

This supplementary material accompanies the ACE Clinical Guideline "[Management of mild and moderate dementia in older adults](#)"

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ACE Clinical Guideline



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view the ACE Clinical Guideline
"Management of mild and moderate
dementia in older adults"

References



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material

Annex A. Deprescribing medications which increase anticholinergic burden

Long-term use of medications with anticholinergic properties, particularly in older adults and those with dementia, may lead to significant adverse effects, including:^{1,2}

Worsening cognitive decline

Increased risk of falls and fractures

Increased risk of delirium

Urinary retention and constipation

Examples of common medications with significant anticholinergic activity and alternatives with lower anticholinergic burden are listed in **Table S1**.

Table S1. Examples of common medications^a with significant anticholinergic activity and suggested alternatives

Medication class	Examples	Alternatives to consider
Antidepressants	Amitriptyline, paroxetine	SSRIs with lower anticholinergic activity (e.g. escitalopram, sertraline)
Antihistamines	1 st generation (sedating) antihistamines (e.g. chlorpheniramine, hydroxyzine)	2 nd or 3 rd generation antihistamines (e.g. bilastine, cetirizine, fexofenadine, loratadine)
Antipsychotics	Chlorpromazine, olanzapine, quetiapine, risperidone	May involve considered continuation of the same medication or trialling another medication, based on the pros and cons for an individual patient and their circumstances (e.g. balancing the risk of anticholinergic effects against the risk of extrapyramidal side effects)
Gastrointestinal medications	Dicyclerine, hyoscine	Dietary modifications
Skeletal muscle relaxants ^b	Orphenadrine for musculoskeletal complaints (usually found in orphenadrine + paracetamol combination products)	Paracetamol, topical analgesics
Urological medications	Oxybutynin, tolterodine	Behavioural strategies such as prompted voiding, scheduled toileting; dietary and lifestyle modifications such as limiting caffeine, limiting fluid intake after dinner (for nocturia); avoiding constipation. If pharmacological treatment is needed, beta-adrenergic agonists (e.g. mirabegron) may be considered

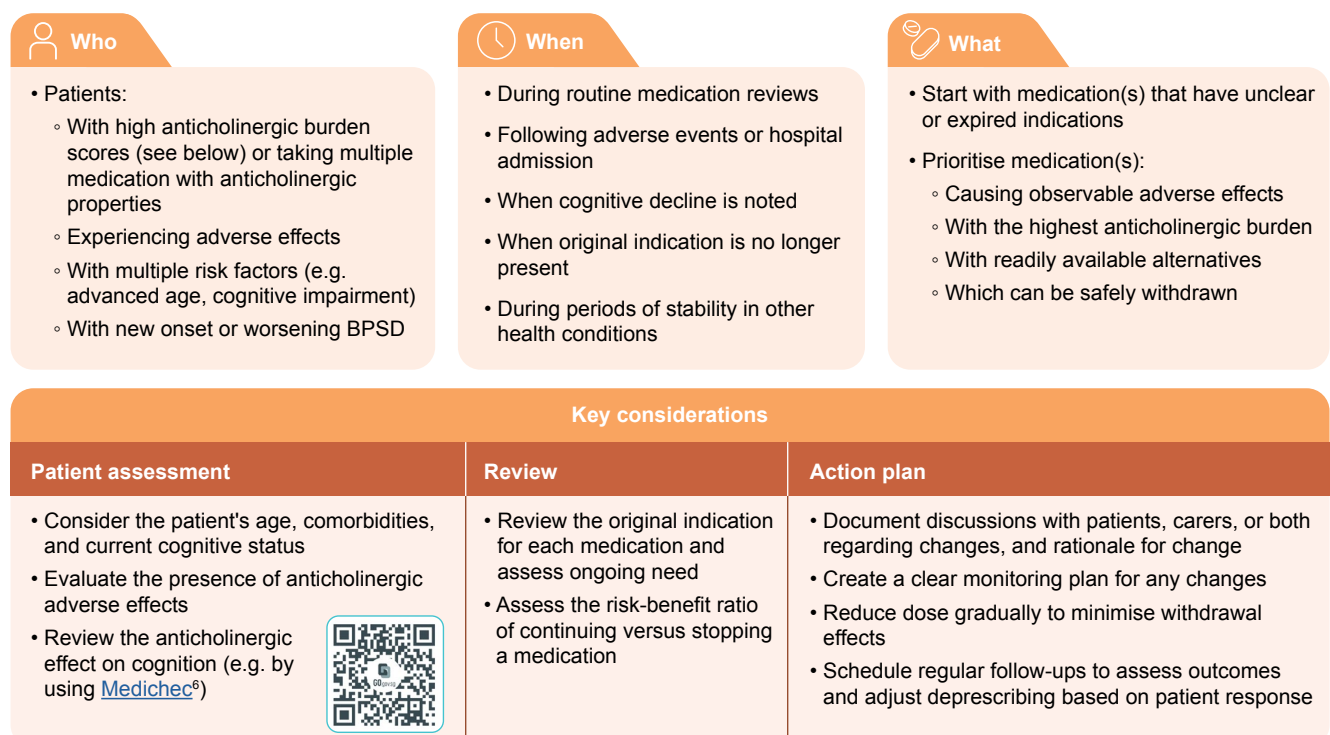
SSRIs, selective serotonin reuptake inhibitors.

