Olanzapine and Samidorphan Combination for Early and Sustained Treatment of Schizophrenia and Bipolar I Disorder: A Plain Language Summary

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Why consider OLZ/SAM across the treatment course?

Olanzapine is one of the most effective medications for schizophrenia and bipolar I disorder (BD-I).[1,2] However, many patients who take it experience weight gain and metabolic changes.[1,3]

- Clinicians may hesitate to prescribe olanzapine early in treatment due to weight gain and metabolic concerns that can affect treatment decisions[4]
- Patients with schizophrenia or BD-I who are early in their illness are at higher risk for weight gain on olanzapine,[5] which may limit its long-term use
- The combination of olanzapine and samidorphan (OLZ/SAM) was developed to retain the effectiveness of olanzapine but with less weight gain

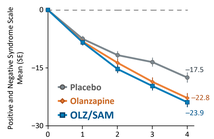
The effectiveness, weight, and metabolic profile of OLZ/SAM may support long-term treatment across the course of illness

What happens in clinical studies after starting OLZ/SAM?

OLZ/SAM improved symptoms similar to olanzapine, with less weight gain and small metabolic changes.[4,6] These effects were also seen in early-in-illness patients, who are at greater metabolic risk with olanzapine.[6,7]

ESTABLISHED EFFICACY

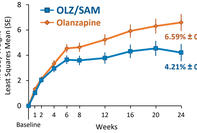
- OLZ/SAM improved symptoms in the 4 weeks after treatment started[4,6,8]



- Symptom control was maintained over longer treatment durations of 3 months and 6 months[4,6]

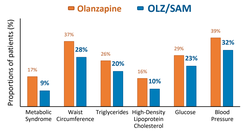
LESS WEIGHT GAIN

- Patients on OLZ/SAM treatment gained 3 to 4 pounds less than those taking olanzapine, over 12 and 24 weeks, respectively[4,6]
- After about 4 weeks of treatment, weight stabilized for patients taking OLZ/SAM, but those taking olanzapine kept gaining weight[4,6]



MINIMAL METABOLIC CHANGES

- OLZ/SAM had a lower risk than olanzapine of worsening metabolic health, including developing obesity, hypertension, and metabolic syndrome[9]
- Fewer patients developed metabolic syndrome during OLZ/SAM treatment[9]



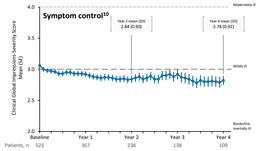
OLZ/SAM offers a treatment approach that improves symptoms with less weight gain and metabolic changes compared with olanzapine treatment

Are OLZ/SAM's outcomes maintained over time?

With long-term OLZ/SAM treatment, patients' symptoms remained stable for up to 4 years.[10] Across long-term studies, changes in weight were small, and changes in metabolic health were minimal.[10-12]

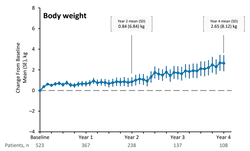
SUSTAINED EFFECTIVENESS

- A concern when treating schizophrenia and BD-I is whether symptom control can be sustained over long-term treatment[13]
- OLZ/SAM's symptom control was maintained for up to 4 years of treatment[10-12]



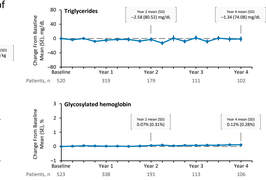
SMALL CHANGES IN BODY WEIGHT

- Patients experienced small changes in body weight during up to 4 years of OLZ/SAM treatment[10-12]
- For context, in a study of 120,000 adults between 1986 and 2006, participants gained an average of 1.52 kg over each 4-year period[10]



MINIMAL METABOLIC CHANGES

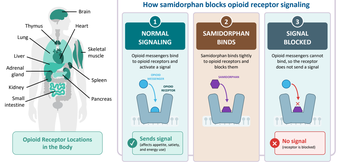
- Minimal changes in fat and sugar levels in the blood were reported for up to 4 years of OLZ/SAM treatment[10-12]



Sustained effectiveness, small changes in body weight, and minimal changes in metabolic health support using OLZ/SAM as a long-term treatment option

Why combine samidorphan with olanzapine?

The opioid system is a communication network in the body.[14] It uses naturally occurring chemical messengers called endogenous opioids that help to regulate hunger, satisfaction after eating, and how the body stores and uses energy.[14,15] These chemical messengers work by attaching to opioid receptors found in the brain and other parts of the body.[14,15] Samidorphan blocks these receptors, stopping activation of opioid receptors, which may impact body weight and metabolic parameters.[14,16]



By targeting the opioid system, OLZ/SAM influences body weight and metabolic health

How well was OLZ/SAM tolerated?

Most common side effects in studies

Across the OLZ/SAM research program, most adverse events were mild to moderate in severity.[4,6,8] Serious adverse events were rare. In early-in-illness patients and in long-term studies, the safety profile was generally consistent with previous studies of OLZ/SAM.[6,10-12]

OLZ/SAM is generally well tolerated, with a safety profile that has been consistent throughout the clinical research program

How many patients completed OLZ/SAM clinical studies?

Overall, 70% of patients treated with OLZ/SAM completed studies lasting up to 1 year.[16] In one 4-year study, more than 50% completed at least 2 years of treatment and 32.5% completed 4 years.

Percentages of patients who completed OLZ/SAM studies

Many patients completed OLZ/SAM treatment throughout both short- and long-term studies

CLINICAL PEARLS

OLZ/SAM may enable earlier and sustained use across the treatment course of schizophrenia and BD-I

KEY TAKEAWAYS

Symptom control maintained

In studies, **OLZ/SAM** provided symptom improvement similar to that of olanzapine while resulting in less weight gain, helping address a common reason that clinicians may hesitate to use olanzapine

Less weight gain, minimal metabolic changes

Small changes in weight and minimal changes in metabolic measures suggest that physical health considerations may be less of a barrier when considering treatment with **OLZ/SAM**

Consistent findings in early-in-illness patients

Similar weight outcomes were seen in patients earlier in their illness, when treatment choices may shape long-term outcomes and future treatment success

Sustained benefits

Many patients completed **OLZ/SAM** treatment in short- and long-term clinical studies, suggesting that the benefits seen early in treatment can be maintained over time

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