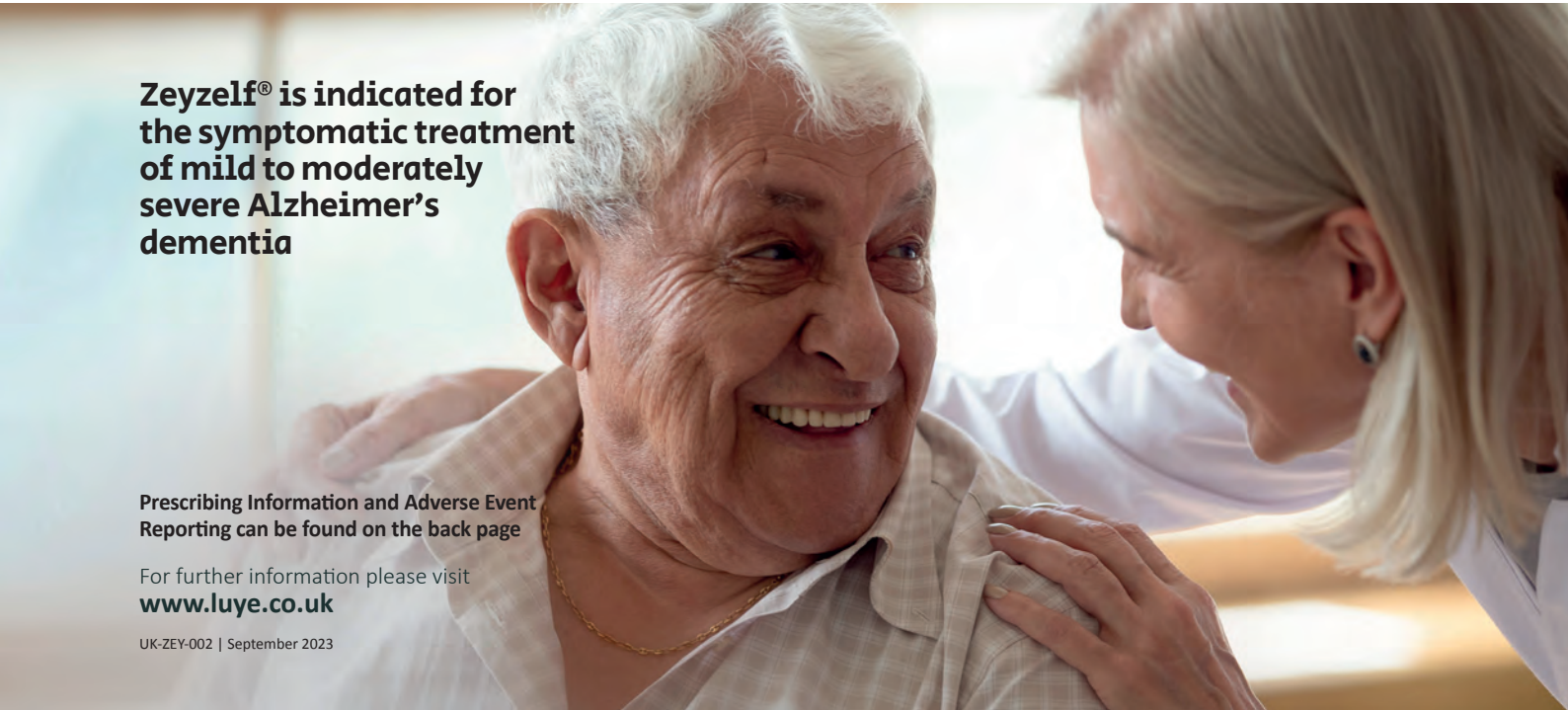
Zeyzelf®
rivastigmine transdermal patch

Luye Pharma

New Zeyzelf® rivastigmine twice weekly transdermal patch



Zeyzelf® is indicated for the symptomatic treatment of mild to moderately severe Alzheimer's dementia

