Studies for approval of new drugs have insufficient patients to evaluate safety

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For medicines intended for chronic use, the number of patients studied before regulatory approval is insufficient to properly evaluate safety and long-term efficacy, requiring the need for new legislation, according to a study by European researchers published in this week's *PLOS Medicine*.

Current European guidelines specify that in order to fully evaluate the safety of medicines being developed for chronic (long-term) treatment of non-life threatening diseases, at least 1000 patients must take the new drug and that 300 and 100 patients must use the drug for 6 and 12 months, respectively, before approval by the European Medicines Agency.

In an analysis led by Ruben Duijnhoven from Utrecht University, the authors used information from the European Commission about 200 medicines approved between 2000 and 2010 to investigate whether the number of patients included were in compliance with the International Conference on Harmonisation E1 guidelines.

The authors found that the average number of patients studied before approval was 1708 for standard medicines and 438 for orphan medicines, medicines used to treat rare diseases. On average, medicines for chronic use (for example, asthma medications) were studied in more patients (2338) than those for intermediate use such as anti-cancer drugs (878) or short-term use such as antibiotics (1315). The safety and efficacy of chronic use was studied in fewer than 1000 patients for at least 6 and 12 months in 46.4% and 58.3% of new medicines,

respectively. Finally, the authors found that among the 84 medicines intended for chronic use, 69 were studied in at least 300 patients for 6 months and 67 were studied in at least 100 patients for 12 months.

The authors say: "For medicines intended for chronic use, the number of patients studied before marketing is insufficient to evaluate safety and long-term efficacy. Both safety and efficacy require continued study after approval."

They conclude: "In light of new scientific and legislative tools to monitor benefits and risks in clinical use, discussion of the long-term exposure requirements for approval of medicines, particularly for medicines intended for chronic use, seems warranted."

The authors add: "Such a discussion should involve healthcare providers, patients, and academia, as well as industry and regulators, and should include debate on the level of acceptable uncertainty, especially for adverse events and the long-term outcomes for chronic medication."

More information: Duijnhoven RG, Straus SMJM, Raine JM, de Boer A, Hoes AW, et al. (2013) Number of Patients Studied Prior to Approval of New Medicines: A Database Analysis. PLoS Med 10(3): e1001407. doi:10.1371/journal.pmed.1001407