PHARMACY BULLETIN HOSPITAL KUALA PENYU

MANAGEMENT OF DEMENTIA

15 Aug 2023

Special points of interest:

- *Introduction*
- *Pathophysiology*
- *Risk Factors & Risk Reduction Strategies*
- *Treatment*
- *Counseling*

Inside this issue:

DEMENTIA– Alzheimer's Disease

Dementia is a syndrome in which cognitive function (i.e. ability to process thought) deteriorates progressively. It is not part of a normal ageing process. It affects memory, thinking, orientation, calculation, learning capacity, language, judgement, emotional control, social behaviour, or motivation.

However, consciousness is not affected. It is commonly associated with behavioural and psychological symptoms which can lead to increased dependency on caregivers and subsequent nursing home admission. The lack of awareness and understanding of dementia can lead to stigmatisation and, delay in diagnosis and care.

There are estimated 50 million People With Dementia (PWD) worldwide and 60% of them live in low- or middle-income countries. There are nearly 10 million new cases every year.

According to Alzheimer's disease International, the estimated number of PWD in Malaysia was 123,000 in 2015

Alzheimer's disease (AD) is the commonest type of dementia (60 - 70%), followed by vascular dementia (VaD), mixed dementia, frontotemporal dementia (FTD), Dementia with Lewy bodies (DLB), Parkinson's disease dementia (PDD) and others.

Patient is unable to remember the date or tell the time

Pathophysiology of Alzheimer's Disease (AD)

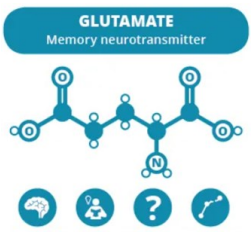
Neurotransmitter Involve in AD

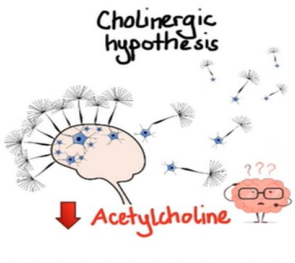
Acetylcholine: Principal neurotransmitter involved in thought, learning and memory, attention and enhancement of sensory perception upon waking.

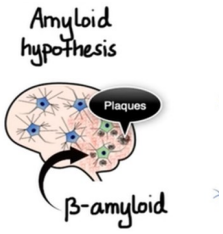
Reduction of acetylcholine in the brain has been linked with the memory deficits associated with Alzheimer's disease.

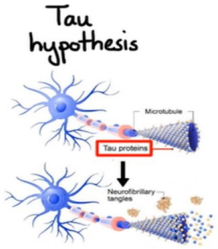
Glutamate: Involved in cognitive functions- learning and memory regulates and brain development

Glutamate is toxic to neurons in larger quantities. Too much Glutamate can destroy neurons.









Cholinergic Hypothesis:

Lost of central cholinergic neurons and deficiency of acetylcholine. Reduce memory and learning process

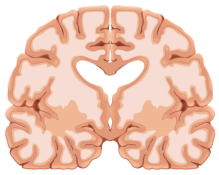
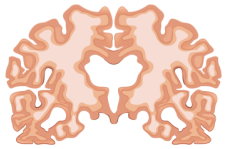
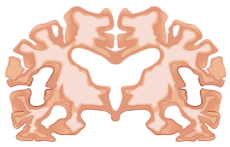
Amyloid Cascade Hypothesis:

Progressive accumulation of beta-amyloid along the microtubule. Triggers a complex cascade of events ending in neuronal cell death

Tau Hypothesis:

Excessive or abnormal phosphorylation of tau results in the transformation of PHF tau (paired helical filament). It cause aggregation of this protein along the neuron, blocking impulse

