REAGILA®
CARIPRAZINE

DOSING GUIDE

Available doses

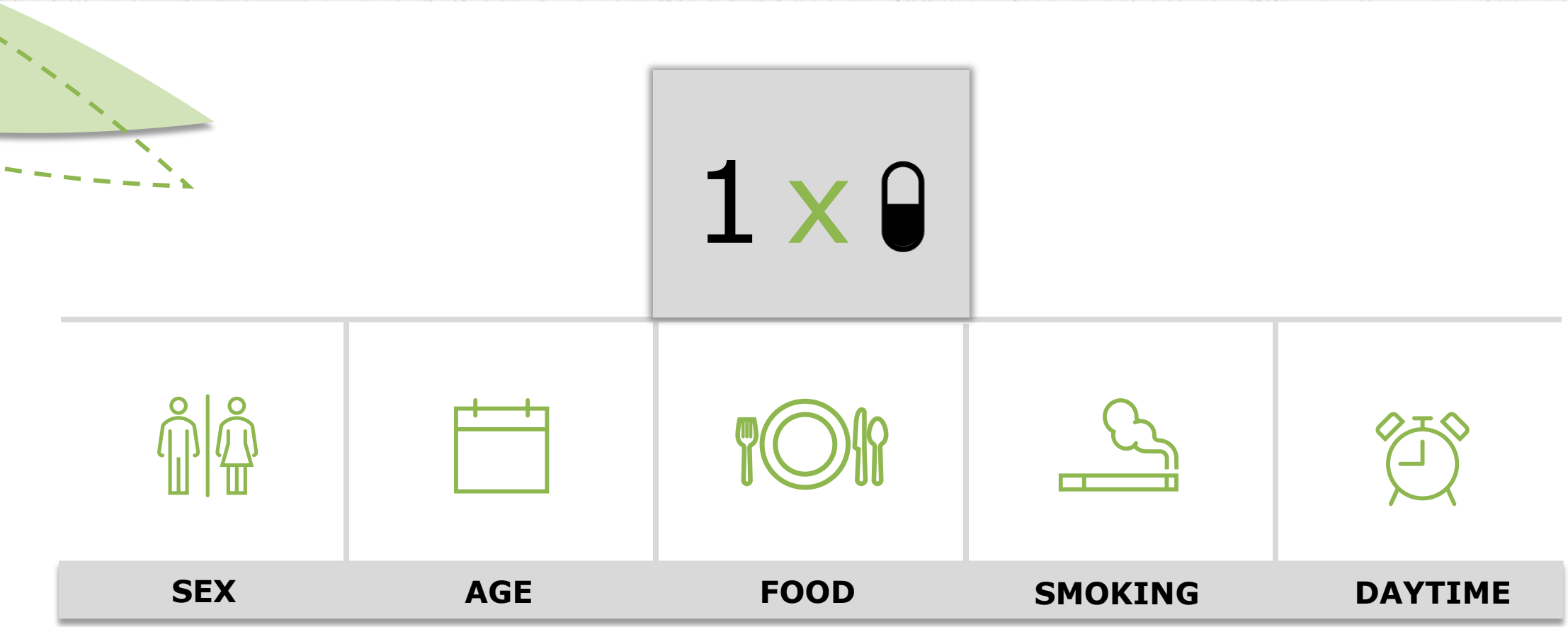
Reagila® is available in four dosages: 1.5 mg, 3.0 mg, 4.5 mg and 6.0 mg for the treatment of schizophrenia in adult patients.[1]

1.5 mg/day	DAILY DOSE	4.5 mg/day	MAXIMUM DOSE
			
STARTING DOSE	**3.0 mg/day**	**OPTIMAL DOSE**	**6.0 mg/day**

START

Method of Administration

Reagila® should be taken once daily at any time during the day without requiring dose adjustments according to:[1]



START

Up-Titration: Fast Dose Escalation

Reagila® dose can be increased **fast** [2-4] (increase by 1.5 mg each day or every second day) until the target dose is achieved.

TITRATION

FAST	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
	1.5 mg/day	3.0 mg/day	4.5 mg/day	6.0 mg/day	6.0 mg/day
	1.5 mg/day	1.5 mg/day	3.0 mg/day	3.0 mg/day	4.5 mg/day

Up-Titration: Slow Dose Escalation

Reagila® dose can be increased **slowly**[5] (increase by 1.5 mg weekly) until the target dose is achieved.