^a For full list, refer to the updated American Geriatric Society (AGS) Beers Criteria.³

^b Does not include skeletal muscle relaxants typically used for the management of spasticity (e.g. baclofen).

Use the framework in **Figure S1** to guide deprescribing to reduce anticholinergic burden by identifying suitable patients (Who), recognising appropriate timing for intervention (When), and selecting priority medication(s) for deprescribing (What).

Figure S1. Deprescribing decision framework for reducing anticholinergic burden^{4,5}



Annex B. Pharmacological options in primary care to support cognition, function, and behaviour

Table S2 provides an overview of cognitive enhancers registered in Singapore to manage Alzheimer's disease. There are no medications with approved indications for other types of dementia. Information references local product information leaflets (PILs); refer to the PIL for full details before prescribing. Clinical judgement should always be exercised when making decisions for an individual patient. Therapy should only be started if a carer is available to regularly administer and monitor the treatment.

Table S2. Cognitive enhancers registered in Singapore to manage Alzheimer's disease

Medication ^c (strength)	Dosing and titration – may need to be further tailored to suit patient profile and response	Hepatic impairment dose adjustment	Renal impairment dose adjustment	Key adverse effects ^d	Warnings or precautions
Acetylcholinesterase inhibitor					
<u>Donepezil hydrochloride tablet (5 mg, 10 mg, 23 mg)^e</u> Approved indication: mild to moderately severe ^f and severe Alzheimer's disease	Initial: 5 mg OD Increase to 10 mg OD after clinical assessment of 4 to 6 weeks' treatment on 5 mg OD, depending on patient response	Mild to moderate impairment: not required, but due to decreased clearance, titrate according to individual tolerability Severe impairment: no data available	Not required	Very common: diarrhoea, nausea, headache Common: vomiting, insomnia, fatigue, common cold, anorexia, hallucinations, agitation, aggressive behaviour, abnormal dreams and nightmares, syncope, dizziness, abnormal disturbance, rash pruritis, urinary incontinence, pain, accidents including falls	All AChE inhibitors Caution in cardiac conditions (e.g. sinus node dysfunction, conduction defects, uncompensated CHF, recent MI) due to vagotonic effects (resulting in bradycardia, heart block), and history of QT prolongation risk, or electrolyte disturbances. Monitor clinically; ECG may be needed Caution for patients with predisposition to increased gastric acid secretion, peptic ulcers, urinary obstruction, seizures, and history of asthma or COPD Caution: associated with neuropsychiatric events in some patients ^{7,8} Patients with lower body weight (<55 kg for donepezil; <50 kg for rivastigmine) may experience more adverse effects; may need lower starting and maintenance doses (e.g. 2.5mg OD for donepezil)
Galantamine prolonged release capsule (8 mg, 16 mg, 24 mg) ^g Approved indication: mild to moderately severe ^f Alzheimer's disease	Initial: 8 mg OD Increase to 16 mg/day if well tolerated after a minimum of 4 weeks' treatment on 8 mg/day. Maintain for at least 4 weeks before considering increase to max recommended maintenance dose 24 mg OD after appropriate assessment including evaluation of clinical benefit and tolerability	Moderate impairment: start with 8 mg EOD for at least 1 week (preferably in morning), then 8 mg OD for at least 4 weeks. Max dose 16 mg/day Severe impairment (Child-Pugh score >9): use not recommended	Moderate impairment: CrCl 9–59 mL/min: max dose 16 mg/day CrCl <9 mL/min: use not recommended due to lack of data	Very common: nausea, vomiting Common: diarrhoea, abdominal pain, dyspepsia, decreased appetite, weight loss, depression, dizziness, headache, tremor, muscle spasms, syncope, lethargy, somnolence, bradycardia, fatigue, falls, asthenia, malaise, hallucinations, hypertension	Galantamine only • Warning: <u>serious skin reactions</u> ⁹ ; patients should be informed about signs of serious skin reactions and discontinue use at the first appearance of skin rash • Caution: not recommended in patients with urinary outflow obstruction or recovering from bladder surgery
