CLINICIAN & PATIENT BRIEFING · PRINT EDITION

Surviving Zyprexa

What 12 recent studies say about olanzapine — and one patient's documented recovery protocol

A one-page, plain-language briefing on the harm mechanisms of olanzapine (Zyprexa), the evidence behind a five-part recovery protocol, and the questions a patient should ask before changing anything.

It is written to be read in a consultation, handed to a doctor, or given to a friend. It is deliberately blunt about what the evidence does and does not show.

Prepared from the published dossier at surviving-zyprexa.com
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IMPORTANT — READ FIRST

This document is a patient-reported experience combined with a summary of published literature. It is NOT medical advice, NOT a prescription, and NOT a treatment recommendation.

Do not start, stop, increase or decrease any medication because of anything written here. Stopping olanzapine abruptly can cause severe withdrawal and relapse. Any change must be planned and supervised by a qualified clinician who knows your history.

Every claim about a study is referenced so it can be checked at source. Verify before you rely on it.

1. The two-minute summary

For the clinician: this is what the patient is bringing you, in one page.

The situation

A patient took olanzapine from 1998. Over 27 years he developed profound weight gain (145 kg peak), emotional blunting, loss of musical and affective response, and metabolic deterioration. He reports that these were repeatedly attributed to his psychiatric illness. From 2021 he researched the pharmacology himself and assembled a five-part protocol. He reports functional recovery.

What the recent literature establishes (this part is well supported)

- **Hunger and weight gain are pharmacological.** Olanzapine blocks histamine H1 and serotonin 5-HT2C receptors in the hypothalamus and activates AMPK in the arcuate nucleus. This is the accepted mechanism of its hunger and weight-gain effect — not a behavioural failure by the patient.
- **It is an inflammatory cascade, not overeating.** Weight gain on olanzapine is accompanied by measurable systemic inflammation (IL-6, IL-17, TNF-α) and paradoxical ghrelin suppression. [2]
- **Damage is organ-resolved and weight-independent.** Olanzapine produces organ-level damage independent of weight: skeletal-muscle DNA methylation of PPARGC1A, brown-fat thermogenic shutdown (UCP1), pancreatic β-cell ER stress, and liver fat accumulation. [3][9]
- **Liver injury can appear within two weeks.** A multicentre study of 487 patients found acute hepatotoxicity in 24.2% of olanzapine patients with a median onset of 13 days. A cohort of 9,565 patients found raised diabetes and dyslipidaemia risk even at doses of 1.25 mg or less. [5][10]
- **Betahistine has human safety data.** High-dose betahistine has been studied in humans up to 480 mg/day with linear pharmacokinetics and good tolerability; a randomised trial at 72 mg/day in schizophrenia reported cognitive improvement with unchanged PANSS. [11][17]

What the literature does NOT establish (state this plainly)

- **The protocol itself is unproven.** No randomised controlled trial has tested this five-part protocol, in any population.
- The 12 studies mostly describe how olanzapine causes harm. They are not trials of a treatment.
- Berberine, ketogenic diet, vitamin D3, sulforaphane and NAC have mechanistic and adjacent-disease evidence, not olanzapine-specific outcome data.
- The author's own recovery is a single unblinded case with no control, confounded by simultaneous dietary change and substantial weight loss.

What the patient is asking of you

Not a prescription. He is asking for monitoring and a supervised, safe plan — and for the metabolic damage to be treated as a medical problem in its own right rather than as a symptom of his diagnosis.

THE PRACTICAL ASK

1. Baseline and serial monitoring: LFTs, fasting glucose and HbA1c, lipids, weight, waist circumference, vitamin D and calcium.
2. A supervised taper plan if discontinuation is being considered — never abrupt.
3. A discussion of drug interactions before adding berberine or any supplement.
4. Honest acknowledgment that the metabolic picture is iatrogenic and treatable.

2. What this document is — and what it is not

This document IS	This document IS NOT
A plain-language summary of 12 published papers, each with a DOI you can check.	A peer-reviewed article, a clinical guideline, or a substitute for one.
One person's detailed account of his own drug experience and recovery.	Evidence that the same protocol will work for anyone else.
A structured list of topics, questions and monitoring points for a consultation.	A prescription, a dosing schedule to follow on your own, or a diagnosis.
A record of corrections the author has published against his own earlier claims.	A claim of certainty. Several mechanisms remain hypotheses.
Something designed to be printed, marked up and handed over.	Something that should stop or change any medication you are taking.

