Product Sheet of Exelon

Distinctive Name: Exelon.
Generic Name: Rivastigmine.
Pharmaceutical Form: Patch.
Formulation: Each patch contains Rivastigmine 9mg, 18mg, and 27mg. Vehicle qs > 1 patch.

Patch	Rivastigmine Dose	Rivastigmine Release Rate in 24 hours in vivo
Each 5 cm^2 patch	9 mg	4.6 mg
Each 10 cm^2 patch	18 mg	9.5 mg
Each 15 cm^2 patch	27 mg	13.3 mg

Therapeutic Indications:
Treatment of patients with:

- Mild to moderately severe dementia of the Alzheimer's type.
- Severe Alzheimer's dementia.
- Mild to moderately severe dementia associated with Parkinson's disease.

Pharmacokinetics:

- **Absorption:** Rivastigmine from Exelon patches is slowly absorbed. After the first dose, concentrations of the active ingredient in the plasma are detected with a delay of half an hour to an hour. Plasma concentrations then gradually increase to near maximum levels, usually after 8 hours, with the peak occurring between 10 and 16 hours. From this point, plasma concentrations decrease gently over the 24-hour application period. With repeated administration (at steady state), plasma concentrations decline slowly for an average of 40 minutes after replacing the previous patch with a new one, until the absorption rate of the active ingredient from the new patch surpasses the elimination rate, at which point concentrations rise again to reach a new peak around 8 hours. Rivastigmine is adequately released from the transdermal patch over the 24-hour application period, with approximately 50% of the drug load being released. The pharmacokinetic profile of rivastigmine transdermal patches is comparable in patients with Alzheimer's disease and those with dementia associated with Parkinson's disease.
- **Distribution:** Rivastigmine moderately binds to plasma proteins (approximately 40%). It easily crosses the blood-brain barrier and has an apparent volume of distribution of 1.8 to 2.7 L/kg.
- **Metabolism:** Rivastigmine is rapidly and extensively metabolized with an apparent plasma elimination half-life of approximately 3.4 hours after patch removal.

- **Elimination:** Trace amounts of unchanged rivastigmine are found in urine; renal excretion of metabolites is the primary route of elimination. Following the administration of 14C-rivastigmine, renal elimination over 24 hours is rapid and virtually complete (> 90%). Less than 1% of the administered dose is excreted in feces.

Geriatric Patients:
Age does not affect rivastigmine exposure in Alzheimer's patients treated with Exelon patches.

Contraindications:
The use of Exelon is contraindicated in patients with:

- Known hypersensitivity to rivastigmine, other carbamate derivatives, or the excipients in the formulation (Vitamin E, poly(butylmethacrylate-co-methylmethacrylate), acrylic copolymer, silicone oil).
- History of reactions at the site of application of a rivastigmine transdermal patch indicative of allergic contact dermatitis (see GENERAL PRECAUTIONS - Skin reactions at the application site).

Adverse Reactions:
Nausea and vomiting were the most frequently observed adverse events among patients treated with the active ingredient.

Drug and Other Interactions:
No specific interaction studies have been conducted with Exelon patches. Hydrolysis by esterases is the primary metabolic pathway for Rivastigmine. The major cytochrome P450 isoforms barely metabolize the active ingredient; therefore, pharmacokinetic interactions with other drug substrates of these enzymes are not expected.

Dosage and Administration:

- **Mild to moderately severe dementia of the Alzheimer's type.**
- **Severe Alzheimer's dementia:** Initial dose and dosage adjustment to achieve an effective dose: Treatment is initiated with one 5 cm² Exelon patch once daily. Subsequently, the dose should be increased to a 10 cm² Exelon patch, and then a 15 cm² Exelon patch, which is the demonstrated effective dose. These dose increases will always depend on the adequate tolerability of the previous patch and will only be made after a minimum therapeutic period of four weeks with the previous patch.
- **Mild to moderately severe dementia associated with Parkinson's disease:** Initial dose and dosage adjustment to achieve an effective dose: Treatment is initiated with one 5 cm² Exelon patch once daily. After a minimum of four weeks of treatment and if the dose is well tolerated, the 10 cm² Exelon patch can be administered, which is the recommended effective dose and can be administered as long as it provides therapeutic benefit to the patient. The response to Rivastigmine varies according to the individual; some patients may obtain greater benefits with higher doses. The subsequent administration of the 15 cm² patch will

always depend on the adequate tolerability of the previous patch dose and will only be made after a minimum therapeutic period of four weeks with each pharmaceutical dose.

