Ministry of Health

Al Masarra Hospital

CLINICAL GUIDELINE FOR MANAGEMENT OF DEMENTIA (MAJOR NEUROCOGNITIVE DISORDER) OF ALZHEIMER'S DISEASE

General Psychiatry/ Geriatric unit-1

Document Title	Clinical Guideline for Management of Dementia of Alzheimer's Disease
Document Type	Guideline
Directorate/Institution	Al Masarra Hospital
Targeted Group	Geriatric Psychiatrists, general psychiatrists, neurologists, Family physicians, internal medicine physicians, general practitioners
Document Author	Task Force listed at acknowledgment section
Designation	Geriatric unit-1
Document Reviewer	**Directorate General of Quality Assurance Center**
Esignation	**Directorate General of Quality Assurance Center**
Release Date	**09/12/2024**
Review Frequency	**Three Years**

Validated by		**Approved by**	
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Signature		Signature	
Date	December 2024	Date	December 2024

Acknowledgement

We would like to thank every member of the task force for their dedication, hard work, and expertise in contributing to the development of this guideline. Their commitment to improving patient care has been instrumental in ensuring that this guideline reflect the most current, evidence-based practices. Together, we aim to enhance the quality of life for those living with Alzheimer's disease by providing compassionate, comprehensive, and personalized care that meets the highest standards of medical excellence.

We hope this guideline will serve as a valuable resource for all healthcare providers involved in the care of patients with Alzheimer's disease, enabling them to deliver effective and empathetic care, in line with the international best practices. We would like to thank also Quality department , reviewing team and administration for great help in releasing this guideline.

The task force was comprised of:

- **Dr. Saleha Al-Jadidi**, Consultant and Head of Geriatric Unit-1
- **Dr. Mervat Said**, Psychiatrist Specialist, Geriatric Unit-1
- **Dr. Hazim Mohammed**, Medical Officer, Geriatric Unit-1

Each member of this team brought invaluable expertise, insight, and dedication to the creation of these guidelines. Their collaborative efforts were key in ensuring that the guideline is comprehensive, evidence-based, and aligned with international standards for the management of Alzheimer's disease. Their hard work and commitment are deeply appreciated

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Acronyms

AMRH	Al Masarra Hospital
(DSM-5)	Diagnostic Statistical Manual of Mental Disorders Edition 5
FTD	Frontotemporal Dementia
MMSE	Mini-mental Status Examination
MoCA	Montreal Cognitive Assessment.
AD	Dementia of the Alzheimer's type (AD).
APP	Amyloid Precursor Protein
RUDAS	Rowland Universal Dementia Assessment Scale
MRI	Magnetic resonance Imaging
fMRI	Functional Magnetic resonance Imaging
SPECT	Single-photon emission computed tomography
IADLs	Instrumental Activities of Daily Living
ADLs	Basic Activities of Daily Living
DHA	Docosahexaenoic Acid
EPA	(Eicosapentaenoic Acid
NMDA receptors	N-methyl-d-asperatate receptors,
MCABs	Mono-Clonal Antibodies
FDA	Food and Drug Administration

Definitions

- **Dementia:** Is an old term describing a progressive neurodegenerative disorder associated with **marked** impairment in memory, judgments, orientation, and cognition. It also refers to a disease process with progressive cognitive impairment with clear consciousness, presents a decline from a previous level of functioning, and involves multiple cognitive domains deficits, leading to significant impairments in social and occupational functioning.
- **Major neurocognitive disorder**: is the new term that substitutes dementia according to the Diagnostic Statistical Manual of Mental Disorders Edition 5 (DSM-5)
- **Pick's disease (FTD)**: is a type of neurocognitive disorder associated with Fronto-Temporal Degeneration.
- **Mini-mental Status Examination (MMSE):** is a scale that probes cognitive impairment, used as a screening tool for assessing dementia.
- **Montreal Cognitive Assessment (MoCA)**: is another type of scale that is more sensitive to mild cognitive impairment.