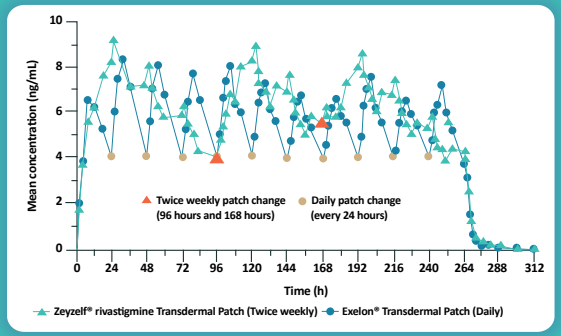
Prescribing Information and Adverse Event Reporting can be found on the back page

For further information please visit
www.luye.co.uk

UK-ZEY-002 | September 2023

Introducing Zeyzelf® rivastigmine twice weekly transdermal patch

Zeyzelf®(twice weekly) is bioequivalent to the originator Exelon (daily) transdermal patch.[1]



Adapted from Schurad B et al.

Rivastigmine mean plasma concentrations over time

Image not to scale

Zeyzelf® is a translucent polymer matrix patch designed to allow release of rivastigmine for up to 4 days.

The only twice weekly rivastigmine transdermal patch

By establishing fixed days for patch changes, for example Monday and Friday, this will help the patient and caregiver to maintain adherence.[2]

	Mon	Tue	Wed	Thur	Fri	Sat	Sun
Zeyzelf® twice weekly Transdermal Patch	■				■		
Exelon daily Transdermal Patch	●	●	●	●	●	●	●

Schematic representation of patch application

Initial dose
Treatment is started with 4.6 mg/24 h.

Maintenance dose
After a minimum of four weeks of treatment and if well tolerated according to the treating physician, the dose of 4.6 mg/24 h should be increased to 9.5 mg/24 h, the daily recommended effective dose, which should be continued for as long as the patient continues to demonstrate therapeutic benefit.

The advantages of transdermal delivery

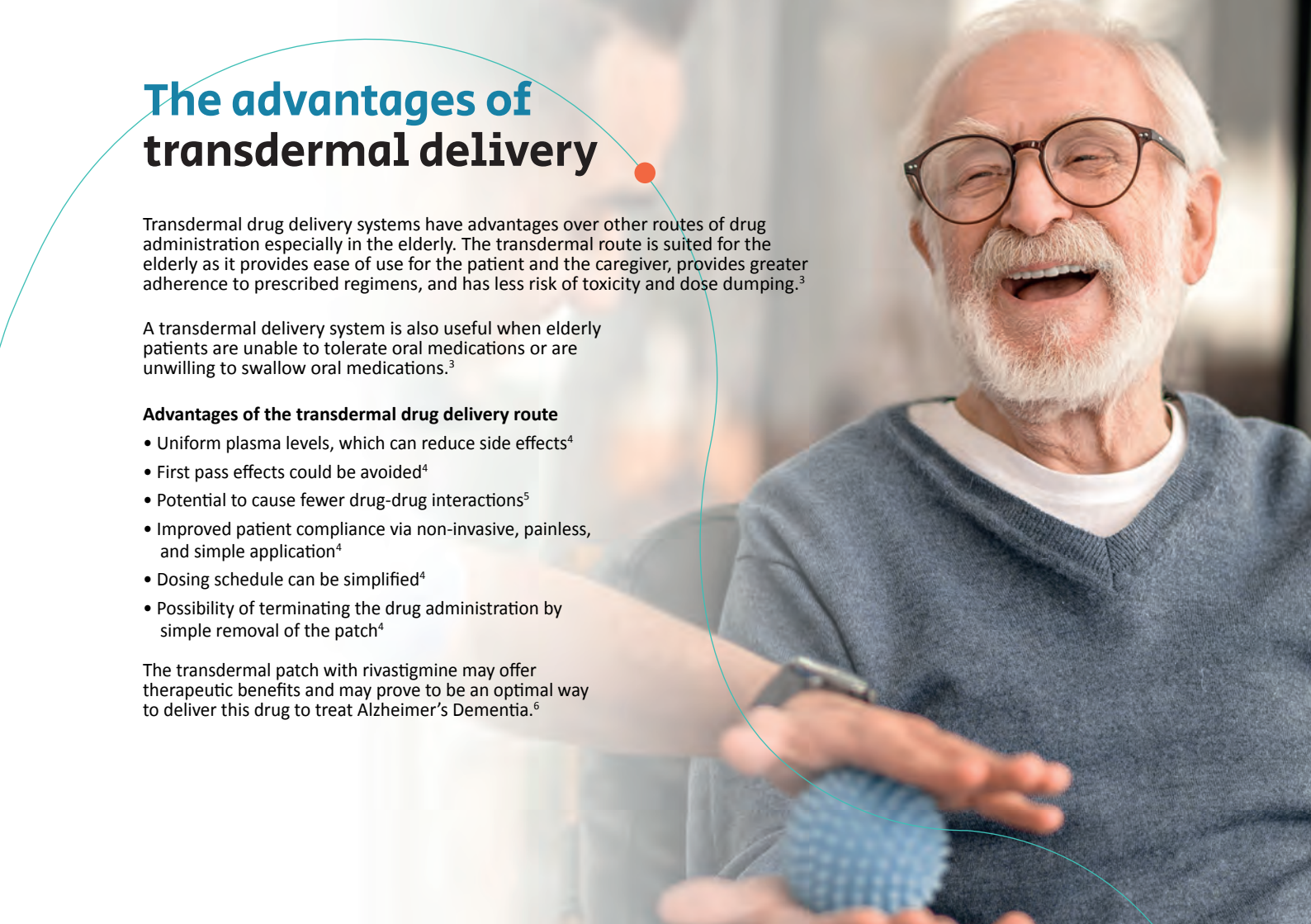
Transdermal drug delivery systems have advantages over other routes of drug administration especially in the elderly. The transdermal route is suited for the elderly as it provides ease of use for the patient and the caregiver, provides greater adherence to prescribed regimens, and has less risk of toxicity and dose dumping.[3]