How to use it

- **If you are the patient:** Read section 1 (the two-minute summary) — that is the part a clinician needs.
- **If you are the doctor:** Read sections 3 to 6. Check the DOIs. Decide what you think.
- **If you are a friend or relative:** Give them section 1 and section 9. Both fit on single pages.

A note on language and honesty

The original website presents this material in an advocacy voice, with language such as “institutional silence” and “the eviction of psychiatry”. That framing has been deliberately removed from this edition. Advocacy rhetoric costs credibility in a consulting room, and the underlying science does not need it. What is left is the evidence, graded and referenced — including the places where the evidence is weak, and the corrections the author has issued against his own earlier claims (section 9).

A CLAIM OF PRIORITY, STATED FACTUALLY

The author's book was first published on 23 August 2025 (ISBN 979-8299396690). Several independent papers describing the same organ-level injury mechanisms appeared afterwards, in 2025–2026. Whether that constitutes priority is a matter for readers to judge; the dates are the dates. The author's own synthesis paper is listed as reference [19].

3. The patient's timeline

Reported by the patient. Not independently verified. Reproduced because the sequence matters clinically — a slow, decades-long metabolic decline eventually attributed to the illness itself.

Year	What happened	What the literature now says
1995	First psychotic episode, Amsterdam. Cannabis cited as a trigger.	Cannabis is a recognised risk factor for first-episode psychosis.
1998	Olanzapine prescribed — 1 tablet at night. Described as “new, very effective”.	FDA approval 1996. H1/5-HT2C antagonism begins immediately. [1]
1998–99	Rapid weight gain, +20 kg. Facial swelling (“moon face”).	H1 antagonism → arcuate-nucleus AMPK activation → hyperphagia. [13] [14]
2000–10	Music and emotion flatten. Social withdrawal. Heavy cannabis and alcohol use.	Mesolimbic/cortical dopaminergic blunting; reward-circuit silencing. [7]
2017	Peak weight 145 kg.	Cumulative metabolic syndrome; MASLD risk. [3][4]
2020–21	Names the condition himself: “chemical lobotomy”. Begins independent research.	A lay term. Described as persistent functional injury in the author's paper. [19]
2023	Begins betahistine.	H3 antagonism → selective cortical dopamine/acetylcholine release. [17]
2024	Adds berberine and vitamin D3. Liver and lipid markers reported stabilised.	AMPK activation → SREBP-1/2 suppression, CPT1A unblocking. [4]
2025	Therapeutic ketogenic diet; reports the “first thaw” in affect and cognition.	Ketones bypass ER-stressed glucose pathways. [3][9]
2025	Book published; five-pillar protocol documented.	Single case. No control. Confounded by weight loss.

Current reported status — to be completed by the patient before the appointment

Measurement	Patient's value	Date	Notes for the clinician
Weight / waist circumference			
ALT / AST / GGT			
Fasting glucose / HbA1c			
Lipid panel (LDL, HDL, triglycerides)			
25-OH vitamin D / calcium			
Blood pressure			
Current olanzapine dose			
Other medications / supplements			

Patient signature: _____ Date: _____

Clinician comments / plan:

_____

_____

_____

_____

4. What olanzapine does — six mechanisms in plain language

1. It switches off the brain's “I am full” signal

Olanzapine blocks the histamine H1 receptor in the hypothalamus, the brain's appetite control centre. That blockade activates a cellular switch called AMPK in the arcuate nucleus, which tells the body it is starving even after a full meal. The result is genuine, drug-driven hunger — not a failure of willpower. This is the best-established mechanism in the entire dossier. [1][13][14]

2. It inflames the body

Patients on olanzapine show elevated inflammatory cytokines (IL-6, IL-17, TNF-α), endothelial stress, and the paradoxical combination of suppressed ghrelin with expanding waist circumference. One paper describes this as dismantling the idea that the weight gain is simply overeating. [2]

3. It damages organs independently of weight

Even when weight is accounted for, olanzapine is associated with methylation of PPARGC1A in skeletal muscle, shutdown of brown-fat thermogenesis (UCP1), ER stress in pancreatic β-cells, and fat accumulation in the liver. These are changes in how cells make and burn energy. [3]

4. It silences the liver's fat-burning programme

In the liver, antipsychotics force on the lipogenesis programme (SREBP-1/2) and block the enzyme CPT1A that would otherwise burn fat. The result is classified in the literature as MASLD — metabolic dysfunction-associated steatotic liver disease. [4]

