Multiple Technology Appraisal (MTA)

Immunosuppressive therapy for kidney transplantation in adults (review of technology appraisal guidance 85)

Submission for Adoport® (tacrolimus)

Sandoz

Executive Summary

23rd July 2015

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1. Executive summary

- Adoport® (tacrolimus) is an immediate-release generic tacrolimus formulation containing tacrolimus monohydrate, which has the same approved indication as the originator product, Prograf®.[1-4]
- Adoport is indicated for the prophylaxis of transplant rejection in liver, kidney or heart allograft recipients and for the treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products.[3]
- Adoport has demonstrated bioequivalence to Prograf at the stricter 90–111% criteria set out by the European Medicines Agency (EMA) for all drug strengths based on data derived from healthy volunteers.[1]
- The pharmacokinetics and therapeutic drug monitoring of Adoport are similar to those of Prograf in renal transplant recipients (RTRs), with respect to:
  - Dosing requirements and adjustments, whether in patients:
    - Treated *de novo*[5-7]
    - Converted from Prograf[8]
  - The pharmacokinetic profile of subgroup populations, such as in those with diabetes, as shown by exploratory analyses[9]
  - Achieving and maintaining therapeutic blood concentrations in patients treated *de novo*[10]
  - Inter/intrapatient variability, which is common to both formulations in patients converted from Prograf to Adoport[11,12]
  - Predicting trough tacrolimus levels in *de novo* patients[7,13]
  - Requirements for therapeutic monitoring and patient management, including:
    - Area under the plasma concentration curve (AUC) to minimum plasma concentration (C_{min}) analyses. Even converting from Prograf may not warrant additional tacrolimus trough monitoring.[14]
- Efficacy of Adoport at a similar dose and exposure to Prograf in *de novo* patients shows:
  - Comparable results to those achieved with Prograf[10]
  - Comparable short-term rejection rates to those seen with Prograf[15,16]
  - Treatment can be initiated without compromising short-term kidney allograft outcomes.[7,13]
- Safety of Adoport at a similar dose and exposure to Prograf shows:

  - The risk of acute rejection and graft loss following conversion of Prograf to be similar to, and no greater than, the risk of remaining on Prograf, with numerous studies showing no or a smaller than 0.1% risk of rejection[11,12,17-19]
  - A consistent safety profile to that of Prograf.[14,20]
- The clinical experience of Adoport in *de novo* and stable conversion RTRs is supported by peer-reviewed papers, reviews and abstracts, many from authors from transplant centres in Europe and the USA.[5-31]
- Evidence presented demonstrates that, in addition to healthy volunteers, bioequivalence of Adoport to Prograf in RTRs is also shown.
- Healthcare professionals can use Adoport in the same manner in which they would have used Prograf, and switching from Prograf can be safely achieved with good communication and minimal additional monitoring.[11,14]
- Adoport provides cost savings compared with Prograf. Costs savings in terms of reduced drug acquisition and prescription costs can be achieved with the use of Adoport rather than with Prograf in *de novo* RTRs and in stable RTRs converted to Adoport from Prograf.[7,8,20,22,23,27,29] Studies evaluating cost savings specifically from the UK perspective have produced encouraging results:
  - Annual cost savings of £1.3 million were reported for 96 patients receiving a transplant (which included renal, pancreas and islet transplants) when converted to Adoport from Prograf[29]
  - The use of Adoport in 44 RTRs resulted in annual savings of £2,444 per patient when compared with costs incurred for 51 RTRs on Prograf, based on 2011 prices for both formulations.[7]
- A discounted hospital tender price for Adoport is available to all UK hospitals. The provision of this discount can help secondary care providers achieve greater cost savings at the drug procurement level.

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