How do you prepare and administer intravenous co-trimoxazole in fluid restricted patients?
Date prepared: 28th September 2011

Background

Patients requiring treatment with high doses of IV co-trimoxazole (e.g. for the treatment of *Pneumocystis jiroveci* (*P. carinii*) pneumonia) are often at risk of fluid overload when co-trimoxazole is diluted and infused in accordance with instructions in the summary of product characteristics (SPC). For example, treating *Pneumocystis jiroveci* in an adult patient in need of fluid restriction could result in the patient receiving in excess of 1.5 litres of fluid per day.

The Septrin brand of IV co-trimoxazole available in the UK contains propylene glycol, which easily precipitates out of solution when diluted (1,2,3). Therefore, careful management is required in ensuring product integrity without compromising on the fluid balance status of patients.

Answer

IV co-trimoxazole can be administered via a licensed or unlicensed route depending on the severity of the fluid restriction.

1. Licensed administration of co-trimoxazole when fluid restriction is required (1,2)
The SPCs provides instructions for dilution when fluid restriction is necessary. This is summarised in the table below.

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Septrin for Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufactured by</td>
<td>Laboratories Genopharm</td>
</tr>
<tr>
<td>Presentation</td>
<td>480mg/5ml ampoules</td>
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<tr>
<td>Posology &amp; method of administration</td>
<td>Dilute 5ml (1 ampoule) with 75ml of glucose 5%.</td>
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<td></td>
<td>The solution should be infused over a period not exceeding one hour.</td>
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<td></td>
<td>Infuse into a central line or a large peripheral vein</td>
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<tr>
<td>Minimum volume necessary to administer a dose of 120mg/kg to a 75kg adult</td>
<td>1425ml</td>
</tr>
<tr>
<td>Comments</td>
<td>Inspect for cloudiness at time of preparation and immediately before and during administration. Discard if there are any signs of particle formation. At this concentration, the resultant solution may appear clear to the naked eye but could exceed BP limits set for particulate matter in large volume parenterals.</td>
</tr>
</tbody>
</table>

Note: For some patients, administration of co-trimoxazole at these concentrations could still result in fluid overload.

Before selecting a suitable IV administration schedule, it might be valuable to consider whether IV therapy is really necessary – it is noted within the SPC that the intravenous route should only be used when the oral route is not practical or desirable (1). Also it is worth checking that the dose prescribed is appropriate in patients with impaired renal function – once creatinine clearance falls below 30ml/minute the dose of co-trimoxazole should be reduced (1,3,4).
2. Unlicensed administration of co-trimoxazole in strict fluid restriction

Administration through a central line: co-trimoxazole can be given as an undiluted solution by IV infusion through a central venous catheter via a syringe pump (2,5,6,7,8) over 90 minutes, but infusion may be prolonged to 2 to 3 hours if patients experience nausea (5). This route is usually only used in critical care areas. (2,5) This information is based on anecdotal reports that GSK is aware of, but for which they have no supportive published information (8).

Summary

IV administration of co-trimoxazole in fluid restricted patients may be given in one of the following ways based on individual patient circumstance:

1. Licensed recommendations:
   Dilute and infuse as per licensed recommendations for the particular brand of co-trimoxazole. Note however, this may still exceed the fluid requirements of patients under severe fluid restriction.

   GSK advise against diluting to lower than a 1 to 15 dilution as in-house data revealed significant precipitation with a 1 to 10 dilution (8).

2. Unlicensed recommendations:
   IV administration through a central line: infuse the undiluted solution via a syringe pump over 90 minutes. This may be increased to 2 to 3 hours in the event of the patient experiencing nausea. This route of administration is based on anecdotal reports that GSK is aware of, but is unable to support with any published references.

Limitations

Careful interpretation of data from American reference sources is required as GSK have advised of slight differences in formulation between Septra (US) and Septrin (UK). Cross-referencing information from various sources (e.g. Trissel) is not advised as many sources relate to formulations containing the excipients, diethanolamine and benzyl alcohol, which is not applicable to the current UK formulation (8).

References

2. Pharmacy Department. UCL Hospitals Injectable Medicines Administration Guide. 3rd edition. Blackwell Publishing
3. BNF 61 (March 2011). Accessed online via http://www.bnf.org.uk on 09/09/11
8. Written correspondence from Medical Information Advisor, GlaxoSmithKline UK. 13 July 2005 (and confirmed 05/01/2009)
Quality Assurance

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Search strategy (Sept 2011)
1. eMC http://www.emc.medicines.org.uk searched 09/09/2011
4. Micromedex (Drugdex). Date: 28/09/2011
4. Specialist Textbooks:
   a) BNF 61 accessed online 09/09/11
   b) UCL Hospitals Injectable Drug Guide 3rd Edition
   d) Guy’s & St Thomas Paediatric Formulary. 8th Edition
5. Manufacturer
6. Medline:
   1. *TRIMETHOPRIM-SULFAMETHOXAZOLE COMBINATION/; 1697 results.
   2. INJECTIONS, INTRAVENOUS/ OR INFUSIONS, INTRAVENOUS/; 116820 results.
   3. 1 AND 2; 40 results.
7. Embase:
   1. *COTRIMOXAZOLE/iv [iv=Intravenous Drug Administration]; 89 results.
   3. FLUID BALANCE/; 5942 results.
   4. 1 AND 3; 0 results.
   5. *COTRIMOXAZOLE/; 13066 results.
   6. 3 AND 5; 3 results.