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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

DELPRIM (trimethoprim), antibiotic

No clinical benefit demonstrated in the treatment of acute uncomplicated cystitis in women and adolescents.

Main points

- DELPRIM has Marketing Authorisation in the treatment of acute uncomplicated cystitis in women and adolescents, at the dosage of 300 mg/day for 3 days.
- The efficacy of trimethoprim, although poorly evaluated at this dosage, seems to be similar to that of alternative medicinal products. Data in adolescents are limited.
- DELPRIM is not indicated for use in empirical therapy.
- It is a new treatment option in case of documented infection with ESBL-producing E. coli, as an alternative to trimethoprim-sulfamethoxazole combination therapy and to a fluoroquinolone, prescription of which should be considered in case of more severe infections.

Therapeutic use

In the treatment of uncomplicated urinary tract infections in women and adolescents, antibiotic treatment is usually empirical. Single-dose fosfomycin-trometamol is recommended in first-line. Pivmecillinam for 5 days is an alternative. Prescription of a fluoroquinolone taken alone (ciprofloxacin or ofloxacin) or of nitrofurantoin for 5 days should not be considered until third-line.
In case of unfavourable progress (persistence of clinical symptoms after 3 days) or early recurrence within two weeks, after a UCT positive for ESBL-producing E. coli, it is possible to use, in addition to the antibiotics mentioned above and according to the data of the antibiogram, trimethoprim (TMP) or trimethoprim-sulfamethoxazole combination therapy for 3 days, as well as amoxicillin-clavulanic acid combination therapy for 5 to 7 days.

Role of the medicinal product in the therapeutic strategy

Although the risk of emergence of resistance to trimethoprim seems to be lower than that observed with fluoroquinolones, its use as an empirical treatment is not currently recommended due to uncertainties in the epidemiology of resistance to this antibiotic.

DELPRIM is a supplemental alternative for the treatment of uncomplicated urinary infections in case of unfavourable progress (persistence of clinical signs after 3 days) or early recurrence within two weeks. Its benefit is essentially in case of documented infection with ESBL-producing E. coli, as an alternative to trimethoprim-sulfamethoxazole combination therapy to reduce the risk of occurrence of adverse effects related to the use of sulfamide, and as an alternative to fluoroquinolones.

Clinical data

- In the treatment of uncomplicated acute cystitis in women and adolescents, trimethoprim seems to have an efficacy similar to that of antibiotics that can be used (fosfomycin-trometamol, fluoroquinolone and trimethoprim-sulfamethoxazole, in particular). However, the available studies are old studies and evaluated dosage regimens different from that currently recommended. No study has assessed the quantity of effect of trimethoprim at the dosage validated by the Marketing Authorisation, i.e. 300 mg/day in a single dose for 3 days.
- The most common adverse effects of trimethoprim were nausea, vomiting and gastralgia.

- Serious adverse effects were reported. There were haematological incidents (leukopenia, thrombocytopenia, megaloblastic anaemia) during prolonged- or high-dose therapy and in subjects with a pre-existing folate deficiency. Skin disorders (pruritus, maculopapular rash) not generally severe and, exceptionally, severe skin reactions (erythema multiforme, Lyell syndrome, Stevens-Johnson syndrome, fixed drug reaction) are also possible under trimethoprim.

Benefit of the medicinal product

- The actual clinical benefit* is substantial and justifies reimbursement by National Health Insurance.
- In view of:
  - the efficacy of trimethoprim, similar to that of antibiotics that may be used in the treatment of uncomplicated acute cystitis, and
  - the lack of data about the efficacy of the dose of 300 mg for 3 days versus clinically relevant comparators,

  DELPRIM 300 mg does not provide improvement of actual clinical benefit**(IACB V) in the treatment of uncomplicated acute cystitis of women and adolescents.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 22 June 2016 (CT-13148) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The improvement of actual clinical benefit (IACB) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of IACB on a scale from I (major) to IV (minor). A level V IACB (equivalent of “no IACB”) means "no clinical added value".