Rivastigmine capsule (1.5 mg, 3 mg, 4.5 mg, 6 mg) Approved indication: mild to moderately severe ^f Alzheimer's disease	Initial: 1.5 mg BD Increase to 3 mg BD if well tolerated after a minimum of two weeks' treatment on 1.5 mg BD. Consider subsequent increases to 4.5 mg BD and then 6 mg BD after a minimum of two weeks' treatment at each dose level, subject to tolerability	Mild to moderate impairment: Not required, but due to decreased clearance, titrate according to individual tolerability Severe impairment: no data available	Moderate impairment: not required, but due to increased exposure or decreased clearance, titrate according to individual tolerability	Very common: nausea, vomiting, dizziness, diarrhoea, decreased appetite Common: abdominal pain, weight loss, agitation, confusion, nightmares, anxiety, somnolence, tremor, dyspepsia, hyperhydrosis, fatigue, asthenia, malaise, headache	
<u>Rivastigmine transdermal patch (4.6 mg/24 h, 9.5 mg/24 h, 13.3 mg/24 h)</u> Approved indication: mild to moderately severe ^f and severe Alzheimer's disease	Initial: 4.6 mg/24 h OD Mild to moderately severe dementia: • Increase to 9.5 mg/24 h if well tolerated after a minimum of 4 weeks' treatment on 4.6 mg/24 h • Consider increasing to 13.3 mg/24 h if patient demonstrates meaningful cognitive deterioration (e.g. decrease in MMSE) and/or functional decline (based on clinician judgement), and if well tolerated after a minimum of 6 months' treatment on 9.5 mg/24 h Severe dementia: • Consider increasing to 13.3 mg/24 h if there is good tolerability of current dose, and only after a minimum of 4 weeks' treatment at each dose level		Not required	Very common: nausea Common: anorexia, decreased appetite, anxiety, depression, insomnia, headache, dizziness, vomiting, diarrhoea, dyspepsia, abdominal pain, urinary incontinence, rash, application site reactions (erythema, pruritus, oedema), weight loss, urinary tract infection	
N-methyl-D-aspartate antagonist					
<u>Memantine tablet (10 mg)</u> Approved indication: moderate to severe Alzheimer's disease	Initial 5 mg/day (half of a 10 mg tablet) Increase gradually by 5 mg every 7 days to reduce the risk of undesirable effects, until maintenance dose (and max dose) of 20 mg/day is reached	Severe impairment: not recommended due to lack of data	CrCl 30–49 mL/min: maintenance dose 10 mg/day for at least 7 days before considering increasing until 20 mg/day as per standard titration, subject to tolerability CrCl 5–29 mL/min: maintenance dose max 10 mg/day	Common: dizziness, headache, constipation, somnolence, hypertension, balance disorders, dyspnoea, elevated liver function test	• Caution due to limited data in cardiac conditions (e.g. recent MI, uncompensated CHF, or uncontrolled hypertension) • Caution for patients with a history of seizure disorders (e.g. epilepsy)

AChE inhibitor, acetylcholinesterase inhibitor; BD, twice daily; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CrCl, creatinine clearance in mL/min; ECG, electrocardiogram; EOD, every other day; max, maximum; MI, myocardial infarction; MMSE, Mini-Mental State Examination; OD, once daily.

^c Medications underlined denote availability on [government subsidy list](#) at the time of publication; medications **bolded** denote availability on [Healthier SG Medication List](#) at the time of publication.

^d Only very common (>1/10) and common (>1/100, <1/10) adverse effects are listed, refer to PIL for the full list.

^e All donepezil strengths available as standard oral tablet; 5 mg and 10 mg donepezil also available as oral disintegrating tablet.

^f The term 'moderately severe' appears in certain assessment tools and scales used in clinical studies but is not commonly used in literature or local clinical practice. For the purposes of this ACG, cases classified as 'moderately severe' are considered under the 'moderate' category.

^g Galantamine is not commonly used and not available in some practice settings.

Table S3 has been adapted^h from the [ACG on major depressive disorder](#) and provides an overview of second-generation antidepressants commonly used off-label to manage behavioural and psychological symptoms of dementia (BPSD) in primary care. For the full range of antidepressants registered in Singapore, please refer to the ACG on major depressive disorder. Tricyclic antidepressants should be avoided for patients with dementia due to their anticholinergic effects.