Treatment Discontinuation:
If gastrointestinal adverse reactions or a worsening of existing conditions (e.g., tremors) are observed, treatment should be temporarily discontinued until these effects disappear. If treatment with a patch has been interrupted for more than three days, it can be resumed at the same dose. Otherwise, it should be resumed with the 5 cm² Exelon patch. If adverse effects persist upon restarting treatment, the dose should be reduced to the previous tolerated dose.

Administration Instructions:
Exelon patches should be applied once daily to healthy, hairless, dry, clean skin on the upper or lower back, upper arm, or chest, avoiding areas where tight clothing may rub. The patch should be replaced with a new one after 24 hours.

Important Administration Instructions (Patients and caregivers must be instructed):

- The previous day's patch should be removed before applying a new one.
- The patch should be replaced with a new one after 24 hours. Only one patch should be applied at a time.
- The patch should not be applied to red, irritated, or wounded skin. It is recommended to change the application site daily to avoid irritation, although consecutive patches can be applied to the same general area (e.g., another location on the upper back).
- Press the patch firmly with the palm of the hand until the edges adhere perfectly for at least 30 seconds.
- If the patch comes off, apply a new one until the end of the day, then replace it the next day at the usual time.
- The patch can be used in any daily situation, including bathing and in hot weather.
- Do not expose the patch to any external heat source (e.g., intense sunlight, saunas, tanning beds) for long periods.
- Do not cut the patch into pieces.
- Wash hands with soap and water after removing the patch. In case of contact with the eyes, or if eyes become red after handling the patch, rinse immediately with plenty of water and consult a doctor if symptoms persist.

Presentations:
Box with 30 patches of 5cm². Box with 30 patches of 10cm² and 15cm².

Storage Recommendations:
Store at no more than 25°C. Keep the box tightly closed.

Protective Legends:
Do not administer to individuals under 18 years old. Do not administer during pregnancy and lactation. Keep out of reach of children. Sale requires a prescription. Literature is for physicians only.

Customer Profile Questions:

1. Do you regularly treat patients with Alzheimer's or Parkinson's disease-associated dementia?
2. Have you used transdermal treatments for dementia before?
3. How important is ease of use and patient convenience in your treatment choice?
4. How do you value the controlled release profile of medications in the treatment of dementia?
5. Have you encountered challenges with gastrointestinal side effects in oral treatments for dementia?
6. Is adherence to treatment a common challenge in your dementia patients?

Frequently Asked Questions:

1.- What is the mechanism of action of Exelon?
It has a dual mechanism that inhibits acetylcholinesterase and butyrylcholinesterase.

2.- How does your treatment help my patient and their caregiver?
Exelon demonstrated significant functional, cognitive, and behavioral improvements, leading to a better quality of life for the patient and caregiver.

3.- Do you have any evidence or studies showing a delay in cognitive decline with your treatment?
Yes, Dr. Martínez, it is demonstrated that patients who remain on Rivastigmine treatment for up to 5 years have less cognitive decline. As shown in this graph (show and explain AV S6), you can see the scores of treated and untreated patients with Exelon in the Mini-Mental State Examination test.

4.- My patients have excellent results with Donepezil, I see no reason to change their treatment.
Dr. Martínez, Donepezil is an excellent medication; however, Donepezil does not have a patch formulation, and the oral formulation is more challenging to administer, which can lead to a high dropout rate. Exelon inhibits acetylcholinesterase and, unlike Donepezil, also inhibits butyrylcholinesterase.

5.- As you know, my patients are on multiple medications. Does your treatment have any restrictions?
Dr. Exelon is a safe treatment for patients on multiple medications, thanks to its patch formulation that avoids liver metabolism. It has a low risk of drug interactions, as seen in this table (show AV S12). Its use is safe with medications for diabetes mellitus, antacids, and anti-ulcer drugs, benzodiazepines, analgesics, and non-steroidal anti-inflammatory drugs, antidepressants, and cardiovascular medications.