5. It rewrites part of the genome's regulation

In healthy volunteers — not people with psychiatric illness — olanzapine directly induced DNA methylation of metabolic genes in skeletal muscle (PPARGC1A, PRKAR1B, RPTOR). Methylation is a chemical tag that can silence a gene. This is one of the strongest findings in the dossier, because the participants had no psychiatric diagnosis, so the effect cannot be attributed to the illness. [9]

6. It can damage the liver within two weeks

A multicentre real-world study of 487 patients found acute hepatotoxicity in 24.2% of olanzapine patients, with the median onset at just 13 days. This is the single most clinically actionable number in the dossier. It argues for liver monitoring early, not at six months. [5]

CLINICAL TAKEAWAY

The metabolic and hepatic picture in a long-term olanzapine patient should not be assumed to be behavioural or psychiatric. The literature describes a measurable, drug-induced, partly epigenetic injury process — and it is monitorable with ordinary blood tests.

One caution: a cohort of 9,565 patients found raised diabetes and dyslipidaemia risk even at microdoses (≤ 1.25 mg), so there is no reassuringly low dose to point to. [10]

5. The 12 studies

Summarised in plain language. Every DOI is given so you can read the original. The "strength" column is an honest assessment of study design — see section 8 for how to read it.

#	Study	What they did	What they found	Strength
1	[1] Oruch et al. 2025 J Clin Med	Review of olanzapine's metabolic effects and discontinuation.	Mapped H1 and 5-HT2C blockade, mitochondrial depolarisation, fat-soluble accumulation, and dopamine supersensitivity after stopping.	Review
2	[2] Alharbi et al. 2026 Front Pharmacol	Compared systemic, metabolic and inflammatory effects of olanzapine, haloperidol and both together, in patients.	Systemic inflammation (IL-6, IL-17, TNF-α), endothelial stress, suppressed ghrelin, rapid waist growth. Weight gain is inflammatory, not behavioural.	Clinical observational
3	[3] Weng et al. 2026 Front Pharmacol	Organ-by-organ review of olanzapine's peripheral metabolic damage.	Muscle PPARGC1A methylation, brown-fat UCP1 shutdown, pancreatic β-cell ER stress, liver fat. Damage is weight-independent.	Review
4	[4] Gonzalez-Pena et al. 2026 Ann Hepatol	Molecular and clinical review of antipsychotic liver injury as MASLD.	Forced SREBP-1/2 lipogenesis, blocked CPT1A fat oxidation, mitochondrial dysfunction, liver fat trapping.	Review
5	[5] Wang et al. 2026 Drug Des Devel Ther	Multicentre retrospective study of 487 real patients on olanzapine.	24.2% incidence of acute hepatotoxicity; median onset 13 days (raised ALT, AST, GGT).	Cohort N=487
6	[6] Peisley et al. 2026 Nat Commun	Cryo-EM structural study of the Kir7.1 potassium channel and MC4R.	Mapped the structural coupling of MC4R–Kir7.1 in energy homeostasis. NOTE: this pathway belongs to clozapine and risperidone, not olanzapine.	Basic science

The 12 studies (continued)

#	Study	What they did	What they found	Strength
7	[7] Huang et al. 2026 Front Pharmacol	Circuit-level study of metabolic synaptic signalling in the dorsal raphe nucleus.	Central serotonergic changes affect autonomic control and affective circuits — a mechanism for flattened emotion and reward.	Basic science
8	[8] Li et al. 2026 Nat Commun	Functional study of MC4R–Kir7.1 coupling in antipsychotic weight gain.	Confirms the coupling drives clozapine/risperidone weight gain. Explicitly shows olanzapine does NOT work this way — a useful boundary.	Basic science
9	[9] Frond, Rettig & Burghardt 2025/26 Epigenomics	Genome-wide DNA methylation profiling in healthy human volunteers taking olanzapine.	Direct methylation of metabolic genes in skeletal muscle (PPARGC1A, PRKAR1B, RPTOR) in people with no psychiatric illness.	Human experimental
10	[10] Kang et al. 2025 J Pers Med	Nationwide cohort of 9,565 patients on olanzapine.	Raised glucose dysregulation, hypertriglyceridaemia and new-onset diabetes even at ≤ 1.25 mg. No safe threshold identified.	Large cohort
11	[11] Strupp et al. 2023 Front Neurol	Prospective randomised dose-escalation pharmacokinetic and safety trial of betahistine, up to 480 mg/day, in Ménière's disease.	Linear pharmacokinetics, good tolerability, no central toxicity at multiples of the standard dose. Safety and PK only — not efficacy.	Human trial (safety)
12	[12] ADA cohort 2026 Diabetes (abstract)	Conference abstract on the Systemic Immune-Inflammation Index in antipsychotic cohorts.	Raised SII, GLP-1 axis breakdown, NLRP3 inflammasome activation, accelerated insulin resistance. Authorship to be confirmed.	Abstract (weakest)

Study strength key: Abstract < Basic science < Review < Cohort < Human experimental < Randomised trial. None of the 12 is a randomised controlled trial of the five-pillar protocol.

