Abstract ID: 4CPS-272

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ANALYSIS OF ADVERSE REACTION REPORTS BEFORE AND AFTER THE USE OF EQUIVALENT IMATINIB IN A TERTIARY HOSPITAL

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BACKGROUND AND PURPOSE

Several patients treated with Glivec® for chronic myeloid leukemia were switched to the equivalent drug Imatinib, after the expiry of the patent. However, the switch in some patients has revealed a suspected adverse reaction, which led to the re-use of the originator drug.
The aim of the study was to analyze the incidence and type of reports of adverse reactions before and after the switch by comparing them with national data.

MATERIALS AND METHODS

At our hospital, the use of equivalent imatinib began massively in October 2017. For the analysis of 7 months, two periods were compared: October 2016 - May 2017 (period 1: pre-switch) and October 2017 - May 2018 (period 2: post-switch). The source of the reports is the pharmacovigilance's database of the Italian drug agency. The formulations in the market were also analyzed in terms of composition.

RESULTS

In period 1, 77 patients were treated with Glivec® and one adverse drug reaction was reported (1.3% eczema) (Table 3). During the period 2, 69 patients were treated and there were 5 reports (2 epigastric pain, diarrhea, pruritus, 1 vomiting, 1 stomatitis, edema, dyspnea, 1 skin rash) (Table 3), all with the equivalent drug (7.2 %). None of these were serious. Because of the intolerance, three patients were re-switch to Glivec®. The increase in the number of reports is also reflected in the national data. From the authorization of the marketing to the expiration of the patent (192 months) 351 reports of adverse reactions of Glivec® were sent (1.8 ADR / month) (Table 1). While from the patent expiry to May 2018 296 adverse reactions were reported and at least 122 were from Imatinib equivalent (7 ADR / month). The increase in reports post-switch was 89%. Regarding the formulation, there are differences in terms of pharmaceutical form (capsules/tablets), excipients and type of coating (Table 2).

	From the authorization of the marketing to the expiration of the patent (22/12/16)	From the expiry date of the patent to May 2018
Glivec®	351	74
Imatinib equivalent	Not applicable	122
Not specificated		100
Total	351	296

Tab. 1: Number of ADRs entered in RNF before and after patent expiration.

	Adverse reaction	N. Pt
Glivec®	Edema, eczema	1
Imatinib equivalent	Epigastric pain, diarrhea, pruritus, urticaria	2
	Vomiting	1
	Stomatitis of the oral cavity, lip edema, dyspnea	1

Tab. 3: Types of adverse reactions reported at our Hospital.

	GLIVEC	IMATINIB TEVA	IMATINIB REDDY	IMATINIB ACCORD
PHARMACEUTICAL FORMULATION	Hard capsule	Hard capsule	Film-coated tablet	Film-coated tablet
CONTENT	Microcrystalline cellulose	Mannitol	Magnesium stearate	Hypromellose 6 cps (E464)
	Crospovidone	Crospovidone	Imatinib mesylate	Microcrystalline cellulose pH 102
	Magnesium stearate	Magnesium stearate		Crospovidone
	Colloidal silica, anhydrous	Colloidal silica, anhydrous		Colloidal silica, anhydrous
	Imatinib mesylate	Imatinib mesylate		Magnesium stearate
				Imatinib mesylate
ENVELOPE	Gelatin	Gelatin	Hypromellose (E464)	Hypromellose 6 cps (E464)
	Red oxide iron (E172)	Red oxide iron (E172)	Talc (E553b)	Talc (E553b)
	Iron oxide yellow (E172)	Iron oxide yellow (E172)	Macrogol (E1521)	Polyethylene glycol
	Titanium dioxide (E171)	Titanium dioxide (E171)	Titanium dioxide (E171)	Iron oxide yellow (E172)
				Red oxide iron (E172)
PRINT INK	Red oxide iron (E172)	Lacquer		
	Shellac	Black iron oxide (E172)		
		Propylene glycol		

Tab. 2: Components of the various pharmaceutical specialties.

CONCLUSION

Results suggest a possible correlation between the switch and the increase in the number of reports. However, as pointed out by AIFA whenever a new equivalent drug comes into commerce the attention to reports may increase. It would be interesting to understand which components have caused adverse reactions and to identify patients at risk.

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