TITRATION

SLOW	WEEK 1	WEEK 2	WEEK 3	WEEK 4	WEEK 5
	1.5 mg/day	3.0 mg/day	4.5 mg/day	6.0 mg/day	6.0 mg/day

As each patient is individually different, slower or faster dose escalation might be necessary depending on the patient's needs and treatment response.[6]

Switching from Another Antipsychotic

In general, when switching from another antipsychotic to Reagila® a gradual cross-titration is advised for patients with schizophrenia.[7]

1-WEEK CROSS-TITRATION

A 1-week cross-titration is recommended when switching from other antipsychotics that have similar receptor profile as cariprazine i.e. other D2 partial agonists. The previous antipsychotic should be tapered off within 1 week, while introducing and escalating the dose of cariprazine within that same week.[7-9]

2-WEEK CROSS-TITRATION

About 2 weeks is necessary if switching from a second-generation antipsychotic that has D2 antagonism. This is necessary in order to avoid dopaminergic rebound causing increased psychotic symptoms, agitation and dyskinesia.[7-9]

ARI – Aripiprazole; BRE – Brexpiprazole; LUR – Lurasidone; RIS – Risperidone

Switching from Another Antipsychotic

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3-WEEK CROSS-TITRATION

Most time should be given when switching from antipsychotics with completely different receptor profiles such as antipsychotics with stronger antihistaminic and/or anticholinergic affinity. By giving enough time, histaminergic and cholinergic rebound can be avoided hence reducing the risk of insomnia, nausea and vomiting.[7-9]

4-WEEK CROSS-TITRATION

Based on US data from the field, a 4-week cross-titration is advised for clozapine. This is also the time when depot neuroleptics get eliminated from the body.[7]

OLA – Olanzapine; QUE – Quetiapine; CLO – Clozapine

Switching from Another Antipsychotic

A full-dose overlap is recommended when switching from another antipsychotic to Reagila®.[8-10] If discontinuation is necessary, no gradual cross-titration is needed.[1]

SWITCHING

FULL-DOSE OVERLAP

A period of overlap with the previous antipsychotic for about 2 weeks, followed by de-escalation of the previous antipsychotic dose (5%-20% every 15 days depending on the previous antipsychotic) **is recommended by various expert panels**.[8-10]

STOPPING

Due to the long half-life of Reagila® (50% decline in ~1 week, greater than 90% decline in ~3 weeks) **the dose can be stopped at once.** The new antipsychotic should be initiated in its lowest dose and potentially maintained low until Reagila is eliminated from the body.[1]

AP – Antipsychotic

Switching from Another Antipsychotic

Complications during switching can arise which should be mitigated accordingly.[8]

SWITCHING

DOPAMINERGIC REBOUND

Dose increase of previous antipsychotic is recommended.

CHOLINERGIC REBOUND

Dose increase of previous antipsychotic or anticholinergic drug e.g. biperiden is recommended.

HISTAMINERGIC REBOUND

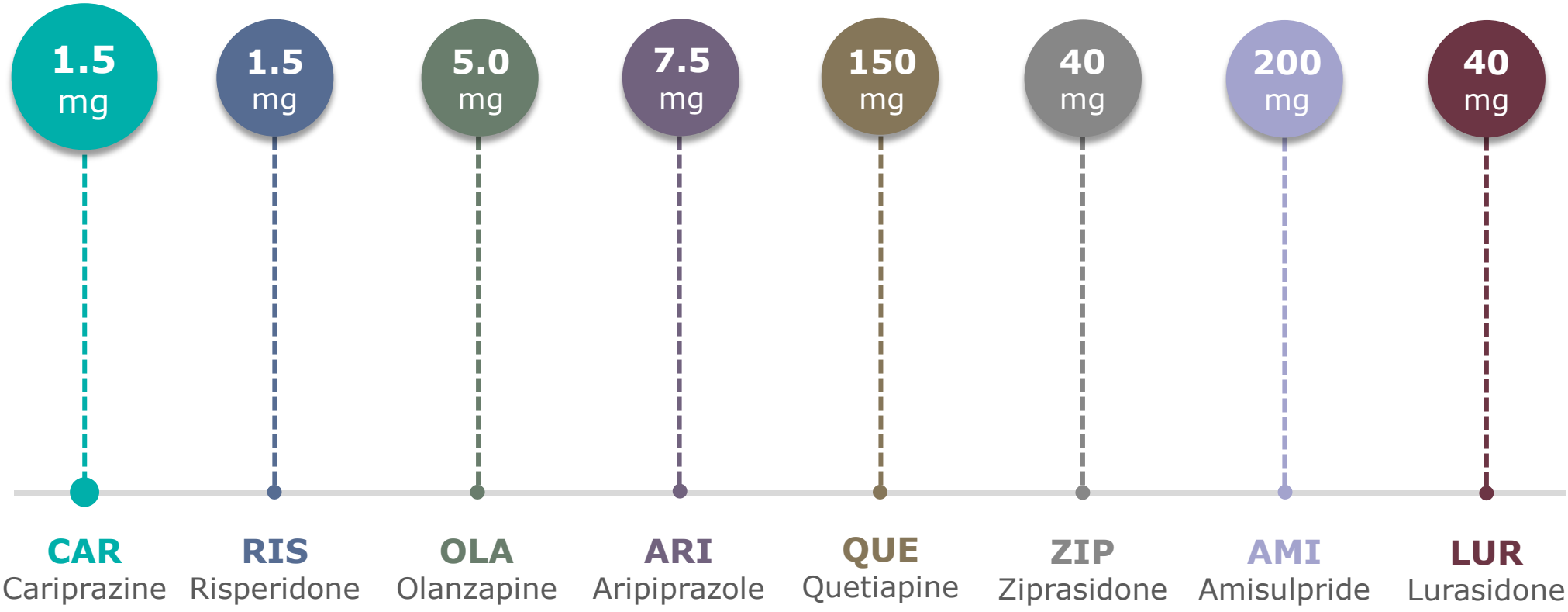
Dose increase of previous antipsychotic or antihistamine drug e.g. hydroxyzine is recommended.