A transdermal delivery system is also useful when elderly patients are unable to tolerate oral medications or are unwilling to swallow oral medications.[3]

Advantages of the transdermal drug delivery route

- Uniform plasma levels, which can reduce side effects[4]
- First pass effects could be avoided[4]
- Potential to cause fewer drug-drug interactions[5]
- Improved patient compliance via non-invasive, painless, and simple application[4]
- Dosing schedule can be simplified[4]
- Possibility of terminating the drug administration by simple removal of the patch[4]

The transdermal patch with rivastigmine may offer therapeutic benefits and may prove to be an optimal way to deliver this drug to treat Alzheimer's Dementia.[6]



The importance of adhesion

Skin adhesion is one of the most important functional properties for a transdermal patch and is critical to the safety, efficacy and quality of the patch.[7]

Poor adhesion results in improper dosing of patients and may result in additional patches having to be used and consume additional carer and Health Care Professional time.[7]

In a study comparing the twice weekly Zeyzelf® patch and Exelon daily patch, Zeyzelf® showed better adhesion properties than the Exelon daily patch despite the longer dosing intervals.[1]

Almost 95% of Zeyzelf® assessments showed adhesion ≥ 90% and there were no cases of complete patch detachments.[1]

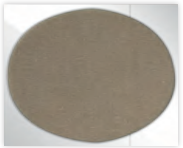
	% of assessments showing adhesion ≥ 90% adherence
Zeyzelf® twice weekly transdermal patch	94.83%
Exelon daily transdermal patch	66.77%

The EMA Guideline defines satisfactory adhesion as ≥ 90% of area that remained adhered at assessment. Assessments were taken 24h post application of the patches.[8]

Zeyzelf® delivers adhesion you can trust

Active patch

Adhesive cover



Images not to scale

The Zeyzelf® twice weekly patch with its adhesive cover provides security with peace of mind for the patients and their caregivers.

