

Recent information on opioid substitution treatments

Initial results of a reimbursement data analysis on more than 4,500 patients in 2006 and 2007

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Introduction

Slightly over 100,000 people in France receive opioid substitution treatment, as a result of the policy adopted from the middle of the 1990s onwards to make opiate substitution treatments (OST), either High Dose Buprenorphine (HDB) or methadone, accessible. It is estimated that 120,000 people were being treated with OST in 2007, with a marked predominance of HDB, which made up 80% of the total (a specific French feature).

Almost 15 years after they were first marketed [1], the impact of OST in people with opiate dependency is clearly extremely positive, but cases of misuse have also occurred, making it necessary to monitor the prescription of these substances.

It was in this context that co-operation between CNAMTS and the OFDT was set up. The study described here is the third part of this work. An initial joint study led to the publication of a report on the accessibility of HDB and methadone on five French geographic sites between 1999 and 2000 [2], followed by a complementary version published in 2004, extending this review to include data for 2003 and 2004 while covering a larger area (13 regional sites) [3]. These two studies described the change in the number of patients treated and also the dissemination of OST prescribing practices and the types of prescriptions (dosages and any associations of psychotropic drugs). Misuse on the black market by some people – particularly for HDB – has also been investigated using indicators including the mean daily dose and number of healthcare professionals consulted (prescribers and pharmacists).

This new study is based, for the first time, on the whole country rather than regional sites, from two representative samples of beneficiaries of the general scheme of French health insurance selected at random for the years 2006 and 2007. It sets out to describe both the methods of use of OST over these

two years (levels of use, therapeutic associations) and also their intended uses (therapeutic or misuse), particularly from the length of treatments, and describes any abuse or misuse encountered. Only the main results of this work are presented in this document. An OFDT report to be published shortly will provide a more detailed review of access to OST nationally over these two years and will describe any changes in profiles of use since the initial work.

This new co-operation is taking place at a time when the availability of OST is broadening in France, as 2006 and 2007 saw the arrival of two generic forms of HDB (HDB Arrow® in March 2006 followed by HDB Merck¹® the following year) onto the market. In addition, a National Health Insurance monitoring plan for suspected OST misuse (specifically relating to HDB) was set up as of 2004 [4].

Methods

Two samples of people were created, one for 2006 and one for 2007, randomly selected² from among members of the general social security scheme who had received at least one reimbursement for HDB and/or methadone during the year. These samples were independent of each other and it was not therefore possible to monitor any courses of treatment beyond the period of one year³. After processing the National Health Insurance database (see box) and removing incomplete or incorrectly completed entries, the analysis was based on 4,736 people in 2006 and 4,607 in 2007.

The substitution treatments identified in this reimbursement database from their CIP⁴ codes were those dispensed by primary care

1. HDB Merck® became HDB Mylan® in 2008.

2. Conducted in the 26 French regions in 2007 and in 25 of them in 2006 (no patients randomly selected in Guyana).

3. The patient anonymisation numbers were not kept from one year to the next and it is therefore not possible to determine whether they were selected again or not.

4. CIP Code: identifier allocated by the Club Inter Pharmaceutique representing the Marketing Authorisation number for a presentation of a given medicine (one identifier per dose of medicine).

pharmacies, whether or not they were initially prescribed by a primary care or hospital physician (general practitioner or specialist).

Results

General features of patients receiving substitution treatments

Predominance of HDB; gradual increase in generic drugs.

The vast majority of patients in these studies were receiving HDB (82% in 2006 and 80.5% in 2007), with approximately one out of five people receiving methadone.

Of those receiving HDB in 2006, the primary substance Subutex® was prescribed, most often alone (72% of cases) or in association with the generic Arrow® (28%); the generic was only prescribed alone to 12 people (0.3%). The penetration of generics increased markedly in 2007, with only 47.3% of people receiving Subutex® alone; the association of Subutex® and generics (Arrow®

and/or Merck®) rose to almost half of the total (48.8%). The number of people receiving only generics therefore increased by a factor of 10 over one year (3.9%).

The majority are men with an average age of 35

Men made up 78% of the sample (Table 1), a figure which is consistent with the sex distribution of all opiate drug users which has been found in the different existing surveys.

The average age of people receiving HDB was 34.5 in 2006 and 35 in 2007; average ages for methadone were similar (35.1 and 34.7 years old respectively).