CHAPTER ONE:

- **Introduction:**

- The prevalence of dementia in general is 5% in the population older than 65 years, and 20 to 40% in the population older than 85 years of age.
- There are four major subcategories of Dementia (1) Dementia of the Alzheimer's type, which usually occurs in persons above 65 years of age, it manifests by progressive decline of cognitive function (2) Vascular Dementia, which is caused by micro/ Marco-cerebral vascular diseases (3)Front-temporal Dementia- **FTD (Pick's Disease**), which caused by degeneration of front-temporal lobes (4) Lew-Body Dementia, which caused by Protein deposits, called Lewy bodies, develop in nerve cells in the brain regions (5) Dementia of Parkinson's disease caused by abnormal microvascular deposits composed chiefly of alpha-synuclein protein. Other causes of dementia include; human immunodeficiency virus (HIV), head trauma, Prion disease (Creutzfeldt-Jakob disease, substance induced by toxin, medications, multiple etiologies, and not specific (Table 1).
- There are multiple steps required to diagnose Dementia, including obtaining a detailed change of daily routine, and understanding the past life of the patient and baseline functions, also requires extensive assessment and investigations, which are discussed in these guidelines. Upon confirmation of diagnosis, management should involve both pharmacological and non-pharmacological management. In this clinical guideline, we will focus on Dementia of Alzheimer's type as it is a major form of Dementia.

- **Dementia of Alzheimer's type**

  With aging, the prevalence of Dementia is increasing and 50 -70 present of all Dementia cases have the Alzheimer's type (AD). The World Alzheimer Report (2009) estimated that 36 million people will be living with dementia in 2010, nearly doubling every 20 years to 66 million by 2030 and 130 million by 2050. Therefore, a strategic major needs to be undertaken for early diagnosis and treatment. AD is commonly diagnosed in clinical settings after other causes of dementia have been excluded.

- A major risk factor of AD is a heterogeneous genetic disorder with familial form mutation in a gene associated with the **amyloid precursor protein (APP)** on chromosomal 21, as well as the presenilin 1 and 2 genes on chromosomal 14 and 1, respectively. In addition, other several genes are unknown may increase risk, but do not determine the occurrence as the apolipoprotein (APOE-4).
-

- Studies showed that genetic and environmental risk factors decrease the clearance of amyloid, which leads to the accumulation of toxic depositions in the brain and the emergence of symptoms. Other causes found as well.

- **Purpose:**

  - To standardize the management plan of patients who are diagnosed with Alzheimer's disease.

  - To improve the Quality of life of patients and their caregivers.

  - To minimize the burden on the families of the patients

- **Scope**

  This policy applies to all healthcare providers who assess and manage geriatric patients in the 1ry healthcare facilities and the other facilities.

- **Structure**

  This is the first version of this guideline and it consists of (3) chapters.

- **Responsibilities**

  All healthcare providers, who assess and manage geriatric patients in all healthcare facilities shall comply with this protocol.

CHAPTER TWO:

- **Guideline/Procedure:**

  - **Diagnosis and Clinical Features**

  To diagnose Major neurocognitive disorder due to Alzheimer's disease, the patient needs extensive history taking and workup. The history includes onset, course duration, precipitating factors, type of cognitive domain/s affected, the impact on the functional level, associated, behavioral and psychological symptoms, and severity of symptoms. Criteria of diagnosis conform with the Diagnostic and Statistical Manual of Mental

Disorders 5thEdition (DSM-5) (Table 1) The investigation and lab work are done to exclude the other organic causes +/- helping to confirm the diagnosis as illustrated in Table2.

