Translated from ***Rev Prescrire*** **July 2008; 28 (297): 500**

rivastigmine patches

LINE EXTENSION

No therapeutic advantage and less convenient than capsules

rivastigmine
(EXELON°)

Transdermal patches

4.6 mg/24 h (9 mg/patch)

9.5 mg/24 h (18 mg/patch)

NOT ACCEPTABLE

In April 2008 a new transdermal patch formulation of rivastigmine, a cholinesterase inhibitor, was added to the products marketed under the brand name Exelon° (Novartis) (1). The patches are only marketed for symptomatic treatment of *"mild to moderately severe Alzheimer's dementia"* (1). The capsules and oral solution are also approved for the treatment of dementia in patients with Parkinson's disease, but they have a negative risk-benefit balance (1,2).

A 24-week double-blind trial in 1195 patients compared rivastigmine patches (9.5 mg/24 h) versus rivastigmine patches (17.4 mg/24 h) versus rivastigmine capsules (12 mg/day) versus placebo patches. Validated scales were used to assess cognitive function, the physician's global clinical impression and the patient's ability to conduct activities of daily life. The 9.5 mg/24h patches were statistically more effective than the placebo patches but the benefit was modest at best and similar to that of the 12 mg/day capsules (3-5).

The main adverse effects observed in patients using the patches delivering 9.5 mg/24h were skin reactions at the application site, gastrointestinal disorders (nausea, vomiting, loss of appetite, diarrhoea), neuropsychiatric disorders (headache, syncope, anxiety, depression), bradycardia, and even death (1,3,4). Nausea was more frequent with the capsules than with the patches delivering 9.5 mg/24 h (23% versus 6.2%) as was vomiting (17% versus 6.2%) (1,3,4). The 12 mg/day dose is the maximum oral dose, and there might be less difference in the incidence of adverse effects with an oral dose of 6 or 9 mg/day (**a**)(1).

The CHMP did not approve the patches delivering 17.4 mg/24h, due to a negative risk-benefit balance (3).

According to the summary of product characteristics (SPC), the doses to be used with the transdermal patches differ from those with capsules or oral solution (1). Details concerning dose equivalents when switching from oral to patch administration are provided in the summary of product characteristics (1).

Patches are less convenient to use than capsules. They must be changed every day and applied to the upper arm, chest or back, on a hairless area. Application to *"the exact same skin location within 14 days should be avoided to minimise the potential risk of skin irritation"* (1).

Rivastigmine, similarly to other cholinesterase inhibitors, has only limited and transient benefits in the treatment of mild to moderate forms of Alzheimer's disease (6). In summary, rivastigmine patches provide no practical advantages over rivastigmine capsules. It is therefore better to avoid using them.

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a- The French Transparency committee that assesses the medical benefits of new drugs and advises on drug reimbursement concluded that the patches provided "no therapeutic advantage" compared to capsules and oral solution (ref 5).

Selected references from Prescrire's literature search.

1- European Commission "SPC-Exelon" 17 September 2007: 83 pages.

2- Prescrire Editorial Staff "Rivastigmine" *Prescrire Int* 2007; **16** (88): 66.

3- EMEA - CHMP "EPAR Exelon (rev. 16) - Scientific discussion" 17 September 2007: 19 pages.

4- Winblad B et al. "A six-month double-blind, randomized, placebo-controlled study of a patch in Alzheimer's disease-Rivastigmine patch versus capsule" *Int J Geriatr Psychiatry* 2007; **22**: 456-467.

5- HAS - Commission de la transparence "Avis-Exelon dispositif transdermique" 5 December 2007: 11 pages.

6- Prescrire Rédaction "12-5. Patients ayant une maladie d'Alzheimer" *Rev Prescrire* 2007; **27** (290 suppl. interactions médicamenteuses).

PRESCRIRE'S RATINGS

Our judgement is based on the degree of therapeutic advance of the new product. It takes into account not only the inherent value of each product in terms of its risk-benefit balance, but also its advantages and disadvantages relative to existing products available in France. Note that the relative value of new products can vary from one country to another.

BRAVO: The product is a major therapeutic advance in an area where previously no treatment was available.

A REAL ADVANCE: The product is an important therapeutic innovation but has certain limitations.

OFFERS AN ADVANTAGE: The product has some value but does not fundamentally change the present therapeutic practice.

POSSIBLY HELPFUL: The product has minimal additional value, and should not change prescribing habits except in rare circumstances.

NOTHING NEW: The product may be a new substance but is superfluous because it does not add to the clinical possibilities offered by previous products available. In most cases it concerns a me-too product.

JUDGEMENT RESERVED: The editors postpone their rating until better data and a more thorough evaluation of the drug are available.

NOT ACCEPTABLE: Product without evident benefit but with potential or real disadvantages.

Quality of information from pharmaceutical companies

In response to our systematic requests

Company provided detailed information including unpublished data and packaging items.

Company provided information limited to administrative and published data.

Company provided minimal information, mainly administrative data.

Company provided no information.

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