6.- What common side effects does your treatment have?
Typical gastrointestinal reactions of this therapeutic class include nausea, diarrhea, vomiting, and headache.

7.- I prefer Galantamine; my experience with its dual mechanism of action has been excellent.
Dr., Galantamine is only available orally, making administration more challenging, and it has the potential for more drug interactions than Exelon. Furthermore, the transdermal patch gives Exelon the unique feature of providing a visual reminder, giving the caregiver confidence that the medication has been administered and preventing forgetfulness.

8.- The price of Exelon is very high; both Donepezil and Galantamine have excellent prices.
Dr., I understand your point, but I can assure you that your patients and their caregivers will be very grateful for providing them with the most modern, innovative, safe, and convenient treatment for Alzheimer's disease. It is easy to administer, has few side effects, and shows significant and demonstrable results. We also have a Patient Support Program called Caminando Juntos, which also attends to caregivers, offering educational materials, psychological support for patients and caregivers, and access to exclusive discounts. The Caminando Juntos Program also includes a purchase reminder and free home delivery, resulting in proper patient adherence to treatment.

9.- I know your program, but my patients complain about the complicated registration process.
Dr., I understand perfectly; we now have the possibility to register for the program by phone and online, providing only basic prescription information. I remind you that it is important for your patients and/or caregivers to have it on hand. In some offices I visit, assistants are helping a lot with this process. Dr., I will be happy to leave you these program cards where you can find the registration phone number, the website, and a QR code that, when scanned, directs you directly to the registration page to confirm the patient's virtual card number. The program's affiliated distributors are also listed.

10.- How does the absorption of the Exelon patch work?
Rivastigmine from Exelon patches is slowly absorbed. After the first dose, plasma concentrations of the active ingredient are detected with a delay of half an hour to an hour, then plasma concentrations gradually increase to near maximum levels, usually after 8 hours, and the maximum value is reached between 10 and 16 hours. From that point, plasma concentrations decrease gently over the 24-hour application period.

11.- What presentations does Exelon have?

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12.- How is the patch administered and where should it be applied?
The administration route of Exelon patches is transdermal, and they should be applied once daily to healthy, hairless, dry, clean skin in the following areas: upper left or right arm, left or right side of the chest, upper left or right back, lower left or right back. Avoid areas where tight clothing may rub. The patch should be replaced with a new one after 24 hours.

13.- What is the recommended dose?
Dr., the recommended dose for mild to moderately severe dementia of the Alzheimer's type and mild to moderately severe dementia associated with Parkinson's disease is to start with a 9mg patch every 24 hours. After a minimum of four weeks of treatment, if the dose is well tolerated, the 18mg patch can be administered, which is the recommended effective dose. However, some patients may benefit from higher doses, such as the 27mg patch, whose administration will depend on the adequate tolerability of the previous patch dose and will only be made after a minimum therapeutic period of four weeks with each pharmaceutical dose.

14.- What are the most important recommendations for administering Exelon patches?
Before applying a new patch, the previous day's patch should be removed. The patch should be replaced with a new one after 24 hours. Only one patch should be applied at a time. The patch should not be applied to red, irritated, or wounded skin. It is recommended to change the application site daily to avoid irritation, although consecutive patches can be applied to the same general area (e.g., another location on the upper back). Press the patch firmly with the palm of the hand until the edges adhere perfectly for at least 30 seconds. If the patch comes off, a new one should be applied until the end of the day. The patch can be used in any daily situation, including bathing and in hot weather. The patch should not be exposed to any external heat source (intense sunlight, saunas, tanning beds) for long periods. The patch should not be cut into pieces. Hands should be washed with soap and water after removing the patch.

15.- What are the contraindications for the Exelon patch?
Dr., the use of Exelon is contraindicated in patients with known hypersensitivity to Rivastigmine, other carbamate derivatives, or the excipients in the formulation, and in patients with a history of reactions at the application site of a Rivastigmine transdermal patch indicative of allergic contact dermatitis.