6. What the evidence does not show

This section exists because leaving it out would make the rest of the document untrustworthy. If a patient hands you a protocol with no stated limits, treat it with suspicion. Here are the limits.

There is no trial of the protocol

Not one of the 12 studies tested betahistine, berberine, vitamin D3, a ketogenic diet and sulforaphane/NAC together, or in this combination, or in olanzapine-treated patients as a bundle. The protocol is a reasoned hypothesis assembled from separate findings. That is a legitimate way to generate a hypothesis, and an illegitimate way to claim a treatment.

Most of the 12 studies describe harm, not treatment

Eleven of the twelve are about what olanzapine does to the body. They support the argument that the damage is real and pharmacological. They do not support the claim that any particular intervention reverses it.

The intervention evidence is thin and partly animal-based

- Betahistine: human safety data at high dose (Ménière's, not psychiatric) [11], one randomised trial at 72 mg/day in schizophrenia reporting cognitive improvement with unchanged PANSS [17], and animal receptor-binding studies [15][16]. No trial of betahistine for olanzapine-induced weight gain.
- Berberine: mechanistic and metabolic-syndrome literature. No olanzapine-specific outcome trial.
- Ketogenic diet: rationale from ER stress and methylation findings [3][9]. Not studied in olanzapine-treated patients.
- Vitamin D3, sulforaphane, NAC: immunomodulatory and antioxidant rationale [2][12]. Adjacent-disease evidence, not antipsychotic-specific outcomes.

The author's outcome is a single unblinded case

One person, no control group, no blinding, and several changes made at the same time — including major dietary change and substantial weight loss, both of which independently improve metabolic markers and mood. Any recovery cannot be attributed to the protocol rather than to those confounders, or to time, or to placebo. An n=1 observation can justify a hypothesis and a conversation. It cannot justify a prescription.

Two specific off-label points

- Betahistine is not licensed for olanzapine-induced weight gain or for any psychiatric indication in most countries. High doses are outside the licensed range. This is off-label prescribing.
- A recent paper popular in online discussions attributes olanzapine weight gain to the MC4R–Kir7.1 channel. That attribution is wrong for olanzapine — the same studies show olanzapine does not act through it at all [6][8]. The correct olanzapine pathway is H1 → AMPK [13][14].

THE HONEST SUMMARY

The harm mechanisms are well documented and clinically relevant. The recovery protocol is a plausible, mechanistically motivated hypothesis with no direct trial evidence. That distinction should survive every conversation about this document.

7. The three-step sequence behind the protocol

The protocol is built on a claim about order: some things have to happen before others can. Presented here as the author's model, not as established fact.

Step 1 — Hypothalamus: stop the false starvation

Goal: switch the “I am starving” signal back off, so hunger returns to normal and the body stops storing fat defensively.

Reasoning: olanzapine blocks H1, which activates AMPK in the arcuate nucleus. Betahistine acts on H1/H3; ketone bodies supply fuel that does not depend on the blocked glucose pathway. [13][14]

Step 2 — Prefrontal cortex: bring emotion and focus back

Goal: relieve the emotional numbness (anhedonia), restore focus, and recover responsiveness to music and reward.

Reasoning: betahistine blocks the presynaptic H3 autoreceptor, which releases dopamine and acetylcholine locally in the cortex. The claim is that this is a cortical effect. [7][17]

Step 3 — Striatum: keep the risk of psychotic rebound at zero

Goal: improve function without provoking psychosis or involuntary movements.

Reasoning: the claim is that H3 modulation is selective for the cortex and does not raise dopamine in the striatum, so supersensitised D2 receptors are not triggered. [1][11][12]

WHY STEP 3 MATTERS MOST TO A CLINICIAN

Any intervention that raises dopamine carries a theoretical risk of precipitating psychosis in a patient with a psychotic history. The entire design argument for betahistine over a dopaminergic agent rests on cortical selectivity. This is a mechanistic hypothesis supported by animal receptor-binding work and human safety data [11][15][16] — it is not proven in this population, and it is the point at which a clinician should be most cautious.