SEVERITY OF THE DISEASE

Mild	Cerebral cortex begins to shrink Difficulties with instrumental activities of daily living Symptoms ●First failures of memory, concentration and attention	
Moderate	Further shrinking of cerebral cortex. Difficulties with basic activities of daily living Symptoms ●Failure to execute simple movements	
Severe	Extreme shrinkage occurs in the brain. Fully dependent Symptoms ●Complete loss of memory and judgment Loss of sphincter control and immobility	

SIGNS & SYMPTOMS

Episodic Memory Impairment

Changes in Mood and Behaviour

Visual Impairment

Poor Speaking and Language

Risk Factors

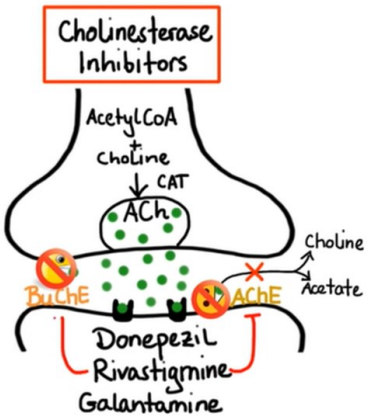
Non-Modifiable Risk Factor :

- Advancing age: age ≥ 65 years is a risk factor for any dementia
- Sex: Female has higher risk of dementia especially in AD
- Genetic: Amyloid β-protein precursor on chromosome 21, presenilin 1 on chromosome 14 and presenilin 2 on chromosome 1

Modifiable Risk Factor:

- Physical inactivity
- Psychiatric illness: late-life depression
- Excessive alcohol consumption
- Lifestyle: Smoking
- Low social participatation, less frequent social contact and more loneliness.

Pharmacological Treatment



Acetylcholinesterase Enzyme Inhibitors, AChEI such as Donpezil, Rivastigmine works by augmenting the levels of acetylcholine in the brain to compensate for the losses of cholinergic function. Additionally, Galantamine also modulates activity at nicotinic receptors. May improve, maintain or slow the decline of cognitive function.

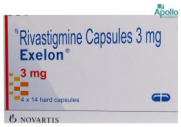
Donepezil

Dose & Frequency	Adjustment	Common adverse effects	Counseling Information/ contraindications
Dosing (mg/day): Initial: 5 mg once daily, may increase to 10 mg once daily after 4 - 6 weeks Max dose 10mg OD	Liver impairment: No dosage adjustment necessary Renal impairment: No dosage adjustment necessary	Diarrhoea, nausea, vomiting, insomnia, fatigue, drowsiness, chest pain, hypertension,	May impair ability to drive or operate machinery Contraindicated to donepezil hypersensitivity, piperidine derivates (haloperidol)

*Oral Donepezil strength: 5mg and 10mg tab
**Orodispersible Tab: 5mg and 10mg tab
Prescriber category: A

Rivastigmine Oral

Dose & Frequency	Adjustment	Common adverse effects	Counseling Information/ contraindications
Dosing: Initial: 1.5 mg twice daily; may increase by 3 mg daily every 2 weeks (based on tolerability). Maximum dose: 6 mg twice daily	Liver impairment: No dosage adjustment necessary Renal impairment: No dosage adjustment necessary	Nausea, vomiting, diarrhoea, dizziness, tremor, hypertension	May impair ability to drive or operate machinery Contraindicated to rivastigmine hypersensitivity, carbamate derivates (disulfiram)



**Oral rivastigmine strength:
1.5 & 3mg Cap
Prescriber category: A*

Rivastigmine TD Patch

Dose & Frequency	Adjustment	Common adverse effects	Counseling Information
Dose. Initial: Apply 4.6 mg/24 hours patch once daily. If well tolerated, may titrate (no sooner than every 4 weeks) to 9.5 mg/24 hours and then to 13.3mg/24 hours (maximum dose)	Liver impairment adjustment. Child-Pugh class A and B: Initial and maximum dose of 4.6mg/24hours. Child-Pugh class C: No dosage adjustment. No renal adjustment	Nausea, vomiting, dizziness, headache, falls, Local: Application site erythema (transdermal), tremor, Hypertension	May impair ability to drive or operate machinery Counsel pt on patch application

