

EXJADE (DEFERASIROX – ICL 670)

At last the new oral chelator of Novartis is on the market. After approval by the Federal Drug Administration (FDA) of the USA and the European Medical Association (EMA) of Europe, its availability is spreading over most countries.

It is coming as a great relief to many patients, who for years have endured long hours of subcutaneous infusions. This new addition will certainly improve quality of life because of the convenience of administration with once per day dosing by mouth. This should improve compliance, especially in those experiencing local and systemic reactions with Desferal.

It allows 'tailored' dosing, according to the amount of iron intake through blood transfusions that each patient receives. Generally, a dose of 20mg/kg/day has been shown to maintain iron balance in regularly transfused patients. A higher dose of 30mg/kg/day will induce a net fall in body iron, as indicated by a reduction in liver iron concentration. It should be taken on an empty stomach 30 minutes before food.

These facts were established by multi-centre trials and the collaboration of many physicians. The results of these were announced in the American Society of Haematology (ASH) meeting in Orlando, in December 2005 and at the Thalassaemia International Conference organised by TIF, in January 2006 in Dubai.

The series of clinical trials are summarized in the table shown below, as follows:

Year of Study	Study Number	Type of Study	Number of Patients involved
1998-1999	101	Single dose Safety and Tolerability	24
2000-2001	104	Multiple dose iron balance	24
2001-2002	105	Randomised deferasirox vs DFO, Safety & LIC Study	71
2002-2004	106	Single arm Safety & LIC	40 children
2003-2004	107	Randomised deferasirox vs DFO, Safety & LIC Study	586 children & adults
2003-2004	108	Single arm LIC & tolerability	184 children & adults
2003-2005	109	Randomised deferasirox vs DFO, Safety & LIC Study	195 children & adults

Some of these studies (105-109) are being extended to obtain information on long-term use.

Side effects:

As with all drugs, some side effects have been noticed, during these trials.

- Skin rashes have appeared in 7% of patients, but these often disappear without needing to decrease the dose or discontinue the drug. If the rash is severe, it may be necessary to discontinue. When the rash goes, the drug may be administered again, starting at a lower dose.
- Mild nausea, vomiting and abdominal pain was recorded in 26% of patients.
- Decreased hearing and disturbances of vision have also been reported, so that hearing and eye testing are recommended every year.
- Non-progressive rises in serum creatinine have been noted in some patients usually, however within normal limits.
- Also elevations of liver enzymes are seen in 2% of patients.

Because of these rare occurrences, monitoring is required as follows:

1. Serum Creatinine, before starting treatment, then monthly. If the level rises by 5% or more above the initial level on two consecutive tests, then the dose must be reduced to 10mg/kg. If there is a progressive increase beyond the upper limit of normal, the drug is discontinued.
2. Liver function should be monitored monthly. If there is a progressive increase in serum transaminase levels (and other causes have to be excluded), then Exjade should be discontinued and may be started again at a lower dose, when they return to normal levels.
3. Body weight and length should be measured every 12 months in children, as a general measure. No adverse effects on growth have been noted.

At present, no studies on the combination of Exjade with other chelators have been conducted. For this reason, this should not be tried in an isolated clinical situation.

The drug has not yet been tried in pregnancy and breastfeeding, so it should be avoided on these situations, pending further studies.

Despite these precautions, EXJADE, in the vast majority of Thalassaemia patients is both effective and safe.

Please visit the official site, for more information: www.exjade.com