8. The five-part protocol, as documented

This is what the author reports taking and doing. It is reproduced for completeness and for discussion — not as a recommendation. Doses are the author's, monitored by his own clinician.

Pillar 1 — High-dose betahistine

Central H1 agonist / H3 antagonist · reported dose 28.8 mg/day at breakfast

What it is: A histamine analogue normally used for Ménière's disease and vertigo.

Why it is included: Acts on the same H1 receptor olanzapine blocks, and blocks the H3 autoreceptor to release dopamine and acetylcholine in the cortex. Aimed at Step 1 and Step 2 of the sequence.

Evidence behind it: Human safety and pharmacokinetics up to 480 mg/day [11]; one randomised trial at 72 mg/day in schizophrenia reporting cognitive improvement with unchanged PANSS [17]; animal receptor-binding studies [15][16]. No trial in olanzapine-induced weight gain.

Safety notes: Off-label in most countries and often prescription-only. Reported adverse effects include nausea, headache and gastric irritation. Contraindicated in phaeochromocytoma and in patients on antihistamines that block H1, which would defeat the purpose.

Pillar 2 — Berberine

Direct AMPK activator · reported dose 500 mg with lunch

What it is: A plant alkaloid used in metabolic and glucose research.

Why it is included: Activates AMPK, suppresses the SREBP-1/2 fat-making programme, and unblocks CPT1A so the liver and muscle can burn fat again — directly aimed at the MASLD mechanism in [4].

Evidence behind it: Mechanistic and metabolic-syndrome evidence, plus the molecular targets identified in [4][3][10]. No olanzapine-specific outcome trial.

Safety notes: Clinically important drug interactions: berberine inhibits CYP3A4 and P-glycoprotein and can raise blood levels of many drugs — including ciclosporin, some statins, and others. It can cause GI upset and may lower blood glucose. It must be reviewed against the full medication list before use.

Pillar 3 — Therapeutic vitamin D3

Circadian and neuro-immune regulation

What it is: Vitamin D3 at therapeutic rather than maintenance dose.

Why it is included: Aimed at the cytokine cascade (IL-6, IL-17, TNF-α) documented in [2], and at the GLP-1 axis changes reported in [12].

Evidence behind it: Immunomodulatory rationale from [2][12]. No antipsychotic-specific outcome data.

Safety notes: SAFETY ALERT — this protocol specifically forbids vitamin K2. The author is heterozygous for Factor V Leiden (F5 rs6025), which raises venous thromboembolism risk 3- to 8-fold, making K2 (MK-7) contraindicated. Most commercial vitamin D products are sold combined with K2. Check the label. High-dose vitamin D requires monitoring of 25-OH vitamin D and calcium for toxicity.

Pillar 4 — Therapeutic ketogenic diet

Alternative neuronal fuel, bypassing ER-stressed glucose pathways

What it is: A ketogenic diet producing beta-hydroxybutyrate.

Why it is included: If glucose uptake is impaired by ER stress and PPARGC1A methylation [3][9], ketone bodies can fuel mitochondria directly, restoring ATP production without depending on the blocked pathway.

Evidence behind it: Mechanistic rationale from [3][9][10]. Not studied in olanzapine-treated patients.

Safety notes: Requires clinical supervision. Risks include electrolyte disturbance, constipation, dyslipidaemia, and — critically — euglycaemic diabetic ketoacidosis when combined with SGLT2 inhibitors. Caution in renal impairment, pancreatitis, and in patients on insulin or sulfonylureas.

Pillar 5 — Targeted cellular nutrition and phase-2 support

Sulforaphane, N-acetylcysteine (NAC), bioavailable protein

What it is: Compounds that support the liver's phase-2 detoxification and glutathione synthesis.

Why it is included: Wang et al. found a 24.2% hepatotoxicity rate with median onset at 13 days [5]. The rationale is to support hepatic clearance during the acute window and to support synaptic repair.

Evidence behind it: Rationale from [5][2][7][9][12]. Adjacent-disease evidence; no antipsychotic-specific outcome trial.

Safety notes: NAC is generally well tolerated but can potentiate nitroglycerin and cause GI upset or bronchospasm in asthma. Sulforaphane from broccoli-sprout sources is generally benign; concentrated supplements are less well characterised. High-risk agents (for example selegiline) are explicitly excluded by the protocol.

