Pharmaceutical medicine can claim many triumphs including the approval last year of a significant number of new medicines for chronic and rare diseases. Yet despite these achievements, the number of diseases for which no treatments are available is worryingly high. The private sector can only do so much to address these needs. Developing medicines de novo is an expensive process, and most companies will only undertake this job if they can expect a return on their investment. At the same time there is a huge reservoir of off-patent medicines on the market that were developed for one medical use but could potentially be redeveloped for other, unmet medical needs.

It is against this background that the Netherlands launched a project in 2011 to study how entrepreneurs could be encouraged, either working on their own or in partnerships, to propose compounds that could form the basis of a drug rediscovery project. This study led to an action plan adopted by the Ministry of Health, containing several aspects. These are to conduct more research into the quality of drug applications currently submitted to the Medicines Evaluation Board (MEB), which is the national regulator; to review possible drug rediscovery projects; and to analyse the business case for drug rediscovery.

There is as yet no formal regulatory pathway for evaluating a drug which has been repurposed for a proposed new indication. But this could change quickly once entrepreneurs and their partners bring new projects forward. The first of these applications was submitted to the MEB in 2012 by a still unidentified partnership. The entrepreneurial team is seeking to develop a new therapeutic use for the chemotherapy agent tioguanine which is used to treat acute myeloid leukaemia, acute lymphoblastic leukaemia and chronic myeloid leukaemia. Marketed under the trade name Lanvis, the drug is cytotoxic to white blood cells. At lower doses it is said to suppress immunity while at higher doses it has an anti-leukaemic effect. The applicant is seeking to have the drug approved for ulcerative colitis, a long-term condition where the colon and the rectum become inflamed, and for Crohn’s disease, a type of inflammatory bowel disease.

In November 2014 the MEB told the applicants that a conditional marketing authorisation will be granted provided they can make a convincing proposal for further clinical development. This proposal is currently being evaluated. A decision is expected on 2 April 2015.

One of the big incentives for rediscovering new uses for existing, marketed medicines is cost. Well-known active substances with an established safety record and a proven benefit-risk profile will be less expensive to develop than new molecular entities. This means that the prices at which they can be sold will be lower. Any policy that promises to ratchet down drug prices at a time when governments are facing pressure to cut costs would be welcome.

There is already a market for the new use of existing medicines and this is called off-label prescribing. A medicine is prescribed off-label when it is used for an indication for which it has not been approved. Off-label prescribing is used by physicians all over the world to treat patients for diseases for which there is no authorised medicine. In recent years however, physicians have been prescribing medicines off-label not only to fill a gap in pharmaceutical coverage, but also to save money.

An example of the economic drive behind off-label prescribing is Avastin (bevacizumab), the cancer medicine, which has been widely used in Europe to treat wet age-related macular degeneration (AMD), a condition for which it has been authorised. The authorised medicine for macular degeneration is Lucentis (ranibizumab), but this medicine carries a much higher price. Both drugs were developed by Genentech (now Roche) and Roche has said it won’t seek a marketing authorisation for Avastin in wet AMD. Roche holds marketing rights for Lucentis in the US, while Novartis holds rights in Europe. In 2011, four hospitals in the UK said that they were planning to make Avastin available on the National Health Service for wet AMD, even though the drug was not approved for this indication. This led to a legal challenge by Novartis, which subsequently ended up in a negotiation with the health service over discounts for Lucentis. Furthermore, some EU member states have even legalised the off-label use of Avastin.

Should off-label prescribing be the route for rediscovering new uses for old medicines? We would argue that a well thought-out policy of drug rediscovery is the better option. It has the advantage of bringing an informal practice, off-label prescribing, into a legal framework so that patients and healthcare professionals can be certain that the new uses for existing drugs have been thoroughly examined for safety and efficacy. If drug rediscovery becomes a European-wide policy it offers the advantage of generating new treatment options for more patients at a lower cost than is currently possible.

Looking across the Atlantic, we can see that steps have already been taken to make better use of existing drug molecules. In December 2011, the US government set up The National Center for Advancing Translational Sciences with a mandate to find new uses for agents that have already progressed in clinical development. The Dutch rediscovery initiative focuses on new uses for off-patent medicines. But the principle is the same: to make more medicines available to patients at a an affordable cost.

References:
2. The countries are Italy and France.

John Lisman is an attorney, consultant and former legal counsel to the Dutch Medicines Evaluation Board. He is also a member of the MedNous Editorial Board.