Tolerability of Cetirizine in children.
Results of a prospective clinical observation study in 305 children suffering from allergic disorders of the upper respiratory tract and allergic pruritus.

Based on the data analysis and final evaluation of the observation study dated from February 17, 1992

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Cetirizine /2-[4-\{(4-chlorophenyl) phenylmethyl]-1-piperazinyl\}ethoxy\} acetic acid, dihydrochloride; Zyrtec\textsuperscript{R} is a strong, selective and long acting blocker of H\textsubscript{1} histaminic receptors with marked antiinflammatory potency. The inhibition of migration of inflammatory cells (eosinophils) leads to an inhibition of the late phase reaction. Cetirizine reduces the platelet cytotoxicity and inhibits the liberation process of histamine. The unchanged polar and hydrophilic molecule is rapidly absorbed and pharmacologically active. Renal excretion predominates. Cetirizine represents the active antiallergic metabolite of hydroxyzine which has been intensively investigated for decades according its tolerability. Concerning safety aspects this is considered to be a crucial advantage of Cetirizine. The plasma half life is about 10 hours; after 4 days Cetirizine is practically eliminated. There is no accumulation after repeated doses. Tachyphylactic effects and sedation typical for antihistaminics have not been registered in objective psychometric investigations. Clinically relevant interactions with drugs are not known.

The tolerability and efficacy of Cetirizine was investigated in a 4-weeks prospective clinical observation study in 305 children suffering from allergic disorders of the upper respiratory tract and/or allergic pruritus. Duration of the observation study: Mai 1991 till February 1992. Tolerability was assessed by physician’s recording of adverse events (AE) and adverse drug reactions (ADR), adverse events were to be recorded if they were reported spontaneously or on questioning to the doctor or if he observed them. A global assessment of the treatment compared to previously administered antiallergic drugs was carried out on a rank scale at the end of the observation period. The data were analyses by using methods of descriptive statistics. Nine documentations out of a total of 314 patients were excluded from the data analysis since the patients were 18 years or older or the records were insufficient. 37 physicians participated in the observation study. All children were outpatients who recieved Cetirizine as a regular treatment. Recommended dose regimen (weight-related): $< 30 \text{ kg} 5 \text{ mg} $; $> 30 \text{ kg} 10 \text{ mg}$ Cetirizine, mean daily dose in the observation group: 6,4 mg; one single evening administration. Mean age: 6,6 years.

Age groups:

| Age | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |11 |12 |13 |14 |15 |16 |17 | Total |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| n   | 10|18 |51 |53 |45 |43 |24 |11 |15 |12 |8 |6  |2  |2  |3  |2  | 305  |
| %   |3.3| 5.9|17 |17 |15 |14 |7.9|3.6|4.9|3.9|2.6|2 |0.7|0.7|1 |0.7 |100\% |

Since 72 per cent of the patients were aged between two and seven years the results of the observation study represent the tolerability of Cetirizine in young children in particular. Sex distribution: 52,2 per cent male, 47,8 per cent female. Mean weight 26,6 kg; mean height 122,4 cm. Distribution of diagnoses: 244 patients with allergies of the upper respiratory tract, 173 patients with skin allergies, 112 patients with both manifestations. Most frequent diseases: allergic rhinitis, neurodermatitis, allergic conjunctivitis, obstructive/spastic bronchitis, asthma. 234 children recieved antiallergic treatment other than
Cetirizine before entering the observation study, most frequently antihistaminic drugs and among them terfenadine, nonsteroidal topical skin treatment, sodium chromoglycate and ketotifen.

There was a marked improvement of any respiratory and skin symptoms during 4 weeks treatment with Cetirizine. In 76 per cent of the cases the treatment with Cetirizine was evaluated substantially better or rather better than previous therapies. There was an overall 81 per cent reduction of symptom scores (mean of 19 scores) after 4 weeks treatment.

During the course of the observation study in 17 patients (5.6 per cent) adverse events were registered, independently of assumed causal relationships. There were no serious adverse events at all. With the exception of one patient there were no indications for stopping the treatment because of adverse events.
Among all adverse events the doctors have assumed in 6 cases a causal relationship with the administration of Cetirizine. These 6 events have been classified as adverse drug reactions: lack of concentration (one week); sleepiness (one week), tiredness (4 days); headache; questionable constipation, feeling of pressure in the stomach. Thus, the initial total frequency of adverse drug reactions has been 1.97 percent with a decrease below the one per cent level after one week of treatment.

\(^{1}\)The results concerning efficacy are not given here in detail.
All adverse drug reactions were considered as mild events. In all cases the administration of Cetirizine was continued. Only two adverse drug reactions were registered in young children (7 years or younger; n=220). So, the initial frequency of adverse drug reactions in the younger age groups was 0.91 per cent.

The results of the observation study confirm an excellent tolerability of Cetirizine in children with allergic disorders, particularly in young children.

It is deducted that Cetirizine represents a safe and highly relevant improvement of opportunities for antiallergic therapy in children which especially fulfills the requirements of a long term treatment and prophylaxis at the current state of the art.