Letters

The Editorial Executive Committee welcomes letters, which should be less than 250 words. Before a decision to publish is made, letters which refer to a published article may be sent to the author for a response. Any letter may be sent to an expert for comment. Letters are usually published together with their responses or comments in the same issue. The Editorial Executive Committee screens out discourteous, inaccurate or libellous statements and sub-edits letters before publication. The Committee's decision on publication is final.

Biosimilars are not (bio)generics

Editor, – The Generic Medicines Industry Association wishes to comment on the editorial 'Biosimilars are not (bio)generics' (Aust Prescr 2009;32:146–7) by Professor McKinnon and Dr Lu.

The authors raise several key issues surrounding the important introduction of quality cost-effective 'biosimilars'. Many of the concerns raised are equally pertinent to the originator biologic reference products, and so are neither new nor unique to 'biosimilars'.

Of note, there exists a broad spectrum of 'biosimilar' medicines, ranging from small unglycosylated proteins (for example filgrastim) – which can be extremely well characterised – to much larger molecules (for example monoclonal antibodies) that currently are more difficult to characterise. Therefore, as with all pharmaceuticals, each product should be assessed on a case by case basis, and not be subject to conclusions based on broad generalisations.

It is critical to appreciate that very high levels of data are demanded by regulatory agencies for establishing the quality, safety and efficacy of all 'biosimilars'. These include product characterisation, comparative trials between the 'biosimilar' and the originator, and robust postmarketing surveillance plans.

It is well acknowledged that the Therapeutic Goods Administration is the competent authority to determine on every occasion whether these criteria are met, and there is no reason in the case of 'biosimilars' to believe or suggest otherwise.

Kate Lynch
Chief Executive Officer
Generic Medicines Industry Association

Professor R McKinnon and Dr C Lu, authors of the article, comment:

The comments by the Generic Medicines Industry Association are welcome and we generally endorse the views expressed. We would, however, note that the emphasis of our editorial was deliberately on contrasting biosimilars with generic products based on traditional small chemical entities, rather than on a detailed comparison of biosimilar approval processes with those relating to the approval of the originator biological reference products.

Flying and thromboembolism

Editor, – I refer to the article 'Flying and thromboembolism' (Aust Prescr 2009;32:148–50) and the patient's perspective on the same topic (Aust Prescr 2009;32:150–1).

I recall with relish the media exposure the 'economy class syndrome' had at the turn of the millennium and the impact this had on the airline industry in terms of seating standards and raising consumer awareness. The article revisited the relevance of both mechanical and chemical prophylaxis in different at-risk groups. However, it failed to address the more controversial issues about practical management of patients with treated venous thromboembolism – particularly with advice on mobilisation and flying – which was elegantly illustrated by the patient's perspective article.

Even with available research showing the benefits of early mobilisation in deep vein thrombosis with no significant risk in pulmonary embolism, there is still hesitation in the medical community in recommending continuing mobilisation in massive deep vein thrombosis, particularly those proximal to the femoral veins. Practical advice on flying and other activities after deep vein thrombosis should be addressed early in conjunction with patient handouts.

Ms Hannah Baird should be congratulated for her remarkable ability to manage her deep vein thrombosis in spite of the limited support she received. I wonder what would be the outcome if she was neither well-informed nor motivated to take charge of her condition.

Shyan Lii Goh
Orthopaedic registrar
Dubbo Base Hospital, NSW

Associate Professor Frank Firkin and Associate Professor Harshal Nandurkar, authors of the article, comment:

The purpose of the article was to discuss the relative degrees of risk conferred by in-flight and pre-existing medical factors. Prophylactic measures for patients at high risk, including those with a history of venous thrombosis, were discussed in the article.

The question of management of a patient with newly diagnosed venous thrombosis on therapy in relation to taking flights is a different issue. Dr Goh raises the issue of the extent to which early mobilisation confers risk despite administration of standard therapy for deep vein

thrombosis. Various factors may play a part, including physical limitations imposed by the impact of the thrombus on venous return, sequelae of pulmonary emboli and imaging results that raise concerns about thrombus stability.

More pertinent issues relate to the period in which there is an increased risk of venous thrombosis following the onset of deep vein thrombosis, amounting to many weeks, and thus delayed diagnosis and suboptimal therapy are disadvantageous. This enhanced risk is normally suppressed by appropriate treatment with low molecular weight heparin and warfarin, and regular monitoring to ensure the INR is maintained.

Editor, – In reference to the article 'Flying and thromboembolism' (Aust Prescr 2009;32:148–50), is there any place for rivaroxaban – currently only listed for major orthopaedic surgery – in high-risk long-haul flight patients? If so, at what dosage and for how long? These patients would previously have been offered subcutaneous low molecular weight heparin.

Mick Coward
Medical Adviser
The Travel Doctor – Traveller's Medical and Vaccination Centre
Adelaide

Associate Professor Frank Firkin and Associate Professor Harshal Nandurkar, authors of the article, comment:

There has been no official approval in Australia for low molecular weight heparin for prophylaxis in high-risk subjects on long-haul flights. Its use for this purpose is based on extrapolation from its proven efficacy in thromboembolism prophylaxis in major hip and knee joint surgery, when the venous thromboembolic risk is generally viewed as greater than that posed by a long-haul flight.

Oral rivaroxaban has been shown to be at least as effective as low molecular weight heparin for thromboembolism prophylaxis in major hip and knee joint surgery, and can be viewed as at least as effective for prophylaxis in long-haul flights, with the obvious advantage that it is an oral drug. However, this is a non-approved purpose as is the case with low molecular weight heparin. Prescribers should be aware of the risks associated with using rivaroxaban in patients with renal impairment or liver disease, and that other drugs may affect its metabolism. These issues are addressed in this issue of *Australian Prescriber* and in the August 2009 issue of RADAR (www.nps.org.au/nps_radar/rivaroxaban).

Editor, – I was staggered to read the article on 'Flying and thromboembolism' (Aust Prescr 2009;32:148–50) and not see the word 'pregnancy' mentioned once in the entire article.

I think this glaring omission needs to be corrected as there is too much evidence-based research confirming that pregnancy is associated with a significantly raised incidence of deep vein thrombosis on long-haul flights.

This article omits a significant group of travellers and sends incomplete messages to readers.

Richard Porter
Specialist Obstetrician
Sydney

Associate Professor Frank Firkin and Associate Professor Harshal Nandurkar, authors of the article, comment:

Increased levels of oestrogen are associated with increased thromboembolic risk during long-haul flights, as discussed in our article, and it is natural to consider this to apply to pregnancy.

It is, however, fundamental that guidance on managing risk factors be based on published evidence or consensus that can reasonably be accessed. In the case of pregnancy there are major publications that do not support an unequivocal assertion of an association with pregnancy in general.

In an article describing life-threatening venous thromboembolism manifested by pulmonary embolism after long-haul flights, there were no cases in pregnant women in contrast to a number of cases in women taking oral oestrogens.[1] In addition, the most recent American College of Obstetricians and Gynecologists Committee Opinion states there is a lack of evidence of increased venous thromboembolism risk in pregnant women.[2]

References

1. Lapostolle F, Surget V, Borron SW, Desmaizieres M, Sordelet D, Lapandry C, et al. Severe pulmonary embolism associated with air travel. N Engl J Med 2001;345:779-83.
2. American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 443: Air travel during pregnancy. Obstet Gynecol 2009;114:954-5.