Drugs concerned	The scope of the procedure is extended. The Decree applies not only to medicinal products authorized with a centralized and mutual recognition procedure, but also to those authorised by means of decentralized and national procedures, as well as **for the purpose of including medicines in the list of Law 648/1996 and to some specific categories of medicinal products in class C and Cnn purchased by the NHS bodies** for public health needs.
Negotiation application	The company must now present together with the application the following: • scientific documentation which shows the **added therapeutic value** of the drug in relation to the main treatments with which it is compared, if any; • **self-certified information** on the marketing, consumption and reimbursement of the drug in other countries; • estimated market share expected in Italy in the following 36 months (previously 24 months); • self-certification on its **production capacity and management of possible unexpected events,** as well as an outline of the steps to be implemented to ensure the **adequate supply of the drug**; • self-certified quantification of any public contributions and incentives received for research and development programs; • information on the **patent status** of the drug.
Negotiation procedure	The changes to the procedure are many. The various steps of the procedure not previously contemplated in the CIPE Resolution are now regulated, including the specific competences of the Technical Scientific Commission (TSC) and the Price and Reimbursement Commission (PRC). In a nutshell: • **the procedure can be started**, not only by the company, but **also by AIFA** in various cases: (i) for medicinal products the reimbursement of which has a significant impact in terms of NHS expenditure or of inappropriate prescriptions; (ii) that have never been subject to negotiation (iii) if the previous procedure ended with a failure to agree; • **the procedure must be completed within 180 days** (previously 90) and only one interruption is allowed, which can also be granted further to **AIFA's request**; once the 90-day maximum suspension period has elapsed without any results, the negotiation procedure ends with the failure to agree and the inclusion of the drug in class C; • the **TSC expresses itself on the clinical value of the drug and on the added therapeutic value** compared to the comparative medicinal products, on the basis of the investigation prepared by AIFA and, when available, of the assessments produced in the ambit of the European procedure and, if deemed appropriate, of a "*scoping*

	meeting "between the competent AIFA offices and the pharmaceutical company; • the negotiation procedure **is considered to have been concluded without success** if the clinical superiority of the medicinal product does not emerge with respect to the comparator product and the company does not reformulate a proposal that confers a therapy cost equal to or lower than that of the comparators; • in the absence of comparative products, the company presents economic assessments supplemented by adequate documentation aimed at motivating the price proposal also on the basis of the costs incurred in the research, development and production phase; • once the evaluation is completed, **the TSC sends the documentation to the PRC, which then starts the process for negotiating the price with the company**. The PRC examines the proposals made taking into account the assessments of the TSC and also emphasizing the prices applied to the NHS bodies and the number of treatments expected. Article 3 of the Decree, which governs the procedure, contains an express provision that during the price negotiation phase, AIFA is also required to consider, on the basis of the presumed consumption data, the financial **limits imposed by the current legislation on pharmaceutical expenditure.** In case no agreement is reached, the medicinal product is classified in class C. In addition to the provision of the CIPE Resolution, the Decree now clarifies that AIFA must report the reasons for the decision taken, through a determination or with other suitable methods.
Negotiating the **Agreement**	Transposing the recommendations of WHA Resolution 72/2019, with respect to the CIPE Resolution, the new Decree provides that: • the agreement is reached taking into account, not only the sales volumes, the availability of the product for the NHS and the discounts for supplies to the NHS bodies, but also the **contributions of a public nature to the drug development and research programmes**; • the company is also obliged to communicate to AIFA, annually, in addition to the sales and turnover data, **the marketing costs and the patent status of the medicinal product** in Italy. In the definition of the agreement, the following changes have also been introduced: • the possibility to apply **a price increase**, in exceptional cases, and in any case for low-cost drugs, where there are objective difficulties in obtaining raw materials, or where it is impossible for it to remain on the market on the established conditions and the increases in production costs are adequately demonstrated on the basis of documented objective evidence; • the possibility for AIFA to regulate, for the purpose of streamlining the negotiation procedures, **automatic mechanisms in favour of generic and**

	biosimilar medicines, also following requests for packaging modifications, for medicines for which similar drugs are already reimbursed by the NHS; • AIFA will also be able to indicate the conditions for automatic renewal upon expiry of the agreement, providing for cases in which progressive discounts can be applied; • the possibility that AIFA and the companies agree on **innovative negotiation models**, in addition to the ordinary price-volume schemes, turnover ceilings and pay-back.
Duration of the Agreement	On the duration and renewal of the agreement, the Decree introduces some changes: - the 24-month validity of the agreement and the right for both parties to restart the procedure before the expiry date, in the presence of changes to the therapeutic indications and/or posology, such as to foresee a "**variation**" (not an "increase", as envisaged in the CIPE Resolution) in the level of use of the drug, are confirmed; - AIFA can restart the negotiation procedures to reconsider the conditions of the agreement before expiry, in various circumstances: (i) in the event that there are medium-term **market variations** such as to foresee an increase in the level of use of the medicinal product or to an unfavourable cost-therapy ratio compared to the alternatives present in the national pharmaceutical handbook; (ii) in the presence of **new evidence on the efficacy and safety of the medicinal product**, such as to suggest that the positioning in therapy has been changed or that the clinical benefits estimated at the time of negotiation have been reduced; (iii) in case of **a shortage of the medicinal product.** Pursuant to an express provision contained in the 2019 Finance Law (art.1 paragraph 554, Law 145/2018), AIFA has already been authorized, with effect from **1 January 2019, to restart the negotiation procedures** before their expiry in the event of **market changes**, as indicated in paragraph (i) above. That provision also extends the period of time available to the parties to propose changes to the conditions of the agreement. This period ranges from 90 to 60 days before the agreement expires. In the absence of changes, the agreement is considered as renewed for a further 24 months.