The impact on caregivers

Patient and caregiver satisfaction are essential for good adherence to treatment.[9]

Alzheimer's dementia, like other dementias, generates a significant burden on family members and/or caregivers.[10]

1 in 3 people will care for someone with dementia in their lifetime.[11]

Family caregivers of people with Alzheimer's and related dementias are at greater risk for anxiety, depression, and poorer quality of life than caregivers of people with other conditions.[12]

Unpaid carers, or families and friends providing care to their loved ones, are providing care to a value of **£13.9 billion** a year.[13]

This will increase to **£35.7 billion** by 2040.[13]

In 2021 **700,000** unpaid carers provided 1.3 billion hours of unpaid care to those with dementia.[14]

It's not the cost of the drug but what it can save

The cost of dementia to the UK is currently £34.7 billion a year, which works out as an average annual cost of £32,250 per person with dementia. Two-thirds of this cost is currently being paid by people with dementia and their families, either in unpaid care or in paying for private social care.[15]

Reducing carer burden and time is essential, the cost of the drug prescription represents a very small proportion of the overall annual cost of dementia.

Zeyzelf® twice weekly provides a considerable cost saving compared to the daily transdermal patch Exelon, with >50% cost savings.[16]

	NHS List Price for 28 days treatment (£)		NHS Saving
Product	Zeyzelf twice weekly transdermal patch 8 patches	Exelon daily transdermal patch 28 patches	
4.6mg/24 hr	35.09	72.77	52%
9.5 mg/24 hr	35.09	72.77	52%