Table1. DSM-5 diagnostic criteria for Major Neuro-cognitive Disorder (Dementia) Table 2. Clinical and Laboratory assessment for Dementia (AD)

Diagnosis of dementia should be made only after a comprehensive assessment, which should include the following:
History taking from the patient, if possible
Collateral history from family, relatives…etc.
Mini-mental Status Examination (MMSE) / Montreal Cognitive Assessment (MoCA) or other validated Cognitive, he Rowland Universal Dementia Assessment Scale: A Multicultural Cognitive Assessment Scaland (RUDAS) and Memory testing with validated tools.
Neuropsychological test by clinical psychologist, if clinically indicated/ if applicable
Review of Medical Conditions'
Medical assessment /Physical examination by medical internist / General practitioner
Medications' Review
Consideration of other causes (including delirium or depression).
Functional Assessment by Occupational Therapist
Psychosocial Assessment by Social Worker
Driving Safety assessment, if applicable
Gait and risk of fall assessment by physiotherapist
Dietician assessment
Neurologist assessment if clinically indicated / if applicable
Sensory (hearing/vision assessment if clinically indicated if applicable
Basic Dementia investigations, should be performed at the time of presentation, they should

include the following blood tests:

Routine hematology

Biochemistry tests (including electrolytes, calcium, glucose, and renal and liver function)

Thyroid function tests

Serum vitamin B12 and folate levels.

Testing for syphilis serology or HIV should be undertaken only in those with histories suggesting they are at risk.

CT head should be as clinically indicated e.g. rapid onset, young age ..etc.)

An electrocardiogram must be if the intent to start acetylcholinesterase inhibitors

Chest x-ray as clinically indicated

MRI, fMRI, SPECT as clinically indicated

- **Differential Diagnosis**

  - **Delirium**: in general, it is distinguished by rapid onset, brief duration, and cognitive impairment with fluctuation during the day.
  - **Depression**: the clinical picture of depression refers to pseudo -dementia and those patients have prominent depressive symptoms and they are more insight into their symptoms than demented patients.
  - **Normal aging**: Aging is not necessarily associated with any significant cognitive, but minor problems can occur as a normal part of aging. This is referred to as benign senescent forgetfulness, age-associated memory impairment, or normal age-related senescence.
  - Other disorders include Hypothyroidism, infections ...etc. These disorders can be distinguished via clinical and laboratory assessments.

- **Treatments of Dementia of Alzheimer's Type:**

After verification of the diagnosis, the second step is prevention measures, which may include changes in diet, exercise, and control of chronic disease (Diabetes and hypertension). However, in general treatment of AD (Table 3) depends on the degree of the illness (Mild, Moderate, or severe), and is divided mainly into: Non – Pharmacological interventions and pharmacological interventions.

Table 3. General Principles for Dementia Management

▪ All patients with dementia or suspected to have dementia and their families must be referred to Memory clinic/ Geriatric Psychiatry Outpatient Department (OPD). ▪ Patients with mild to moderate dementia, when admitted to hospitals, should be identified as having the risk of delirium. Therefore, they should be offered multi-component interventions including, orientation, sleep-enhancement strategies, mobilization, hearing aids, and good hydration to minimize the risk of delirium. ▪ Comorbidities of patients with Alzheimer's disease should be appropriately treated. ▪ Recommendation about the use of medications for treating Alzheimer's disease ▪ Safety measures should be maintained in the hospital/ home. ▪ Mandatory psychoeducation to the family and caregiver about the diagnosis, progress, treatment, quality of life ...etc. ▪ Recommend Non- pharmacological management ▪ Genetic counseling when indicated.

A. Non-Pharmacological Interventions for AD

Patients often benefit from support and education psychotherapy in which the nature and the course of illness are explained. They also, benefit from assistance in accepting the extent of disability and form self-esteem issues. There is a must to maximize intact functioning areas of the patient/s. It has been recommended to instruct the patient to find a way to deal with the impairment of memory by keeping calendars for appointments and orientation and by making a schedule to help with daily activities. Family intervention, is necessary in treating Dementia, particularly for those who are taking care of the patient, who may be delayed by guilt and grief,

exhaustion…. etc. Such interventions include; helping families to understand the nature of feelings toward patients with dementia and themselves as shown in (Table 4).