When prescribing a second generation antidepressant, consider potential medication interactions (particularly anticholinergic burden when used with cognitive enhancers) and the risk of adverse effects such as SIADH-induced hyponatraemiaⁱ in older adults. Regular medication reviews and electrolyte monitoring are recommended. Refer to standard dosing for approved indications to guide dosing, and adjust as needed.

Refer to the PILs for full details before prescribing. Clinical judgement should always be exercised when making decisions for a patient.

Table S3. Commonly used second-generation antidepressants to manage BPSD in primary care (off-label use)

Medication ^j	Key precautions		Additional considerations	
				+ Advantageous - Disadvantageous • Advantageous or disadvantageous, depending on the patient's context
Selective serotonin reuptake inhibitor				
Escitalopram Approved indication: GAD, MDD, OCD, panic disorder	Risk of bleeding abnormalities with SSRIs; bleeding tendency may be increased if concurrently used with anticoagulants, or medication that affect platelet function (e.g. NSAIDs and aspirin)	May cause orthostatic hypotension	Dose-dependent QTc prolongation (higher risk than other SSRIs)	+ Lower treatment drop-out due to side effects, compared to other antidepressants • Greater propensity for weight gain compared to other antidepressants
<u>Fluoxetine</u> Approved indication: bulimia nervosa, MDD, OCD, pre-menstrual dysphoric disorder			Strong inhibitor of CYP2D6	+ Lower treatment drop-out due to side effects, compared to other antidepressants + Suitable for patients with poor medication adherence due to a long half-life + Lower risk of discontinuation symptoms compared to other antidepressants - Insomnia very commonly reported - Greater difficulty in switching to another antidepressant due to long half-life • Activating effect
<u>Fluvoxamine</u> Approved indication: MDD, OCD			Strong inhibitor of CYP1A2, CYP2C19, and CYP3A4	• Sedating effect
<u>Sertraline</u> Approved indication: MDD, OCD, panic disorder, pre-menstrual dysphoric disorder, PTSD, social anxiety disorder	Risk of bleeding abnormalities with SSRIs; bleeding tendency may be increased if concurrently used with anticoagulants, or medication that affect platelet function (e.g. NSAIDs and aspirin)		+ Dose adjustment not routinely required in renal insufficiency + Safe to use post-myocardial infarction or heart failure - Insomnia very commonly reported • Activating effect	
Noradrenergic, specific serotonergic antidepressant				
<u>Mirtazapine</u> Approved indication: MDD	May cause orthostatic hypotension		+ Lower propensity for hyponatremia compared to SSRIs and SNRIs¹⁰ - Greater propensity for anticholinergic effects compared to other antidepressants • Greater propensity for weight gain compared to other antidepressants (encourages appetite) • Sedating effect	
Multimodal serotonergic antidepressant				
Vortioxetine Approved indication: MDD	Risk of bleeding abnormalities; bleeding tendency may be increased if concurrently used with anticoagulants, or medications that affect platelet function (e.g. NSAIDs and aspirin)		+ Lower treatment drop-out due to side effects, compared to other antidepressants + Dose adjustment not routinely required in renal and hepatic insufficiency + Evidence of efficacy for improving cognitive function and memory	

CYP1A2, cytochrome P450 family 1 subfamily A member 2; CYP2C19, cytochrome P450 family 2 subfamily C member 19; CYP2D6, cytochrome P450 family 2 subfamily D member 6; CYP3A4, cytochrome P450 family 3 subfamily A member 4; GAD, generalised anxiety disorder; MDD, major depressive disorder; NSAIDs, nonsteroidal anti-inflammatory drugs; OCD, obsessive compulsive disorder; PTSD, post-traumatic stress disorder; QTc, corrected QT interval; SNRIs, serotonin-norepinephrine reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors.

^h Additional information specific to older adults has been added to this table.

ⁱ Syndrome of Inappropriate Antidiuretic Hormone (SIADH) secretion, which causes serum sodium lower than 110 mmol/L (hyponatraemia).

^j Medications underlined denote availability on [government subsidy list](#) at the time of publication; medications **bolded** denote availability on [Healthier SG Medication List](#) at the time of publication.

Cognitive enhancers are the mainstay pharmacological treatment for Alzheimer's disease. The role of other complementary medications and emerging therapies is not yet established. **Table S4** provides two examples.