AKATHISIA

The use of an anticholinergic drug or benzodiazepines or beta-blockers e.g. propranolol is recommended.

Dose Equivalencies

Equivalent dosing is important to guarantee fair comparisons of drugs, for treatment guidelines, and when psychiatrists need to switch from one drug to another.[11,12]



Dose Equivalencies

Equivalent dosing is important to guarantee fair comparisons of drugs, for treatment guidelines, and when psychiatrists need to switch from one drug to another.[11,12]

cariprazine 1.5 mg	cariprazine 3.0 mg	cariprazine 4.5 mg	cariprazine 6.0 mg
			
risperidone 1.5-2.0 mg	risperidone 3.0 mg	risperidone 4.5 mg	risperidone 6.0 mg
aripiprazole 7.5 mg	aripiprazole 15.0 mg	aripiprazole 22.5 mg	aripiprazole 30.0 mg
olanzapine 5.0 mg	olanzapine 10.0 mg	olanzapine 15.0 mg	olanzapine 20.0 mg
clozapine 100.0 mg	clozapine 200.0 mg	clozapine 300.0 mg	clozapine 400.0 mg

Abbreviated Summary of Product Characteristics

Reagila® (cariprazine) 1.5 mg; 3 mg; 4.5 mg; 6 mg hard capsule.[1]

SMPC

Name of the medicinal product
Reagila (cariprazine) 1.5 mg; 3 mg; 4.5 mg; 6 mg hard capsule, ATC code: N05AX15.

Therapeutic indications
Reagila is indicated for the treatment of schizophrenia in adult patients.

Posology
The recommended starting dose of cariprazine is 1.5 mg once daily. Thereafter the dose can be increased slowly in 1.5 mg increments to a maximum dose of 6 mg/day, if needed. Because of the long half-life of cariprazine and its active metabolites, changes in dose will not be fully reflected in plasma for several weeks.

Contraindications
Hypersensitivity to the active substance or to any of the excipients, concomitant administration of strong or moderate CY- P3A4 inhibitors or inducers.

Abbreviated Summary of Product Characteristics

Reagila® (cariprazine) 1.5 mg; 3 mg; 4.5 mg; 6 mg hard capsule.[1]

SMPC

Special warnings

Precautions for use: in case of suicidal thoughts or behaviour; in those who are prone to or already exhibit symptoms of akathisia; in patients with Parkinson disease; in patients with risk factors for stroke; in patients with medical history of seizure, cardiovascular disease (blood pressure changes, QT prolongation, risk for venous thromboembolism), diabetes mellitus. If signs and symptoms of tardive dyskinesia appear discontinuation should be considered. Drug discontinuation is recommended if signs and symptoms of neuroleptic malignant syndrome develops. Patients who would develop symptoms potentially related to cataract should be advised to ophthalmologic examination. Weight should be monitored regularly. Not recommended to treat elderly patients with dementia. Capsules of 3 mg, 4.5 mg and 6 mg contain Allura red AC which can cause allergic reactions.

Most common adverse reactions

Akathisia, extrapyramidal symptoms, body weight increase, increased or decreased appetite, dyslipidaemia, sleep disorders, anxiety, sedation, dizziness, blurred vision, tachyarrhythmia, hypertension, nausea, constipation, vomiting, increased liver enzymes and creatinine phosphokinase in blood, fatigue. Not recommended during pregnancy or for fertile women not using reliable contraception. The medicinal product has minor or moderate influence on the ability to drive and use machines.

References

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