Table 4. Types of nonpharmacological approaches

Cognitive training/cognitive rehabilitation Although some studies showed positive results in improving cognition and/or functional performance in persons with dementia, there is insufficient research evidence to any firm conclusions about the effectiveness in improving and/or maintaining cognitive and/or functional performance. Further research is required to be able to conclude the positive findings of cognitive training.
Effectiveness of environmental interventions: No insufficient evidence conclusions about promoting functional performance benefits impact on IADLs and ADLs for mild to moderate dementia.
Individualized exercise: there is good evidence to indicate that programs have an impact on functional performance in persons with mild to moderate dementia
Health diet, evidence showed food with low refined sugars, low saturated fat, and low sodium may improve cognition
Occupational therapy: evidence showed that, it maximizes the level of independency in activities of daily living
Caregiver support: provide day to day support for Alzheimer's caregiver including care training, planning tools and provides tips to cope
Supplements (Souvenaid) is new approach in medical nutrition a dietary management particularly for early dementia**.** It provides a unique combination of nutrients designed to support brain connections (Omega 3, DHA (Docosahexaenoic Acid) and EPA (Eicosapentaenoic Acide), uridine monophosphate, choline, B vitamins and other co- factors) it given once daily drink

B. Pharmacological Interventions

1. Cholinesterase inhibitors

Prevent the breakdown of acetylcholine in the brain. Acetylcholine is involved in learning and memory. Three cholinesterase inhibitors — donepezil, galantamine, and rivastigmine — are used to treat mild to moderate Alzheimer's disease except Donepezil, which also approved for severe cases. They have similar degrees of benefit. The choice of which cholinesterase inhibitor is based on tolerability, adverse effects, ease of use, and cost. And although most people do not experience side effects, the commonest ones are nausea, loss of appetite, vomiting diarrhea, and bradycardia.

If one cholinesterase inhibitor is not well tolerated or the patient develops side effects or is deemed ineffective, patients can be switched to another one or memantine. After initializing of medication, patients should be followed carefully for the development of adverse effects and re-evaluated to determine the response.

Memantine on the other hand is not recommended for patients with mild dementia, but it is an option as either monotherapy or adjunctive therapy (with a cholinesterase inhibitor) for the treatment of moderate to severe Alzheimer's disease. "Namzaric" is a combination of Memantine and Donepezil, also used to treat moderate to severe dementia. Pharmacotherapy for dementia should be stopped if the patient refuses to take the medication, non-adherent, when no response/ no evidence of improvement

Table 5. Medication for Treatment of Dementia

Chemical Class	Generic Name	Trade Name	strengths	Dosage	Side effects
Piperidine	Donepezil	Aricept	5mg, 10mg	Initial does is 5mg/ day taken once daily could be increase to 10mg a day if no side effect is seen after 4-6 weeks. The maximum dose is 10 mg /day	Nausea: 11%• Diarrhea: 10% • Headache: 10% Insomnia: 9%• Pain: 9% <1% CVS – bradycardia, arrhythmias
Carbamate	Rivastigmine	Exlone Exlone patch	1.5mg, 3mg, 4.5mg, 6mg 4.6mg	Initial dose is 1.5mg bid given with meals for 4 weeks. If well tolerated, increase dose to 3 mg twice daily after at least 2 weeks • If well tolerated, increase dose to 4.5 mg twice daily and	Nausea:37% Vomiting: 23% Dizziness: 19% Diarrhea: 16% Headache: 15%

