Government sponsored off label use – new frontiers for Avastin?

The on-going saga of Avastin and Lucentis for the treatment of neovascular age-related macular degeneration (wet-AMD) patients has recently taken an interesting new direction in Italy. New legislation has enabled AIFA to approve reimbursement for Avastin for off-label usage in the treatment of wet-AMD.

Both Avastin (bevacizumab) and Lucentis (ranibizumab) are anti–vascular endothelial growth factor (anti-VEGF). Avastin, marketed by Roche, is indicated predominately for cancer indications, whereas Lucentis, marketed by Novartis, is indicated for wet-AMD, one of the leading causes of blindness in the elderly. Both products have become mega blockbusters in their respective indications, even with Lucentis costing ten times more than Avastin in the treatment of wet-AMD. This price difference and the associated large budget impact of Lucentis in wet AMD has been a significant driver for a number of organisations to investigate if Avastin is as effective and safe as Lucentis (such as the CATT and IVAN trials). Roche has consistently argued that the safety profile of Avastin is not sufficiently robust to seek marketing authorisation, providing evidence of potential microbial contamination during syringe preparation from Avastin vials.

In May 2014, the Italian government approved a decree allowing off-label use of drugs. This decree is partly in response to an anti-trust investigation where Italy’s antitrust regulator fined Novartis and Roche €180m for allegedly colluding to prevent the use of Avastin as a treatment for wet AMD. The decree allows products to be reimbursed off-label if there is no valid alternative but also if a therapeutic alternative exists. The approval of off-label usage must be justified by national and international research showing its cost-effectiveness and suitability. Naturally, the decree caused a significant backlash, particularly from EFPIA and EUCOPE, which accused AIFA of infringing and undermining the European Union's marketing authorisation system.

Nevertheless, several Italian regions have formally asked AIFA to consider Avastin for reimbursement in wet-AMD in response to the new decree. AIFA’s Scientific and Technical Committee (CTS) agreed and gave positive approval for using Avastin in wet-AMD and on the 18th Feb, AIFA’s official decision approving reimbursement for wet-AMD was published in the Gazzetta Ufficiale.

So, what does this mean for the future? It is obvious that there will be an increase in Avastin use in wet-AMD, particularly in the regions that requested the AIFA review. If the budget impact of wet-AMD is significantly decreased, it will be interesting to see the extent to which regions will start to use this new legislation as an additional cost containment tool and which products will be the next ones considered for off-label reimbursement.

It is not only Italy that has expanded the reimbursement for off label drugs. The FDA authorized the off-label use of Avastin for wet AMD in 2008 and France has recently taken steps to allow the Temporary Recommendations for Use (RTU) to be issued to off-label treatments, even if an alternative therapy already exists. Also in the UK, 120 Clinical Commissioning Groups have recently petitioned the General Medical Council, the Department of Health and NHS England to allow them to use Avastin off-label. The CCGs complain there are barriers which are conspiring to stop prescription of Avastin, which could result in yearly saving of £102 million to the NHS.

It is interesting to note that the driving force behind implementation of these measure is coming from the local level budget holders, such as the regions in Italy and the CCGs in the UK, who appear to be convinced of the safety and efficacy and the potential savings that can be made. These measures are all part of a growing trend by governments and budget holders to utilise and reimburse medicines where effectiveness and safety has been clearly demonstrated, despite the lack of regulatory approval, if significant cost savings can be realised.

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We always welcome your thoughts and opinions on the topics raised here. Do contact us (Paul@remapconsulting.com, Tel: +41 79 963 10 59; Graham@remapconsulting.com, Tel: +44 741 594 6778) or share your thoughts with us on Twitter (@remapconsulting), where you can also find the latest news.