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9. Safety alerts

Read this before acting on anything else in this document.

1. DO NOT STOP OLANZAPINE ABRUPTLY

Abrupt discontinuation of olanzapine can cause severe withdrawal symptoms — insomnia, nausea, agitation, anxiety, sweating and tremor — and can precipitate relapse of psychosis, particularly through dopamine supersensitivity [1]. Any reduction must be gradual, planned and supervised. A taper of months, not days, is often appropriate. This is not a reason to stay on a drug indefinitely; it is a reason to stop safely.

2. VITAMIN K2 IS CONTRAINDICATED IN THIS PROTOCOL

The author carries Factor V Leiden (F5 rs6025), which multiplies venous thromboembolism risk several times over. Vitamin K2 (MK-7) is therefore absolutely contraindicated for him, and he has asked that this be treated as a warning rather than a preference. Because most vitamin D supplements are sold combined with K2, read the label. If you have any thrombophilia, discuss this with your clinician before taking any vitamin K-containing product.

3. SUPPLEMENTS INTERACT WITH PRESCRIPTION DRUGS

Berberine inhibits CYP3A4 and P-glycoprotein and can raise the blood concentration of many medicines, including ciclosporin and certain statins. Vitamin D at high dose needs calcium and 25-OH-D monitoring. NAC can potentiate nitroglycerin. Bring the full list — prescription, over-the-counter and supplement — to your clinician before adding anything.

4. THE KETOGENIC DIET IS NOT A CASUAL INTERVENTION

In patients taking SGLT2 inhibitors, a ketogenic diet carries a risk of euglycaemic diabetic ketoacidosis, which can occur with normal blood glucose and is easily missed. It also requires attention to electrolytes, renal function, lipids and pancreatitis risk. Supervise it.

5. THIS IS NOT MEDICAL ADVICE

Nothing in this document is a diagnosis, a prescription, or a treatment recommendation. It is a patient's account and a summary of published papers. Decisions about your medication belong to you and a qualified clinician who knows your history.

10. How to weigh the evidence

A short guide so that the strength of each claim can be judged at a glance.

Tier	Study design	What it can establish	Where it appears here
Highest	Randomised controlled trial	Whether an intervention causes an outcome.	[11] safety/PK only — randomised but not an efficacy trial in this population; [17] betahistine RCT in schizophrenia
	Large prospective cohort	Association and risk over time, better than case series.	[10] N=9,565 olanzapine patients
	Retrospective real-world cohort	Prevalence and timing of harms in practice.	[5] N=487, hepatotoxicity at median 13 days
	Human experimental / mechanistic	That a biological change occurs in humans.	[9] DNA methylation in healthy volunteers
	Clinical observational	That measurements differ between groups.	[2] inflammatory markers in patients
	Narrative review	That evidence has been gathered and interpreted — not new data.	[1][3][4]
	Basic science / animal / in vitro	Plausible mechanism only. Often does not transfer.	[6][7][8][13][14][15][16]
Lowest	Conference abstract / single case report	Hypothesis generation only.	[12] abstract; the author's own n=1

Three questions to ask of any claim in this document

- **1.** What kind of study is this, and does it actually measure the outcome being claimed?
- **2.** Does the study population resemble me, or is it animals, healthy volunteers, or a different disease?
- **3.** Could the outcome be explained by something else — weight loss, diet, time, placebo, or stopping a drug?

Applying those questions to the protocol

Claim	Best available support	Verdict
Olanzapine causes drug-driven hunger and weight gain via H1 → AMPK, not behaviour	Established mechanism, reviews and animal work [1][13][14]	Well supported
Olanzapine causes inflammation and organ-level metabolic injury	Human cohorts and human methylation study [2][3][5][9][10]	Well supported
Liver injury can occur within ~2 weeks	N=487 real-world cohort [5]	Well supported
There is no safe microdose for metabolic risk	N=9,565 cohort [10]	Supported
High-dose betahistine is tolerable in humans	Randomised PK/safety trial [11]	Supported (safety only)
Betahistine improves cortical function in schizophrenia	One randomised trial, 72 mg/day [17]	Preliminary
Betahistine reverses olanzapine-induced weight gain	Mechanistic reasoning; no dedicated trial	Unproven
Berberine reverses MASLD caused by olanzapine	Mechanistic reasoning; adjacent-disease evidence	Unproven
This five-part protocol produces recovery	One unblinded case with major confounders	Unproven

11. Questions to take to your clinician

Print this page, fill it in, and take it to the appointment. Tick the boxes as they are covered.

