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# Adherence with brand versus generic bisphosphonates among newly treated osteoporosis patients: a retrospective cohort study in the French claims database

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## Background and aims

Oral bisphosphonate (BP) are recommended among the first-line treatments for osteoporosis (OP), and a low adherence to oral BP has been associated with an increased risk of further fractures. Several studies documented declines in treatment adherence with generic forms of BP compared to branded forms, possibly related to increased occurrence of gastrointestinal adverse effects, while other studies did not support this relation.

As this topic remains controversial, we conducted an **analysis of the French national database to test the hypothesis of a reduced medication adherence with brand versus generic forms of oral BPs.**

## Results

➤ During the 2009-2015 period, **3,903 patients initiated an oral BP treatment** for primary OP: **1,710 (43.8%) with generic BP and 2,193 (56.2%) with brand BP.** Results of switches and implementation rates according to BP group are presented in Table 1.

➤ **Univariate analyses were conducted to identify factors associated with good implementation (defined by CMA7  $\geq$  0.9).** Factors tested were: exposition of interest (BP group), year of initiation, frequency of BP administration, oral BP molecule, prescriber specialty, age, sex, presence of a major chronic disease, socioeconomic frailty, polypharmacy, history of osteoporotic fracture, Charlson comorbidity index.

➤ **Binary logistic regression modelling** was then used to predict good implementation, by stepwise addition of exposition of interest and variables associated with good implementation at a probability level of 0.2 or less in bivariate analyses. Results of multivariate analysis are presented in Table 2.

Table 1: Implementation and switches with first-line BP initiated during the 2009-2015 period, according to BP group (N=3,903)

	Brand BP N = 2,193	Generic BP N = 1,710
Still on first-line BP at 12 months, n (%)	540 (24.6)	459 (26.8)
BP treatment discontinuation, n (%)		
before 6 months	1,105 (50.4)	860 (50.3)
between 6 and 12 months	189 (8.6)	176 (10.3)
Switch to the other BP group, n (%)		
before 6 months	152 (6.9)	118 (6.9)
between 6 and 12 months	80 (3.6)	38 (2.2)
Switch to another molecule, n (%)		
before 6 months	82 (3.7)	53 (3.1)
between 6 and 12 months	45 (2.1)	6 (0.4)
Mean CMA7 $\pm$ SD*	0.932 $\pm$ 0.071	0.941 $\pm$ 0.071
Class of CMA7, n (%)*		
<90%	202/854 (23.7)	141/679 (20.8)
$\geq$ 90%	652/854 (76.4)	538/679 (79.2)

\* Analysis on the 1,533 patients under BP treatment during at least 6 months

## Methods

➤ **Retrospective, comparative cohort study** carried out using the **Generalist Sample of Beneficiaries (EGB)**, a permanent representative sample of the general population of subjects affiliated with the National French Health Insurance System.

➤ Inclusion of **all patients aged 50 and older, new users of oral BP alone** (alendronic acid, ibandronic acid, risedronic acid or etidronic acid, not associated with vitamin D) **for primary osteoporosis between 01/01/2009 and 31/12/2015.**

➤ Patients **followed from the initiation date until:**

- **switch** (change from generic to brand drug or brand to generic, or change from one oral BP to another),
- or **discontinuation** of BP (no new dispensation during a period greater than 2 times the duration of the previous supply),
- or **12 months.**

➤ Implementation evaluated using the **continuous multiple-interval measure of medication availability version 7 (CMA7)**, for patients under treatment during at least 6 months:

- dosages considered were the defined daily doses,
- hospitalization were taking into account assuming that treatments were supplied by the hospital during the hospitalization period.

Table 2: Multivariate analysis of factors associated with good implementation (CMA7  $\geq$  0.9) among patients under BP treatment during at least 6 months (N=1,530)

	Bivariate OR [IC95%]	Multivariate OR [IC95%] <sup>1</sup>	p-value <sup>1</sup>
BP group			
Generic	1	1	
Brand	0.846 [0.663;1.079]	0.974 [0.713;1.329]	0.8659
Frequency of BP administration			
Daily	1	1	
Weekly	1.011 [0.213;4.806]	1.022 [0.212;4.934]	0.9784
Monthly	0.716 [0.150;3.403]	0.733 [0.149;3.616]	0.7033
Oral BP molecule			
Risedronic acid	1	1	
Alendronic acid	0.967 [0.713;1.312]	0.850 [0.593;1.220]	0.3790
Ibandronic acid	0.735 [0.549;0.985]	0.986 [0.675;1.439]	0.9397
Etidronic acid	0.531 [0.048;5.887]	0.653 [0.058;7.341]	0.7297
Prescriber specialty*			
General practitioner	1	1	
Specialist practitioner	0.711 [0.431;1.171]	1.124 [0.812;1.556]	0.4824
Hospital practitioner	1.486 [0.750;2.946]	1.394 [0.952;2.042]	0.0878
Class of age (years)			
50 to 59	1	1	
60 to 69	1.146 [0.808;1.626]	1.157 [0.813;1.647]	0.4187
70 to 79	1.269 [0.890;1.809]	1.246 [0.871;1.784]	0.2284
$\geq$ 80	1.530 [1.034;2.265]	1.459 [0.982;2.166]	0.0614
Sex			
Male	1	1	
Female	0.587 [0.363;0.949]	0.627 [0.382;1.030]	0.0651

\* Data were missing for 3 patients, who were excluded from multivariate analysis

## Conclusion

In multivariate analysis, once adjusted for confounding factors, there were **no differences in implementation with brand or generic BP** in this population. **Adherence rate was higher in our study** than the mean medication possession ratio of 66.9% presented in the meta-analysis of Imaz et al. (Osteoporos Int, 2010). This difference could be due to the fact that we chose to evaluate the dimensions of persistence and implementation separately, and that our methodology of adherence calculation included hospitalizations.