Biosimilar medicines in inflammatory bowel disease

Treatment of ulcerative colitis and Crohn's disease with biological medicines is usually effective, but costly. The patent on the first medicine to come on the market has expired, and a much cheaper biosimilar medicine has recently been registered.

The new medicine is now recommended as the first choice by the Norwegian Drug Procurement Cooperation, but we believe there is reason for a conservative approach until more studies of the new medicine have been completed.

Therapeutic monoclonal antibodies for medical use are called biological medicines. Their manufacture is difficult and is based on biological processes in which antibodies are produced in genetically modified cell colonies, with the challenges this entails.

When pharmaceutical manufacturers want to make «copies» of existing drugs, the manufacturer of the copy has to develop separate cell colonies and make synthetic genes that code for a protein that is as similar as possible to the original. A process of this nature will never be able to yield a result that is completely identical to the original drug, and therefore these copies are not called generic medicines, but «biosimilar» medicines. The products of this process are biochemically and clinically tested in collaboration with the European Medicines Agency (EMA) according to their own guidelines (1).

A biosimilar medicine must demonstrate equivalent efficacy and have the same safety profile as the drug that it has «imitated». It is a matter of debate whether efficacy must be demonstrated for all diseases for which the original drug has been shown to be effective, or whether it should be sufficient to demonstrate efficacy for one or a few diseases, and then extrapolate to others. The argument for extrapolation is that millions of kroner in development costs can be saved (1, 2). The final result is that the medicines can be offered at a significantly reduced cost, which will naturally be advantageous.

New recommendations

Until now, the therapeutic alternatives with regard to biological medicines for patients with ulcerative colitis and Crohn's disease have been infliximab infusion (Remicade, from MSD), subcutaneous injection of adalimumab (Humira, from Abbvie) or golimumab (Simponi, from MSD), the latter only for patients with ulcerative colitis.

Infusion therapy must be administered in hospital, while subcutaneous injections may be administered by patients themselves. The efficacy of these treatment options is considered to be comparable, and the Norwegian Drug Procurement Cooperation has previously issued recommendations that the least costly alternative should be the first choice (3). However, the costs of the treatment options have been so similar that according to our experience, the choice has been largely based on individual preferences and route of administration. The patent on infliximab recently expired, and biosimilar versions have now come onto the market.

In January, the Norwegian Drug Procurement Cooperation announced its recommendations for 2014 concerning biological medicines in the field of gastroenterology (4). Two biosimilar medicines to infliximab (Remicade) were included in the bidding round: Remsima (from OrionPharma) and Inflectra (from Hospira).

«There is an absence of good documentation on the use of biosimilar medicines for ulcerative colitis and Crohn's disease»

The Norwegian Drug Procurement Cooperation now recommends Remsima as the first choice for biological treatment of ulcerative colitis and Crohn's disease. The cost is 39 % below the 2013 price level for Remicade. This will mean a saving of approximately NOK 50 000 in drug costs alone for the first year of treatment of one patient. The corresponding saving compared to use of Humira will be approximately NOK 40 000 (4).

The alternatives are thus considered comparable by the Norwegian Drug Procurement Cooperation with regard to efficacy and adverse effects, and it is therefore cost and route of administration that will have a bearing on the choice of drug. Use of Humira, which is administered subcutaneously, has turned treatment and monitoring over to outpatient clinics in the specialist health service. Remsima is now clearly the least costly alternative, and the fact of it being the first choice will result in a significant saving in drug costs. At the same time, Remsima is administered as an infusion, and its increased use will therefore also result in more patients requiring admission to hospital to receive treatment, consequently leading to an increased use of resources at the outpatient infusion clinics. The real cost saving will therefore not be as great as the difference in the direct drug costs.

What are the consequences?

For patients starting biological treatment for the first time, the least costly alternative will now be infusion with Remsima. The financial savings available with Remsima will make it likely that this will be the drug of choice. In that case a certain level of uncertainty must be accepted, since the effect of Remsima in Crohn's disease and ulcerative colitis has not been documented in randomised studies. The patient should therefore also be included in the decision regarding choice of treatment and route of administration. Finally, the issue of treatment capacity at the hospital's outpatient infusion clinic may have a decisive impact on the choice.

From a medical standpoint, a much more problematic question is whether those already receiving treatment with Remicade with good results should switch to a much less costly biosimilar alternative. We would now strongly advise against this, as biosimilar is not synonymous with bioidentical and because, as of today, the consequences of such a change are uncertain. Loss of primary efficacy and antibody development with severe infusion reactions as possible adverse effects are not inconceivable. Because of a lack of documented efficacy and safety when switching between biosimilar medicines, an additional allocation of NOK 20 million has been set aside in the state budget for a clinical study in the fields of rheumatology, gastroenterology and dermatology. In our opinion, the natural consequence of this is that no patients with inflammatory bowel disease should switch to a biosimilar medicine before they have received an offer to participate in the planned treatment-switching study. Switching to a biosimilar medicine when Remicade has lost its efficacy, or adverse effects have occurred, is also highly problematic, since the same efficacy and adverse effect profile may be expected after the switch. On the other hand, switching to Remsima due to

lack of efficacy or adverse effects with Humira or Simponi is considered to be a viable alternative, where until now we have tried Remicade.

In summary, we believe that there is an absence of good documentation on the use of biosimilar medicines for ulcerative colitis and Crohn's disease. This creates uncertainty for decision-makers in national and international health policy and in medical communities. Unresolved questions about efficacy and safety are of great concern to the medical community, and new studies are needed to clarify this. Norwegian authorities have allocated tens of millions of kroner for this purpose, and it would have been advantageous to have such a clarification before the Norwegian Drug Procurement Cooperation announced its recommendations.

The decision as to when biosimilar medicines should be chosen now lies with the individual specialist and hospital administration, with the responsibility that this entails. In the absence of a common decision-making arena regarding the medical stance on switching, registers that can follow up patients, and initiation of a study that requires that patients on established treatment switch under close monitoring, it is our opinion that we specialists should lean towards a sceptical, conservative approach.

Bjørn Moum
bjorn.moum@medisin.uio.no
Knut E.A. Lundin

Bjørn Moum (born 1952) is a professor and senior consultant at the Department of Gastroenterology, Oslo University Hospital.
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Knut E.A. Lundin (born 1958) is an associate professor and senior consultant at Oslo University Hospital.
The author has completed the ICMJE form and declares the following conflicts of interest: He has received fees from Abbvie, MSD, Orion-Pharma, Hospira, TakedaNycomed, Meda, Regeneron and GlaxoSmithKline.

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