About monitoring

☐ Can I have baseline liver function tests (ALT, AST, GGT) and a repeat within the first month?

☐ Can we monitor fasting glucose and HbA1c, even though my dose is low?

☐ Can we check a full lipid panel and my waist circumference, not just my weight?

☐ Should we check 25-OH vitamin D and calcium before I take any high-dose vitamin D?

☐ How often should these be repeated, and what change would trigger action?

About the medication itself

☐ Given my results, is my current olanzapine dose still justified?

☐ If we reduce it, what schedule would you use, and how slowly?

☐ What withdrawal symptoms should make me contact you urgently?

☐ Are there signs of dopamine supersensitivity or tardive symptoms I should watch for?

☐ Is there an alternative antipsychotic with a better metabolic profile for me?

About anything I want to add

☐ I am considering betahistine / berberine / vitamin D3 / a ketogenic diet. What do you think of each?

☐ Do any of those interact with my current medication list?

☐ Which of them would you be willing to supervise, and which would you advise against?

☐ If you are not comfortable supervising them, who could I be referred to?

☐ Would a dietitian or endocrinology referral be appropriate for the metabolic side?

Notes from the appointment

12. Corrections the author has published against his own work

Recorded here because it is the strongest available evidence about how carefully this material is maintained. These are the author's own errata, dated 12 October 2026.

#	What was wrong	What was corrected
1	A claim that MC4R–Kir7.1 channel coupling explains olanzapine weight gain.	Not an olanzapine mechanism. The source studies show olanzapine does not act through Kir7.1 at all; the coupling belongs to clozapine and risperidone. Step 1 of the model now rests on the H1 → AMPK pathway [6][8][13][14].
2	Vitamin K2 was included in the vitamin D pillar.	Removed. Absolute contraindication because of the author's Factor V Leiden (F5 rs6025), which multiplies venous thromboembolism risk.
3	PMID 23994047 was described as a human double-blind trial.	It is a rat receptor-binding study (Lian et al., 2013/2014). The genuine human randomised double-blind trial is Wang et al., Front Psychiatry 2021;12:762656 (PMID 34790138, 72 mg/day) [17].
4	Two references could not be traced.	Gjerde et al. (2026) and DOI 10.3390/ijms27088471 were withdrawn pending verification. An earlier LMU Munich reference was replaced with the verified PK-BeST trial [11]. Oruch et al. is now classified as a review, not primary research.

WHY THIS PAGE IS INCLUDED

A document that corrects itself is more trustworthy than one that never does. If you find something in this briefing that does not match the primary source, the source is right and this document is wrong — please say so, and it will be corrected in the next version.

13. References

The 12 studies, plus supporting sources cited in the protocol. All DOIs are given so they can be checked at source. Verify before relying on any of them — this edition reproduces the findings as characterised by the original dossier, not as re-abstracted by a clinician.

The 12 studies

[1] Oruch R. et al. Drawbacks of Olanzapine Therapy: An Emphasis on Its Metabolic Effects and Discontinuation. J Clin Med. 2025;14(22):8125. doi:10.3390/jcm14228125

[2] Alharbi et al. Beyond antipsychotic efficacy and toward an individualized therapeutic strategy: systemic, metabolic and inflammatory effects of olanzapine, haloperidol and their combination. Front Pharmacol. 2026;17:1727959. doi:10.3389/fphar.2026.1727959

[3] Weng et al. Olanzapine and peripheral metabolic dysregulation: organ-resolved mechanisms, risk, and MASLD-aligned care pathways. Front Pharmacol. 2025/2026;16:1729264. doi:10.3389/fphar.2025.1729264

[4] Gonzalez-Pena et al. Clinical and molecular implications of antipsychotics in MASLD. Ann Hepatol. 2026;31(2):102158. doi:10.1016/j.aohep.2025.102158

[5] Wang et al. Olanzapine-Associated Hepatotoxicity in Bipolar Disorder: A Multicenter Real-World Study of Prevalence, Risk Factors, and Outcomes. Drug Des Devel Ther. 2026;20:598447. doi:10.2147/DDDT.S598447

[6] Peisley et al. Structural and functional studies of inward rectifier Kir7.1 and its regulation by the Melanocortin-4 receptor. Nat Commun. 2026;17. doi:10.1038/s41467-026-75941-6

[7] Huang et al. Regulation on the metabolic synaptic pathway in the dorsal raphe nucleus. Front Pharmacol. 2026 (Neuropharmacology). No DOI published at time of writing.