* A pack of Exelon transdermal patches contains 30 patches and costs £77.97

Zeyzelf®

Zeyzelf (rivastigmine) twice weekly transdermal patches.
Abbreviated Prescribing Information.
Please refer to the Zeyzelf Summary of Product Characteristics (SmPC) for full details.
Presentations: Transdermal patches each releasing either 4.6 mg or 9.5mg of rivastigmine per 24 hours. **Indication:** Symptomatic treatment of mild to moderately severe Alzheimer's dementia. **Dosage and administration:** Zeyzelf twice weekly transdermal patches should be applied twice weekly on fixed days (after four and three days, respectively). Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer's dementia. Similar to any treatment initiated in patients with dementia, therapy with rivastigmine should only be started if a caregiver is available to regularly administer and monitor the treatment. Dosage: *Initial dose:* Treatment is started with 4.6 mg/24 h. *Maintenance dose:* After a minimum of four weeks of treatment and if well tolerated according to the treating physician, the dose of 4.6 mg/24 h should be increased to 9.5 mg/24 h, the daily recommended effective dose, which should be continued for as long as the patient continues to demonstrate therapeutic benefit. *Dose escalation:* 9.5 mg/24 h is the recommended daily effective dose which should be continued for as long as the patient continues to demonstrate therapeutic benefit. If well tolerated and only after a minimum of six months of treatment at 9.5 mg/24 h, the treating physician may consider increasing the dose to 13.3 mg/24 h in patients who have demonstrated a meaningful cognitive deterioration while on the recommended daily effective dose of 9.5 mg/24 h. The 13.3 mg/24 h dose strength cannot be achieved with Zeyzelf twice weekly. Treatment should be temporarily interrupted if gastrointestinal adverse reactions are observed until these adverse reactions resolve. Transdermal patch treatment can be resumed at the same dose if treatment is not interrupted for more than three days. Otherwise treatment should be re-initiated with 4.6 mg/24 h. *Switching from capsules or oral solution to transdermal patches:* Refer to SmPC. **Special populations:** Patients with body weight below 50 kg: Particular caution should be exercised in titrating patients with body weight below 50 kg above the recommended effective dose of 9.5mg/24 h. Hepatic impairment: In mild to moderate hepatic impairment dosing recommendations to titrate according to individual tolerability should be closely followed. Patients with clinically significant hepatic impairment may experience more dose-dependent adverse reactions. have not been studied. Particular caution should be exercised in titrating patients with severe hepatic impairment. Renal impairment: No dose adjustment is necessary for patients with renal impairment. **Method of administration:** Zeyzelf twice weekly is for transdermal use. Transdermal patches should be applied twice weekly on fixed days (after four and three days, respectively) to clean, dry, hairless, intact healthy skin on the upper or lower back, upper arm or chest, in a place which will not be rubbed by tight clothing. It is not recommended to apply the transdermal patch to the thigh or to the abdomen due to decreased bioavailability of rivastigmine observed when the transdermal patch is applied to these areas of the body. The transdermal patch should not be applied to skin that is red, irritated or cut. Reapplication to the exact same skin location within 14 days should be avoided to minimise the potential risk of skin irritation. To prevent interference with the adhesive properties of the transdermal patch, no cream, lotion or powder should be applied to the skin area where the medicinal product is to be applied. **Patients and caregivers should be instructed on important administration instructions:** Refer to SmPC. **Common Adverse Reactions:** Application site skin reactions (usually mild to moderate application site erythema) are the most frequent adverse reactions observed with the use of rivastigmine transdermal patch. The next most common adverse reactions are gastrointestinal in nature including nausea and vomiting. List of common adverse reactions reported in 1,670 patients with Alzheimer's dementia treated in randomised, double-blind, placebo and active-controlled clinical studies with rivastigmine transdermal patches for a duration of 24-48 weeks and from post-marketing data: Urinary tract infection. Anorexia, decreased appetite Anxiety, depression, delirium, agitation. Headache, syncope, dizziness. Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain. Rash. Urinary incontinence. Application site skin reactions (application site erythema, pruritus, oedema, dermatitis, irritation), asthenic conditions (e.g. fatigue, asthenia), pyrexia, weight decreased. **Please consult the full SmPC for other adverse reactions. Contraindications:** Hypersensitivity to the active substance rivastigmine, to other carbamate derivatives or to any other excipients. Previous history of application site reactions suggestive of allergic contact dermatitis with rivastigmine patch. **Warnings and Precautions:** Zeyzelf twice weekly transdermal patches are multiday patches. Care should be exercised and application of more than one patch at the same time should be avoided. The incidence and severity of adverse reactions generally increase with increasing doses, particularly at dose changes. If treatment is interrupted for more than three days, it should be re-initiated with 4.6 mg/24 h. *Misuse of the medicinal product and dosing errors resulting in overdose:* Misuse of the medicinal product and dosing errors with rivastigmine transdermal patch have resulted in serious adverse reactions; some cases have required hospitalisation, and rarely led to death. Patients and their caregivers must be instructed on important administration instructions for rivastigmine transdermal patch. *Gastrointestinal disorders:* Gastrointestinal disorders such as nausea, vomiting and diarrhoea are dose related, and may occur when initiating treatment and/or increasing the dose. These adverse reactions occur more commonly in women. *Weight loss:* Patients with Alzheimer's disease may lose weight whilst taking cholinesterase inhibitors, including rivastigmine. The patient's weight should be monitored during therapy. *Bradycardia:* Rivastigmine may cause bradycardia which constitutes a risk factor in the occurrence of torsade de pointes, predominantly in patients with risk factors. *Care must be taken when prescribing Zeyzelf twice weekly transdermal patches to patients* with sick sinus syndrome or conduction defects (sino-atrial block, atrio-ventricular block); patients with active gastric or duodenal ulcers or patients predisposed to these conditions because rivastigmine may cause increased gastric secretions; patients predisposed to urinary obstruction and seizures because cholinomimetics may induce or exacerbate these diseases; patients with a history of asthma or obstructive pulmonary disease. *Skin application site reactions:* Skin application site reactions may occur with rivastigmine patch and are usually mild or moderate in intensity. Patients and caregivers should be instructed accordingly. These reactions are not in themselves an indication of sensitisation. However, use of rivastigmine patch may lead to allergic contact dermatitis. In these cases, treatment should be discontinued. It is possible that some patients sensitised to rivastigmine by exposure to rivastigmine patch may not be able to take rivastigmine in any form. There have been rare post-marketing reports of patients experiencing allergic dermatitis (disseminated) when administered rivastigmine irrespective of the route of administration (oral, transdermal). In these cases, treatment should be discontinued. **Other warnings and precautions:** Rivastigmine may exacerbate or induce extrapyramidal symptoms. Contact with the eyes should be avoided after handling Zeyzelf twice weekly transdermal patches. Hands should be washed with soap and water after removing the patch. In case of contact with eyes or if the eyes become red after handling the patch, rinse immediately with plenty of water and seek medical advice if symptoms do not resolve. **Interactions: Refer to the SmPC for full details.** Rivastigmine may exaggerate the effects of succinylcholine-type muscle relaxants during anaesthesia. Caution is recommended when selecting anaesthetic agents. Possible dose adjustments or temporarily stopping treatment can be considered if needed. Rivastigmine should not be given concomitantly with other cholinomimetic substances. Rivastigmine might interfere with the activity of anticholinergic medicinal products (e.g. oxybutynin, tolterodine). Caution should be exercised when rivastigmine is combined with beta-blockers and other bradycardia medicinal products (e.g.class III antiarrhythmic medicinal products, calcium channel antagonists, digitalis glycoside, pilocarpin). The combination of rivastigmine with torsades de pointes-inducing medicinal products should be observed with caution and clinical monitoring (ECG) may also be required. **Effects on ability to drive and use machines:** Alzheimer's disease may cause gradual impairment of driving performance or compromise the ability to use machines.