**TD rivastigmine patch strength:
4.6mg, 9.5mg,13.3mg/24hrs
Prescriber category: A*

*Available in HKP

**Not Available in HKP

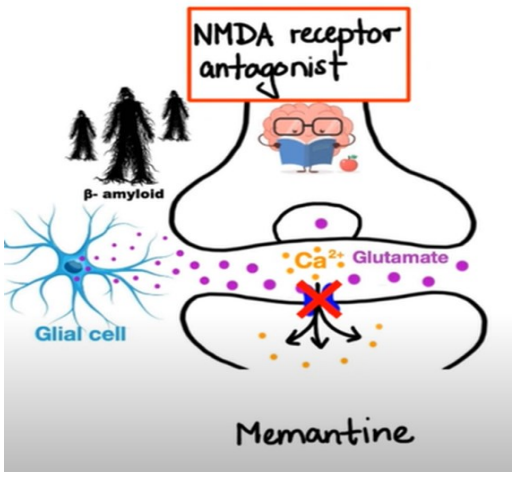
Pharmacological Treatment

Galantamine

Dose & Frequency	Adjustment	Common adverse effects	Counseling Information/ contraindications
Dosing (mg/day): Initial: 4 mg BD x 4 weeks If tolerated, increased to 8 mg BD for more than 4 weeks If tolerated, increase to 12 mg BD •*If treatment interrupted >3 days, to restart at lowest dose	Liver impairment: Moderate: Max dose 16 mg/day. Severe: Use not recommended Renal impairment: Creatinine clearance (CrCl) 9 - 59 ml/min: Max dose 16 mg/day. CrCl <9 ml/min: Max dose 8mg/day	diarrhoea, nausea, vomiting, decreased appetite, abdominal pain/distress, dyspepsia, dizziness, fatigue, tremors, weight loss	May impair ability to drive or operate machinery Contraindicated to galantamine hypersensitivity

**Oral Galantamine strength:

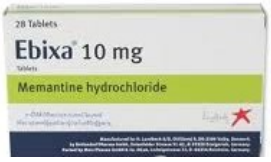
4mg Tab



- MOA: NMDA receptor antagonist that inhibits the effects of pathologically elevated levels of glutamate which then lead to neuron destruction
- NMDAra use for AD treatment is Memantine

Memantine

Dose & Frequency	Adjustment	Common adverse effects	Counseling Information
Dosing (mg/day): Initial: 5 mg once daily; increase dose by 5 mg every week as tolerated to a target maximum dose of 20 mg/day Dose may be administered once daily or two divided doses	Liver impairment: Severe: Use with caution Renal impairment: CrCL 30 - 49 ml/min: Initial 5 mg once daily; CrCL 5 - 29 ml/min Initially 5 mg once daily	Hypertension, dizziness, confusion, headache, diarrhoea, constipation, vomiting, back pain, cough, dyspnoea	May impair ability to drive or operate machinery Counsel pt on patch application Contraindicated to memantine hypersensitivity