[8] Li et al. Functional coupling between MC4R and Kir7.1 contributes to clozapine-induced weight gain. Nat Commun. 2026;17. doi:10.1038/s41467-026-76561-w

[9] Frond, Rettig & Burghardt. Genome-wide DNA methylation profiling in human skeletal muscle reveals olanzapine-induced epigenetic alterations in metabolic pathways. Epigenomics. 2025/2026;17:2489341. doi:10.1080/17501911.2025.2489341

[10] Kang et al. Dose-dependent metabolic dysregulation and new-onset diabetes associated with olanzapine exposure: a nationwide cohort study of 9,565 patients. J Pers Med. 2025;15(8):380. doi:10.3390/jpm15080380

[11] Strupp et al. (LMU Munich). High-dose betahistine in patients with Meniere's disease: a prospective, randomized, open-label, dose-escalation, pharmacokinetic and safety study (PK-BeST). Front Neurol. 2023;14:1271640. doi:10.3389/fneur.2023.1271640

[12] ADA cohort. Systemic Immune-Inflammation Index and Accelerated Cardio-Metabolic Breakdown in Second-Generation Antipsychotic Cohorts. Diabetes. 2026;75(Suppl 1):1644-P. doi:10.2337/db26-1644-P (abstract; authorship to be confirmed)

Supporting sources cited in the protocol

[13] He et al. Psychoneuroendocrinology. 2014;42:153–164. (H1 → AMPK mechanism for olanzapine hyperphagia)

[14] He et al. Endocrinology. 2014;155(12):4895–4904. (ARC AMPK activation and weight gain)

[15] Lian et al. Prog Neuropsychopharmacol Biol Psychiatry. 2013/2014;48:196–203. PMID 23994047. (Rat receptor-binding study — see correction 3)

[16] Lian et al. Prog Neuropsychopharmacol Biol Psychiatry. 2015;56:75–80. PMID 25149912.

[17] Wang et al. Front Psychiatry. 2021;12:762656. PMID 34790138. (Randomised double-blind trial, betahistine 72 mg/day in schizophrenia)

[18] Abbasi Jannatabadi et al. J Psychopharmacol. 2025;39(8):804–814. PMID 40624881. (Weight and metabolic effects under olanzapine/risperidone)

[19] Filippi G.P.S. The Chemical Lobotomy: A Mechanistic Synthesis of Persistent Functional Brain Injury Following Olanzapine Exposure. Academia.edu, version 1.1, 12 October 2026. ORCID 0009-0009-0098-4429

Further reading and primary sources

- Full interactive dossier, all 12 studies and the complete protocol: surviving-zyprexa.com/dossier
- Book: “Surviving Zyprexa” / “Sobrevivendo ao Zyprexa”, Gabriel Filippi, first published 23 August 2025 (ISBN 979-8299396690). Four language editions.
- Author's ORCID record: orcid.org/0009-0009-0098-4429

14. How to share this, and what to do next

If you are the patient

- Print sections 1, 6, 9 and 11. That is five pages and it is enough for most consultations.
- Bring your actual blood test results with it. The document argues for monitoring; the numbers make the case.
- Ask for the monitoring, not the prescription. You are far more likely to be heard, and you are asking for something a clinician can do immediately.
- Do not stop or reduce anything on your own. Re-read Safety Alert 1.
- If your clinician disagrees with the literature, that is a legitimate discussion — but ask them to explain specifically which study they dispute and why, and write it down.

If you are the clinician

- Treat the inflammatory and hepatic findings as testable in your own patient: LFTs early, HbA1c and lipids even at low dose, waist circumference not just weight.
- Sections 6 and 10 state the limits of this evidence explicitly. The protocol is unproven, and the document says so.
- The one point that is defensible on mechanism alone is that a patient's metabolic deterioration should be investigated rather than attributed to their psychiatric diagnosis.

If you are a friend or relative

- Section 1 is the one to read. It explains why the weight gain and the emotional flatness are not a failure of character.
- The most useful thing you can do is help them get blood tests and get to an appointment with this document in hand.

"You are not broken. You were injured. And injuries can be understood, treated, and healed."

Surviving Zyprexa — Patient & Literature Briefing, version 1.0, October 2026.

Compiled from the published dossier at surviving-zyprexa.com. Author of the underlying work: Gabriel Filippi (ORCID 0009-0009-0098-4429).

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