negotiation) | ? |