Table S4. Examples of complementary medication and emerging therapeutic approaches used in dementia

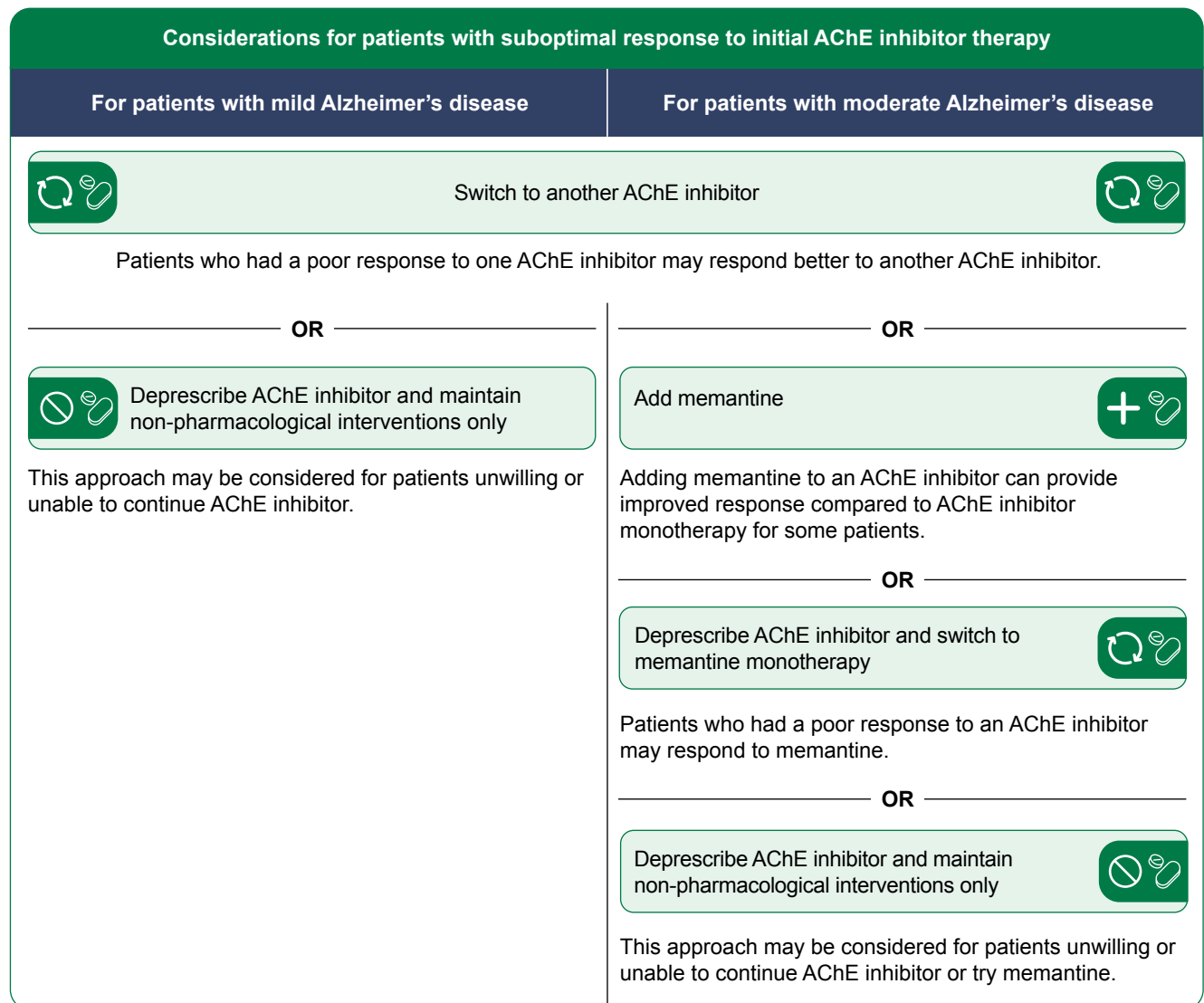
 Ginkgo biloba leaf extract EGb761®	 Amyloid-targeting therapies (donanemab and lecanemab)
• Current evidence shows no consistent benefit in patients with mild or moderate dementia when using 240 mg/day EGb761 for a minimum of 22 weeks, compared to placebo, or to 12 weeks of AChE inhibitor therapy^{11,12} • Clinical judgement is required before prescribing, noting that studies have only been conducted with a specific formulation (EGb761) • Safety considerations include increased risk of bleeding events, particularly when used with blood-thinning medications (e.g. aspirin, warfarin) or in individuals with bleeding tendency¹³	• Current evidence shows modest benefits in reducing cognitive deterioration after 18 months of treatment, compared to placebo in patients with Alzheimer's disease • Safety considerations include risk of brain oedema or bleeding events (known as amyloid-related imaging abnormalities), with increased risk in patients with a double copy of the apolipoprotein E ε4 allele.^{14,15} Long-term effects are unknown and there is a lack of data on patients with multiple comorbidities¹⁶ • The approved indications for donanemab and lecanemab are mild cognitive impairment and mild dementia due to Alzheimer's disease.^{14,16} However, the process to determine patient suitability and eligibility is complex and would involve a referral to a specialist clinic in tertiary setting

