

# PALIPERIDONE: THE EXPERT POINT OF VIEW

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The clinical and scientific interest for in paliperidone is the interest for an goes back to an antipsychotic drug line that was born began in 1958 with the discovery of haloperidol and reached now paliperidone, including antipsychotic drugs with a prevalent and constant antagonist action on the D2 receptors. The initial perception of paliperidone in clinical practice has evolved over time, both for both pharmacodynamic (antagonist action on 5-HT<sub>2A</sub> receptors, rapid drug-receptor dissociation) and pharmacokinetics reasons (width breadth of the therapeutic window, regular kinetics in the therapeutic range, stability of plasma concentrations, minimal hepatic metabolism, reduced interaction with other substances). Overall, these pharmacological characteristics guaranteed paliperidone a clinical ductility flexibility that risperidone itself didoes not present. Given its balanced, persistent and non-irreversible binding to D2 receptors, the high tolerability and low tendency to induce side effects, since its marketing paliperidone has represented an added value in to the treatment of psychosis since it came on the market.

In recent years, clinicians have also witnessed the advent of second-generation long-acting injectables (LAI) antipsychotics. With the introduction of a risperidone LAI formulation, there has been an improvement in adherence of among schizophrenic patients with schizophrenia as well as a reduction in relapses, both in terms of both frequency and intensity. Furthermore, the therapeutic relationships with the psychotic patients was have improved. This was an unprecedented unexpected phenomenon that did not occurred occur with haloperidol decanoate (as well as or with other first-generation depot antipsychotics), but that has occurred with all second-generation LAI antipsychotics. These observations have progressively prompted clinicians to change their perspective on the schizophrenic syndrome. Until then, in fact, tThe course and severity of this psychotic disorder were were previously evaluated mainly on the basis of positive symptoms (more evident), rather than on negative symptoms (difficult to investigate and intertwined with complex dimensions such as affectivity, cognitive functions and socialization). With the advent of second-generation LAI antipsychotics, it has been is understood that the more constant the anti-psychotic therapeutic dosage is constant, the more adaptive the mind-brain system will be. Therefore, the stability of the antipsychotic effect became a fundamental requirement for an effective reparative neuroplastic process. In From this new perspective, the advantages offered by LAI formulations of second-generation antipsychotics is are evident. In practice, the introduction of second-generation LAI antipsychotics has allowed clinicians to focus more on therapeutic programs that include social and emotional rehabilitation and patient empowerment. A patient is no longer “passivated”, as in the past, but “empowered” and involved in care, in from a participatory perspective.

Today, like as yesterday previously, the clinician to whom when a schizo-

phrenic patient with schizophrenia is referred with severe levels of psychotic dissociation is referred, the clinician first considers a drug with a predominant D2 receptor antagonist action. However, bBecause of previously shown its advantages, paliperidone is not only a the first-choice therapeutic option, but also offers the possibility of a rapid conversion to LAI treatment, both from with risperidone and from or oral paliperidone. The starting of tTreatment with paliperidone palmitate begins(which involves with two injections in the first eight 8 days) ; this usually allows a results in rapid reduction of positive symptoms and any pre-existing side effects. In many cases, we observe the rapid passage transformation of the psychotic patient from a phase of simple compliance (often imposed), to a phase of “assisted” adherence (in which the patient is still supported, but already provides contributes a substantial consensus), to a phase of conscious adherence. From this point of view, an important advantage of paliperidone palmitate compared to with risperidone and oral paliperidone seems to be the induction of a greater and faster neuroplasticity, with a more rapid recovery of insight, that which allows the patient to participate in psychoeducation groups and programs of rehabilitation. The discovery of these clinical advantages of paliperidone palmitate occurred by serendipity: ; we started began with from the idea of creating a formulation that would guarantee a less harmful compliance compared to that of with the first-generation depot antipsychotics and instead we reached a completely different therapeutic option, which makes paliperidone palmitate a the first-choice treatment. Its particular pharmacokinetics and constancy of action allow the patient a possibility of to adapt and adaptation, of coping, which in fact activates their resilience already from the

acute phase. It is essential, therefore, the possibility of using that paliperidone palmitate is used, even without a preliminary stabilization with oral treatment in patients with schizophrenia who have previously responded to paliperidone or oral risperidone.

In conclusion, we can state that the antipsychotic effect of LAI treatment is based not only on the drug itself, but also on the constancy and stability of its action. These last features represent the true revolution of the care system. For this reason, many authors support the use of LAI antipsychotic therapy since from the first psychotic episode. Early treatmentActing on time, in fact, guarantees a fundamental qualitative effect: ; first the earlier we intervene on in the degenerative process connected to schizophrenia and the better the results will be. It is a therapeutic choice that represents the beginning of a new phase of life for the in the life of a person with schizophrenic persona from the point of view of planning, especially in view of the availability of paliperidone LAI in a quarterly formulation. The possibility to of implementing effective antipsychotic therapy with four injections per year will, in fact, drastically decrease the stigma associated with schizophrenia. The decrease in Reducing the stigma in surrounding the treatment of schizophrenia is a primary factor, not a secondary one, but a primary factor: reducing Reducing the number of administrations of antipsychotic therapy means decreasing the prejudices, increasing the scope and depth of the doctor-patient relationship, and focusing on rehabilitation work. This is a fundamental difference in the treatment of schizophrenia which, ultimately, can be implemented in a “repressive” sense, as in the case of high-dose haloperidol, or in the “expressive” sense, as in the case of paliperidone palmitate and other second-generation LAI antipsychotics.