			9.8mg	then to 6 mg twice daily, after at least 2 weeks • Maximum dose is 6 mg twice daily Patch 4.6mg /24hrs for 4 weeks if well tolerated increase to 4.8mg/24hrs	
Phenanthrene Alkaloid	Galantamine	Reminyl R Reminyl ER	Tab:4mg,8mg,12 Liquid: 4mg/ml Extended Release:8mg, 16mg,24mg	Initial does IR: 4mg bid with meals for 4 weeks; increase to 8mg bid after4 weeks ; if no side effects increase to 12mg bid. Initial dose ER does is 8mg am for 4 weeks; increase to 16mg am; if no side effects occur, can increase to 24mg am after 4 weeks. The maximum dose is 24 mg/d	Nausea:17% Dizziness: 10% Headache: 8% Injury:8% Vomiting: 7%
***N*-methyl-D-aspartate (NMDA) receptor antagonist**					
NMDA	Memantine	Ebixa	Tab:5mg, 10mg Solution:2mg/ml	Dose escalation over one month ; 5mg od for 7 days, 5mg bid for 7 days, 10mg am and 5 mg in afternoon for 7 days, then 10mg bid can be taken with or without food	7% Dizziness 6%Confusion: 6%Headache: 6%Hypertension: liver failure
N- Methyl-D aspartate inhibitor					
	Memantine/ Donepezil	Namzaric	28/10mg 14/10mg	Given once daily	

2. **Memantine**

It blockade of current flow through channels of N-methyl-d-asperatate (NMDA) receptors, is approved for moderate to severe Alzheimer's disease, initial dose is 5mg once / day which can be increase if tolerated well to maximum 20mg / day

3. **Amyloid modifying Agents – New medications**

Two anti-amyloid monoclonal antibodies (MABs)—lecanemab (Leqembi) and aducanumab (Aduhelm®)—have been approved in the USA for the treatment of Alzheimer's disease (AD). Anti-amyloid monoclonal antibodies are the first disease-modifying therapies for AD that achieve slowing of clinical decline by intervening in the basic biological processes of the disease. These are breakthrough agents that can slow the inevitable progression of AD into more severe cognitive impairment. The results of trials of anti-amyloid MABs support the amyloid hypothesis and amyloid as a target for AD drug development. Donanemab is the 3rd agent (USAN; development code LY3002813), a biological drug in Phase III clinical trials that showed promising results in slowing the progression of cognitive decline.

⇒ **Special Consideration**

- **Patients with severe Alzheimer's disease:** should be monitored by health care providers at least once every 3-4 months particularly those on pharmacotherapy. The goal of management in severe dementia is to improve the quality of life, maintain optimal function, and provide maximum comfort. Monitoring including as well, medical management for treatable conditions.
- **Neurocognitive symptoms of dementia** There is no single approach or medication, that can be used to treat behavior disturbance in dementia; however, non-pharmacological interventions should be initiated first. They include using behavior-modification techniques, Music therapy… etc. Pharmacologic therapies should be initiated concurrently with non-pharmacologic interventions in the presence of severe depression, psychosis, or aggression that puts the patient or others at risk of harm. Medications, must

- Be initiated at the lowest doses, titrated slowly, and monitored for effectiveness and safety.Atypical antipsychotics can be used for severe agitation, aggression, and psychosis.Recently, the FDA approved brexpiprazole as the First Therapy for Alzheimer's Agitation (FDA NEWS, 2023). However, the potential benefit of all antipsychotics must be weighed against the potential risks, such as cerebrovascular events and death. Benzodiazepines should be used only for short periods.