Annex C. Managing suboptimal response to AChE inhibitor therapy

While the evidence for managing suboptimal response to AChE inhibitor therapy is limited, **Figure S2** presents practical strategies for consideration. Healthcare professionals should exercise clinical judgement when selecting and implementing these strategies. Where stepdown is required, refer to the deprescribing section in the ACG (**Figure 2**).

Non-pharmacological interventions to support cognition, reduce BPSD and preserve function are encouraged for all patients; these should be maintained alongside pharmacotherapy as appropriate, throughout all stages of Alzheimer's disease.

Figure S2. Strategies for consideration when initial response to AChE inhibitor therapy is suboptimal



Strategies that are not recommended

Based on current evidence, the following strategies are **not recommended**:

- ✗ Starting with memantine in mild dementia, either as monotherapy or in combination with an AChE inhibitor: memantine demonstrates greater efficacy in moderate and severe stages of Alzheimer's disease, with very limited efficacy in the mild stage (no better than placebo).¹⁷
- ✗ Starting with two AChE inhibitors: there is limited evidence on this approach, and it is likely to result in increased treatment discontinuation due to adverse effects.

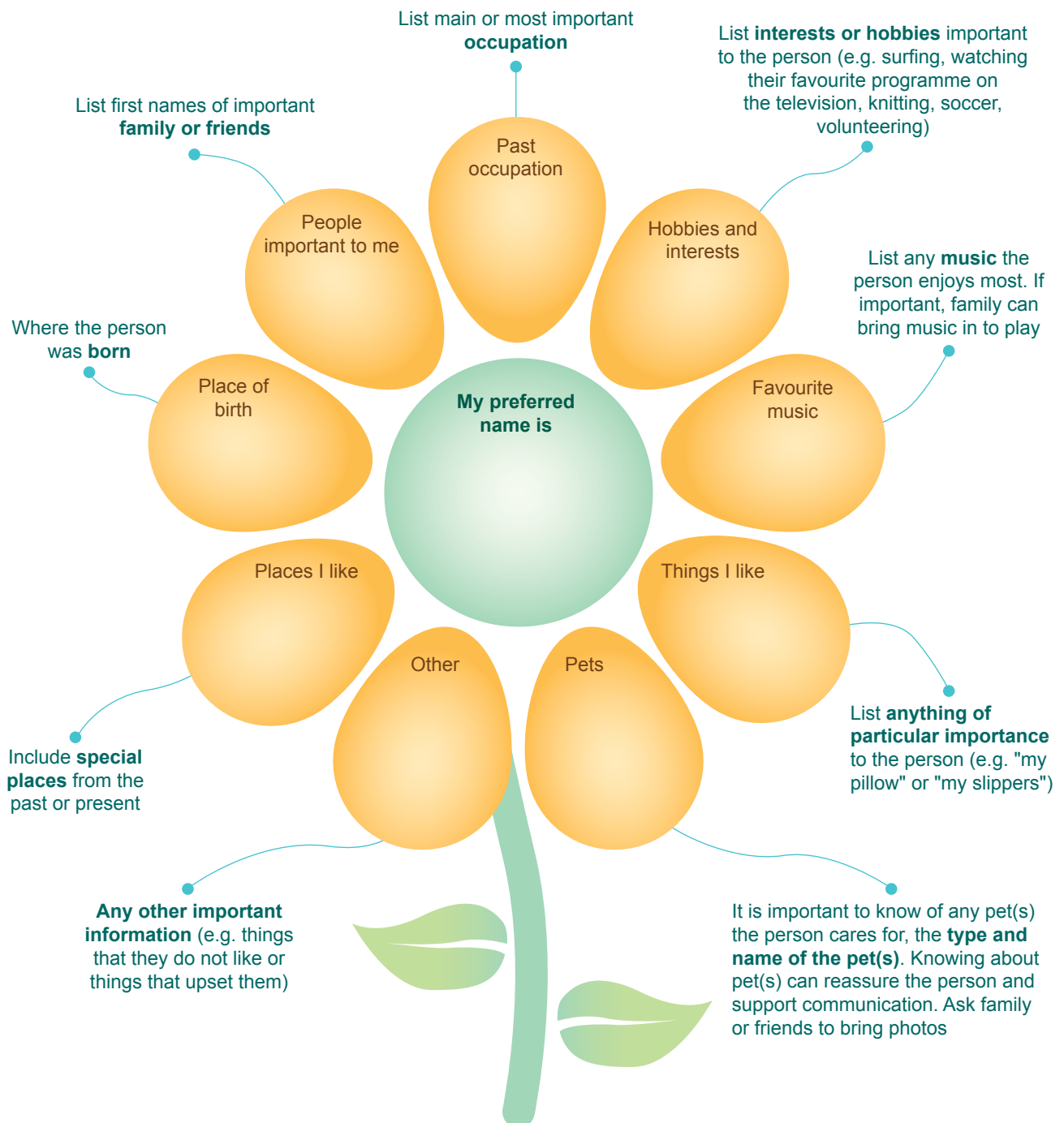
Legend

 Pharmacotherapy
  Switch
  Stop
  Add

Annex D. A reference patient profile framework to guide individualised interventions

The Sunflower Tool is an example of a tool which supports healthcare professionals in understanding a patient's preferences, informing the types of interventions which the patient will enjoy and engage in. Consider using the Sunflower Tool for comprehensive patient profiling when the patient is clinically stable.

Figure S3. The Sunflower Tool: a framework for understanding patient preferences and personalising interventions



Annex E. Supporting carers in identifying and managing common BPSD using non-pharmacological strategies

This section provides strategies that healthcare professionals can share with carers to support them in managing BPSD. Many strategies can be implemented in the home setting. Healthcare professionals can also refer patients and carers to care services listed in **Annex F** and to [Community Outreach Team \(CREST\)](#) or [Community Intervention Team \(COMIT\)](#) service providers as needed.

Tools can be helpful to identify possible triggers of BPSD. For example:

- The [CAUSEd problem-solving tool](#) to **understand why changes in behaviour occur**. It guides users to see behaviour changes as responses to changes in the brain, and consider various factors that can be addressed in response to the behaviour.