Marketing Authorisation Number and Basic NHS Price:
Zeyzelf twice weekly 4.6 mg/24 h transdermal patch PLGB 50827/0023
(8 patches: £35.09);
Zeyzelf twice weekly 9.5 mg/24 h transdermal patch PLGB 50827/0024
(8 patches: £35.09).

Marketing Authorisation Holder: Luye Pharma Ltd. 40 Occam Road, Guildford, GU2 7YG, United Kingdom. Legal Category: POM. Further information: Luye Pharma Ltd., 40 Occam Road, Guildford, GU2 7YG.

Further information: info@luyepharma.co.uk.

Date of preparation: August 2023.

Item number: UKZey001Vers1.0

References
1. Schurad B et al. Current Alzheimer Research, 2022, 19, 541-553.
2. Zeyzelf® rivastigmine transdermal patch, Summary of Product Characteristics, Luye Pharma Ltd. September 2023.
3. Vadivelu N, Hines R L. Clin Interv Aging, 2008 Sep; 3(3): 421–430.
4. Sozio P et al. Neuropsychiatr Dis Treat. 2012;8:361-8.
5. Grossberg G et al. Int J Geriatr Psychiatry. 2000 Mar;15(3):242-7.
6. Winblad B et al. Randomized Controlled Trial. Neurology. 2007 Jul 24;69 (4 Suppl 1):S14-22.
7. Wokovich A M et al. Eur J Pharm Biopharm. 2006 Aug;64(1):1-8.
8. EMA. Guidelines on the pharmacokinetic and clinical evalution of modified release dosage forms. Available online at: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-pharmacokinetic-clinical-evaluation-modified-release-dosage-forms_en.pdf
9. Blesa R et al. Randomized Controlled Trial. Neurology. 2007 Jul 24;69 (4 Suppl 1):S23-8.
10. Burns A. Int J Neuropsychopharmacol. 2000 Jul;3(7):31-38.
11. NHS. Dementia. Available online at: https://www.england.nhs.uk/mental-health/dementia/ [Last accessed: August 2023]
12. CDC. For Caregivers, Family and Friends. Available online at: https://www.cdc.gov/aging/caregiving/alzheimer.htm [Last accessed: August 2023]
13. Alzheimer's Society. What are the costs of dementia care in the UK. Available online at: https://www.alzheimers.org.uk/about-us/policy-and-influencing/dementia-scale-impact-numbers [Last accessed: August 2023]
14. Herron D, Runacres J. Healthcare (Basel). 2023 Jul; 11(14): 1998.
15. Alzheimer's Society. How much does dementia care cost. Available online at: https://www.alzheimers.org.uk/blog/how-much-does-dementia-care-cost [Last accessed: September 2023]
16. NHSBSA Drug Tariff (England and Wales). September 2023

Adverse events should be reported.
Reporting forms and information can be found at: https://yellowcard.mhra.gov.uk/
Adverse events should also be reported to Luye Pharma Ltd at safety@luyepharma.co.uk