

Augustus 2003

Thyrax Duotab 0,025 mg[®] and allergic reaction

Introduction

Thyrax Duotab, containing levothyroxin as active substance, is indicated for the treatment of various kinds of hypothyroidism and for temporary suppression of the thyroid gland for diagnostic purposes. It is available in three formulations: 0.025 mg (blue), 0.100 mg (white), and 0.150 mg (pink).

The most recent SPC dates from February 20, 2002. No allergic phenomena are mentioned. The SPC lacks a list of excipients [1].

Reports

The Lareb database contains 79 reports with Thyrax Duotab as suspect medication. Ten case reports concern allergic reactions.

Table 1. Reports of allergic reactions associated with the use of Thyrax Duotab[®], irrespective of formulation

Patient, Sex, age	Suspect medication	Concomitant medication	Suspected ADR	Time to onset, outcome
A F, 71	Thyrax Duotab 0,025 mg	not reported	rash/drug eruption	3 months, not recovered
B F, 79	Thyrax Duotab 0,025 mg	propranolol, thiamazol	rash maculo-papular	2 days, not recovered 7 days after withdrawal
C F, 66	Thyrax Duotab 0,025 mg Fosamax 10 mg	furosemide, diazepam, temazepam	urticaria	4 days, drug continued and not recovered
D F, 58	Thyrax Duotab 0,025 mg	verapamil, psyllium, Thyrax Duotab 0,100 mg	rash erythematous	3 days, positive de- and rechallenge
E F, 47	Thyrax Duotab 0,025 mg	none	urticaria	1 day, replaced by Thyrax Duotab 0,150 mg without recovery, Thyrax Duotab stop: recovery, start Eltroxin [®] without events
F F, 45	Thyrax Duotab 0,025 mg	rofecoxib, omeprazol, nizatidine	rash erythematous	10 months of dose increment, replaced by Thyrax Duotab 0,100, outcome unknown
G F, 58	Thyrax Duotab 0,025 mg	betaxolol eyedrops	urticaria	5 months, outcome unknown, according to GP not related with Thyrax, drug continued
H F, 20	Thyrax Duotab 0,025 mg	not reported	rash	3 days, positive dechallenge
I F, 78 2	Thyrax Duotab 0,025 mg	salbutamol, latanoprost eyedrops	pruritus	unknown, not recovered, Thyrax Duotab 0,025 mg replaced by Thyrax Duotab 0,150
J F, 28	Thyrax Duotab 0,025 mg	medroxyproges teron	urticaria	1 day, positive dechallenge, start Euthyrox [®] without events

In all 10 reported cases of allergic reactions Thyrax Duotab 0,025 mg[®] was involved. In case D, any role of Thyrax Duotab 0,100 mg[®] could be ruled out by a positive dechallenge and even rechallenge with Thyrax Duotab 0,025 mg[®].

The association between Thyrox Duotab 0,025 mg[®] and allergic reactions could not sufficiently be explained by the low prescription rate of the 0.100 formulation, as is illustrated in Figure 1. The 0.150 formulation has been prescribed less.

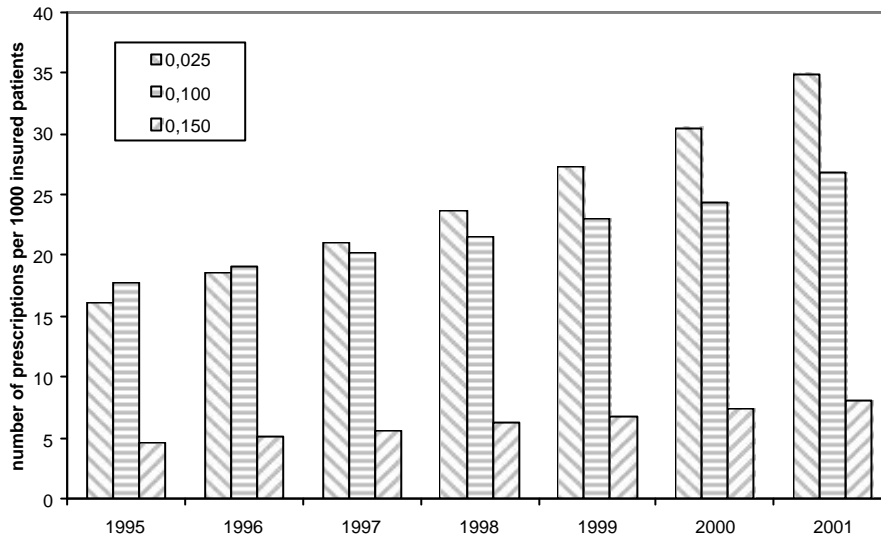


Figure 1. Prescription rates of the various Thyrox Duotab[®] formulations (Source: GIP College Voor Zorgverzekeringen, Diemen)

Other sources of information

Literature

A literature search on Thyrox Duotab did not yield any hits. An advanced search using the terms levothyroxine and hypersensitivity revealed an association with asthma, but not with cutaneous reactions.

Databases

Since the WHO database does not allow searches on trade names and formulations, no search could be performed here.

Mechanism

We hypothesise that indigo carmine, the blue dye present in the Thyrox Duotab 0,025 mg[®] formulation, is responsible for the allergic reactions [2].

Indigo carmine is used as a dye in various diagnostic procedures and is known for its allergenic potential.

As a dye in food and tablets, its use has been approved under code E132 [3].

Thyrox Duotab 0,150 mg[®] contains the pink dye erythrosine, approved as E127 [2].

Conclusion

The strong association between allergic reactions and Thyrox Duotab 0,025 mg[®], and not with the 0.100 and 0.150 mg formulations, suggests causality.

This is supported by the presence of indigo carmine, a known allergenic agent, in the 0.025 mg formulation, which is absent in the other formulations.

References

1. Dutch SPC of Thyrax Duotab (version 20 February 2002). <http://www.cbg-meb.nl/IB-teksten/08389-09334-13683.PDF>
2. Informatorium Medicamentorum 2003, KNMP
3. <http://www.mvo.nl/voeding-en-gezondheid/adar/download/1995L0045.pdf>