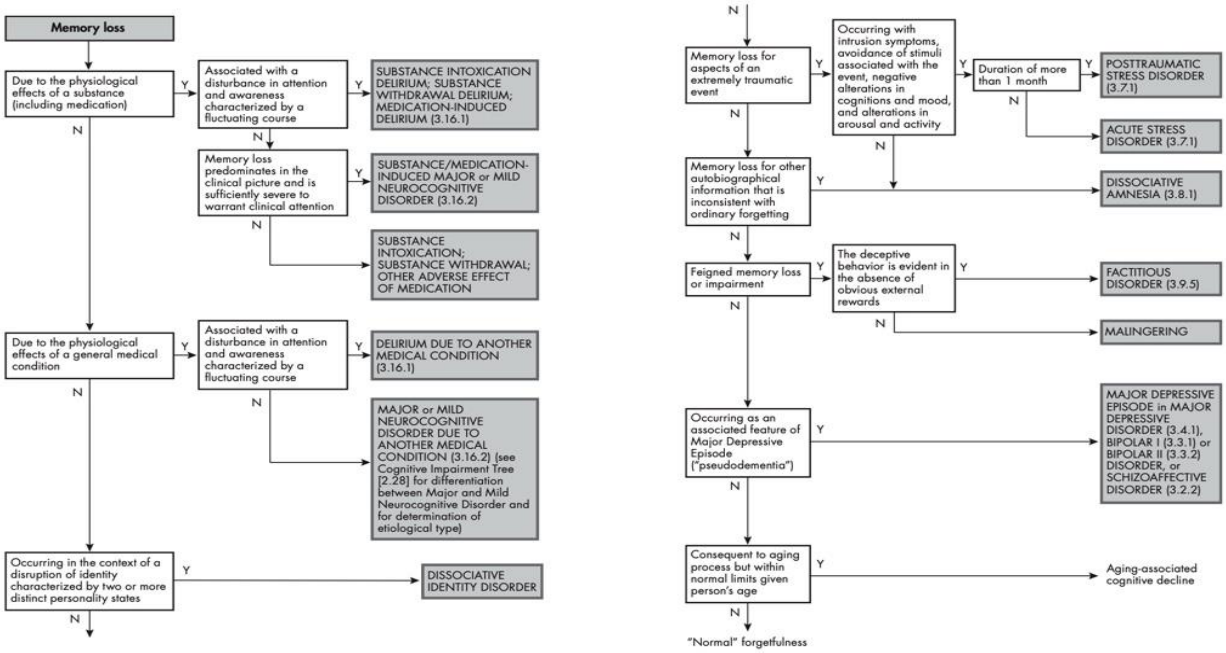
CHAPTER THREE:

- **Responsibilities**

  All healthcare providers, who assess and manage geriatric patients in geriatric specialized unit 1 shall comply with this guideline.

Summery and Decision tree for memory loss and possible diagnosis of Alzheimer disease.

Figure (1): Decision Tree for Memory Loss, American Psychiatric Association, 2014



(Michael, 2014)

Do's and Don'ts of Dementia Care

Providing a positive environment to a person with Alzheimer`s disease with dementia is crucial and easily applicable. The following Dos and Don`ts give a basic approach to the care of persons with dementia.

Dos

==========

- **Do** talk in short, simple sentences of seven words or lesser is better.
- **Do** smile, but not in a mocking way. Facial expression is important.
- **Do** lower your tone of voice as you talk louder and speak clearly if the resident is hard of hearing. Our voice tones tend to get higher when we talk louder, which makes it harder for that person to hear or they may think you are yelling at them.
- **Do** offer food, drinks, or activities according to that person's liking.
- **Do** reminisce with a resident.

Don`ts

==========

- **Don't** ask too many questions. Keep it to minimal choices: "Would you like coffee or juice?"
- **Don't** talk, let the resident think and calmly wait for a response.
- **Don't** stand over the individual in dominance. Instead, talk at eye level.
- **Don't** invade their space, but also **don't** be afraid of touch. A light hand over theirs is reassuring.
- **Don't** disagree, argue, or correct.

CHAPTER FOUR:

Document History and Version Control Table

Version	Description	Review Date
1	**Initial Release**	**December 2027**
2		
3		

References:

Cummings, J. Anti-Amyloid Monoclonal Antibodies are Transformative Treatments that Redefine Alzheimer's Disease Therapeutics. Drugs 83, 569–576 (2023). https://doi.org/10.1007/s40265-023-01858-9

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.Diagnosis and treatment of dementia: 5. Nonpharmacologic and pharmacologic therapy for mild to moderate dementia, *CMAJ* 2008;179(10):1019-26

Diagnosis and treatment of dementia: 3. Mild cognitive impairment and cognitive impairment without dementia CMAJ2008;178(10):1273-85

Diagnosis and treatment of dementia: 3. Mild cognitive impairment and cognitive impairment without dementia, CMAJ 2008;178(10):1273-85

FDA NEWS RELEASE: FDA Approves First Drug to Treat Agitation Symptoms Associated with Dementia due to Alzheimer's Disease, May 11, 2023

Lake, B. B. et al. Alzheimer's drug Donanemqb helps in early disease, Nature 619, 585–594 (2023).