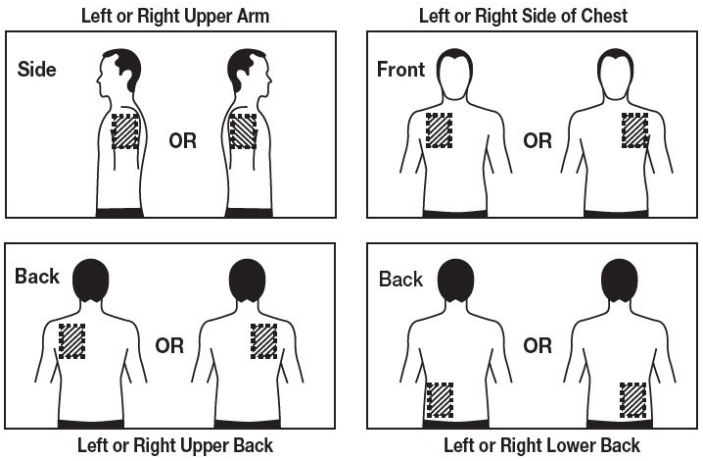


*Oral Memantine strength: 10mg tab
Prescriber category: A*

*Available in HKP

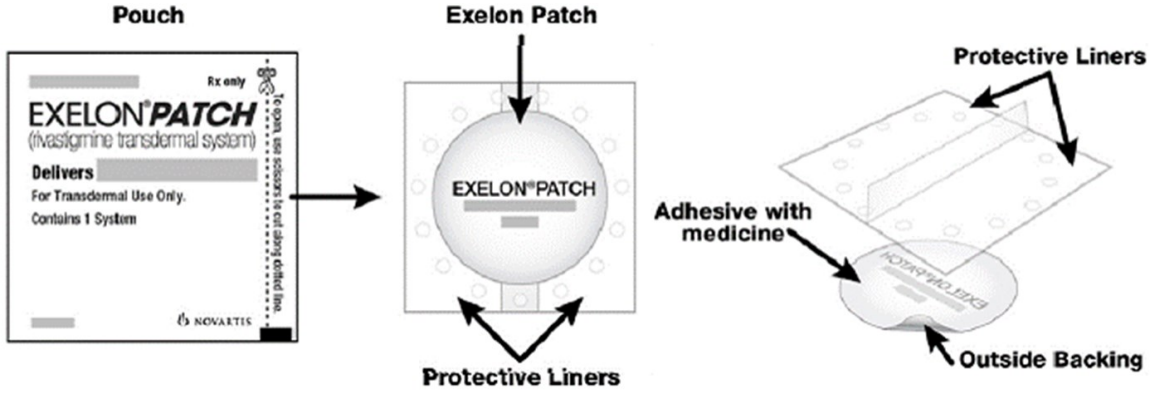
**Not Available in HKP

How to use Rivastigmine TD Patch?



To use it
1. Wash hand
2. Open packaging
3. Choose application site
4. Peel the adhesive film
5. Apply patch on application site

To remove it
1. Peel the edge of film
2. Fold patch inwards the adhesive side, seal it
3. Discard in closed bin



References

1. Management Of Dementia (Third Edition), CPG, Ministry of Health Malaysia, 2021
2. Mohandas E, Rajmohan V, Raghunath B. Neurobiology of Alzheimer's disease. Indian J Psychiatry. 2009;51 (1):55-61. doi:10.4103/0019-5545.44908
3. Ganapathy SS, Sooryanarayana R, Ahmad NA, et al. Prevalence of dementia and quality of life of caregivers of people living with dementia in Malaysia. Geriatr Gerontol Int. 2020;20 Suppl 2:16-20. doi:10.1111/ggi.14031
4. Mat Nuri TH, Hong YH, Ming LC, Mohd Joffry S, Othman MF, Neoh CF. Knowledge on Alzheimer's Disease among Public Hospitals and Health Clinics Pharmacists in the State of Selangor, Malaysia. Front Pharmacol. 2017;8:739. Published 2017 Oct 26. doi:10.3389/fphar.2017.00739
5. Tsolaki A, Kazis D, Kompatsiaris I, Kosmidou V, Tsolaki M. Electroencephalogram and Alzheimer's Disease: Clinical and Research Approaches. International Journal of Alzheimer's Disease. 2014;2014:1-10. doi:10.1155/2014/349249

Prepared By:

Muhammad Alif Iskandar Bin Shahril
Pegawai Farmasi
Hospital Kuala Penyu

Reviewed By:

Siti Khadijah Binti Sahbudin
Ketua Pegawai Farmasi
Hospital Kuala Penyu