- The Antecedent-Behaviour-Consequence (ABC) analysis tool¹⁸ to systematically **document the BPSD and possible triggers**. For example, if the patient becomes agitated (B) every time there is loud television noise (A) and calms down when moved to a quiet room (C), the carer can prevent future episodes by keeping the volume low or moving the patient to a quieter location.

Antecedent (A)	Behaviour (B)	Consequence (C)
What happens before BPSD occur (e.g. time, location, people present, ongoing activities)	Specific behaviours (duration and intensity rated on a 1 to 10 scale)	Immediate responses and outcomes

Table S5 presents commonly reported triggers and examples of strategies for commonly observed BPSD. These strategies focus on addressing underlying triggers and providing appropriate environmental modifications and therapeutic activities to reduce or resolve the BPSD. Strategies should be tailored to the patient's preferences and interests. Where there is a sudden or concerning change in behaviour, carers should contact the person's healthcare professional promptly.

Table S5. Suggested strategies to address frequently encountered BPSD

Behaviour	Commonly reported underlying triggers	Suggested strategies to address frequently encountered BPSD
Agitation or aggression	• Unmet physical needs (e.g. pain, hunger, thirst, or need for toileting) • Environmental factors (e.g. excessive noise, unfamiliar surroundings, changes in routine) • Overstimulation or understimulation • Difficulty communicating needs	• Create a calm and familiar environment, maintain routines, and reduce overstimulation (e.g. limiting noise, crowds, or complex visual patterns) to help de-escalate emotional distress • Facilitate personalised activities, or touch and massage^{19,20}
Apathy	• Lack of meaningful engagement or activity • Loss of usual roles and routines • Understimulation • Side effects of medication (check with healthcare professional if suspected)	• Encourage physical exercise or interaction with pets (to promote engagement)^{20,21} • Provide prompts or cues to encourage participation in familiar activities (e.g. showing photographs, offering familiar objects, or gentle reminders about hobbies they enjoyed)²²
Anxiety	• Change in situations (e.g. transition between activities, changes in routine, unfamiliar environments, separated from familiar carers) • Anxiety increases during 'sundowning' in the late afternoon or evening	• Reduce the need for stressful decision-making by establishing and maintaining structure and routine