Michael B. DSM-5TM Handbook of Differential Diagnosis, Differential Diagnosis by the Trees; Decision Tree forMemoryLoss139-148 Copyright © 2014 American Psychiatric Association.

Annexes

Appendix 1. Audit Tool

Department: _____

Date: _____

Auditor's Name: _____

#	Criteria	Yes	No	N/a	Remarks
Knowledge of the Guideline/Procedure/Protocol (Interview)					
1	Are the doctors and/or healthcare providers who assess and manage geriatric patients in all healthcare facilities aware about this guideline?				
Observation					
2	Does the doctor adhere to the Criteria of diagnosis conform to the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5); in diagnosing dementia in Alzheimer`s disease?				
3	Does the doctor able to exclude other deferential diagnosis?				
4	Does the doctor able to manage elderly patients with dementia in Alzheimer`s disease?				
5	Does the doctor aware about different medications which are used in managing elderly patients dementia in Alzheimer`s disease?				
6	Does the doctor aware about the special consideration during managing elderly patients with dementia in Alzheimer`s disease?				
7	Does the doctor aware about and Dos & Don`ts in providing care to elderly patients with dementia in Alzheimer`s disease?				

Appendix 2: Document Request Form

Document Request Form			
Section A: To be completed by Document Writer			
Writer Details			
Name	Dr. Saleha Al Jadidi	Date of Request	April 2024
Institution	*Al Masarra Hospital*	Contact information	----
Department	Adult Geriatric Psychiatry		
Purpose of Request: ■ Develop new document ☐ Modify existing document ☐ Cancel existing document			
Document Information			
Document title	Clinical Guideline for Management of Dementia of Alzheimer's Disease		
Document code (for existing documents)	AMRH/PSY/G1/GUD/002/Vers. 01		
Section B: To be completed by **Document Section of Quality Management and Patient Safety**			
■ Approved ☐ Rejected ☐ Cancelled			
Comment and Recommendation: Approved			
Name and Title	Kunooz Al Balushi 	Date	April 2024

Appendix 3: Document Validation Checklist

Document Validation Checklist					
Document Title: Clinical Guideline For Management Of Dementia Of Alzheimer's Disease		**Document Code:** AMRH/PSY/G1/GUD/002/Vers. 01			
No	Criteria	**Meets the Criteria**			**Comments**
		Yes	**No**	**N/A**	
1.	**Approved format used**				
1.1	Clear title – Clear Applicability	✓			
1.2	Footer complete	✓			
1.3	Involved departments contributed	✓			
2.	**Document Content**				
2.1	Clear purpose and scope	✓			
2.2	Clear definitions	✓			
3.	**Well defined procedures and steps**				
3.1	Procedures/methods in orderly manner	✓			
3.2	Procedure/methods define personnel to carry out step	✓			
3.3	Procedures/methods define the use of relevant forms	✓			
3.4	Procedures/methods to define flowchart	✓			
3.5	Responsibilities/Requirements are clearly defined	✓			
3.6	Necessary forms/checklist and equipment are listed	✓			
3.7	Forms/Checklist are numbered	✓			
3.8	References are clearly stated	✓			
4.	**General Criteria**				
4.1	Procedures/methods are adherent to MOH rules and regulations	✓			
4.2	Procedures/methods are within hospital/department scope	✓			
4.3	Relevant central policies are reviewed	✓			
4.4	Used of approved font type and size	✓			
4.5	Language is clear, understood and well structured	✓			
Reviewed by : Kunooz Al Balushi					