Behaviour	Commonly reported underlying triggers	Suggested strategies to address frequently encountered BPSD
Depression	• Loneliness or lack of social support • Grief (e.g. awareness of cognitive decline) • Loss of independence and functional mobility	• Encourage social connection and participation in engaging activities, facilitate touch and massage, or exercise such as walking^{23–25}
Disinhibited behaviour	• Impaired judgement or reduced awareness of social norms • Presence of familiar carers or others • Environmental factors (e.g. communal settings, lack of privacy) • Sensory discomfort or unmet need for physical closeness	• Divert the patient's focus to other activities (e.g. craft or puzzles) to distract and redirect attention^{26–29} • Avoid drawing attention to inappropriate behaviours; acknowledge and reinforce appropriate behaviours^{26–29} • Provide clothing that limit the likelihood of these behaviours (e.g. clothing that opens at the back)²⁶
Psychosis (hallucinations and delusions)	• Unfamiliar or complex visual stimuli in the environment • Changes in lighting (e.g. shadows, glare) • Social isolation or reduced sensory input • Unmet needs (e.g. pain, fatigue)	• Acknowledge thoughts and feelings; avoid directly challenging hallucinations or delusions • Maintain a calm and predictable environment and reduce unfamiliar stimuli • Redirect to another topic or distract with other activities (e.g. craft activities) and limit potential triggers/stimuli
Sleep disturbance	• Thirst or hunger • Caffeine in the evening, fluid intake in the hours before bed • Lack of night-time routine, and taking daytime naps • Light and noise intrusions	• Schedule more stimulating activities during daytime (e.g. exercise) and transit to evening with calming activities (e.g. gentle music, familiar routines)^{30,31} • Encourage sleep hygiene (e.g. consistent bedtime routines, limiting evening caffeine and fluid intake, setting comfortable temperature, and minimising noise disturbances) • Prevent nighttime incidents with safety measures (e.g. motion sensors, bed alarms, clear pathways, leaving toilet light switched on)
Vocally disruptive behaviour	• Impaired language or communication skills (e.g. reduced speech) • Unmet needs or uncomfortable environment (e.g. pain, thirst, hunger, and inappropriate room temperature)³² • Social isolation, lack of stimulation, change in carer interaction • Reminiscences and re-emergence of painful memories	• Optimise the environment for comfort (e.g. maintaining appropriate temperature, reducing glare) • Gently redirect attention to a preferred activity or topic³³ • Observe for and report signs of discomfort to the person's healthcare professional (e.g. grimacing, restlessness)
Wandering	• Disorientation to time, place, or person • Trying to return home, looking for a person, escaping a perceived threat • Unmet needs (e.g. regular toileting, pain, hunger, or thirst)	• Modify the environment to allow safe wandering (e.g. circular paths, secure the perimeter with door alarms, locks, or disguised exits, remove hazards, and ensure clear pathways)³⁴ • Improve orientation (e.g. clear signage, consistent lighting, and familiar objects)³⁴ • Redirect attention with preferred activities, or distraction zones with engaging activities near exit points³⁴ • Use technology to monitor movement or improve navigation (e.g. watch with a tracking or navigation system, identity bracelet)³⁴ • Encourage physical exercise (e.g. walks with carer)³⁴ • Maintain a consistent daily routine to reduce confusion

Annex F. Links to additional resources

Table S6 provides links to information, services, and guidance across the care continuum to support patients with dementia, their carers, and healthcare professionals.

Table S6. Dementia and related resources for patients, carers, and healthcare professionals

Support area	Resource	Description	Click or scan QR code
Dementia care information and support 	DementiaHub.SG	Resource portal on dementia care, events, and services	
	Top 5 Dementia Resources and Caregiving Tips	Top 5 curated tips and guides for carers	
	Dementia Helpline	Helpline for dementia care information and service linkages	 6377 0700
	Dementia Singapore	Social service agency specialising in dementia care, carer support, training, consultancy, and advocacy	
Carer support, resources, and respite services 	We See You Care	Resources for carers on self-care, financial assistance, caregiving, and care service recommendations	
	AIC Link	Physical locations advising on care services, assistance schemes, and respite care	
Advance Care Planning (ACP) and Lasting Power of Attorney (LPA) 	Start Your ACP Journey	Information on Advance Care Planning	
	Make an LPA	Information on Lasting Power of Attorney	
Professional resources for GPs 	Community Mental Health Resource Kit for General Practitioners, Section C: Dementia	Toolkit on dementia community health services for GPs supporting patients and carers	

Legend

Target audience:  Patient  Carer  Healthcare professional