The average age of people receiving a generic in 2006 (Arrow®) was lower than for the whole subject group at 25.5 years old. It was higher for the same generic (35.6 years

Table 1 - Numbers, mean age and CMU (Couverture Maladie Universelle, Universal health care coverage) status of patients receiving OST, shown by sex

Number	2006			2007		
	Men	Women	Total	Men	Women	Total
HDB	3 018 (78 %)	866 (22 %)	3 884	2 927 (79 %)	784 (21%)	3 711
Methadone	639 (75 %)	213 (25 %)	852	662 (74 %)	234 (26 %)	896
Mean age	Men	Women	Total	Men	Women	Total
HDB	34.5	34.2	34.5	35.2	34.5	35
Methadone	35.4	34.5	35.1	34.6	34.8	34.7
CMU (%)	Men	Women	Total	Men	Women	Total
All patients	25 %	32 %	27 %	23 %	35 %	25 %

Source : CNAMTS data in 2006-2007, OFDT estimates

old) the following year but lower for the Merck® generic (30.1 years old), suggesting that the new generics are possibly easier to prescribe to young patients at the start of treatment.

A quarter of the people benefit from the CMU, with an over-representation of women

A quarter of people receiving OST were registered with CMU⁷. There is a female predominance in this group with one in three women receiving CMU compared to approximately one out of four men (Table 1). This difference is particularly pronounced in the intermediary age groups (between 30 and 39 years old).

More people receiving HDB, rather than methadone, were registered with CMU, particularly in 2006 (23% vs. 17%, $p < 0.0002$).

Average daily doses of OST and regional disparities in HDB

The recommended maintenance dose of HDB is 8 mg/d, with a maximum dose of 16 mg/d. Mean daily doses of HDB found here for the whole patient group were 9.5 mg/d in 2006 and 8.9 mg/d in 2007⁸ (Table 4). The national mean masks very different situations depending on region, with a minimum of 5.3 mg/d in Limousin ($n = 38$) and a maximum of 19.6 mg/d in Ile-de-France ($n=478$) in 2006. There was less dispersion

5. Erasmie national reimbursement database.

6. As this amount will probably be used after obtaining the last prescription for the year (and overlapping into the next year, if the last dispensing date is at the end of the year being studied).

7. Being registered with the CMU is only based on those people who have only had one CMU status during the year ("CMU+" or "CMU-"), i.e. in 3,907 people in 2006 and 3,793 in 2007 (82% of the people for both years).

8. The 2002 study found a mean daily dose of 9.3 mg/d for the second half of the year.

Processing the CNAMTS 2006 and 2007 databases

For both years an initial search in the National Health Insurance databases⁵ was used to randomly select people from amongst those who had received at least one reimbursement for HDB (Subutex® and/or its generics) and/or methadone between the first and last day of a particular month (in reality, the months of January 2007 and January 2008 in this case). A further search was then used to record reimbursement data for HDB and/or methadone prescriptions for these subjects retrospectively over each of the two previous years (from 1st January to 31st December included). Subjects who had only received a single OST prescription or had received both medicines during the year were studied separately:

	January 2007	January 2008
Search no. 1: Random selection of people who had received at least one OST reimbursement during the month of January	N=5,051 5.5% of the database of OST recipients for this month (N=91,928)	N=4,939 (5% of the database of OST recipients for this month (N=97,985))
↓	↓	↓
Search no. 2: Retrospective analysis of OST prescriptions in these people over the previous 12 months	Year 2006	Year 2007
- Removal of incomplete or incorrectly completed files	n=65	n=59
- Removal and separate study of people receiving a single OST reimbursement and those receiving both OST (mixed treatment) during the year	n=153	n=176
Number of people kept for analysis	N=4,736	N=4,607

Several OST-related variables were created to perform the analysis:

- For each prescription: the **dispensing time** (the time between the prescription and dispensing dates for an OST)
- For each subject: the **dose dispensed** during the year (calculated from the amounts reimbursed for OST identified from the CIP codes), **length of treatment** (difference between the first and last dispensing dates of the OST(s) received in the year), and the **mean daily dose** (defined as the sum of all of the amounts prescribed (HDB or methadone) from the first to the penultimate⁶ treatment dispensed for the year divided by the length of treatment (from the first to the last dispensing date)).

in 2007 because of a marked fall in the mean daily dose in Ile-de-France (13.6 mg/d, n=407). As in the various previous studies [2, 3], the mean daily doses are particularly high, and amongst the highest, in three regions - Ile-de-France followed by the Provence-Alpes-Côte d'Azur (PACA) and Alsace regions⁹.

The mean daily dose in the two years studied was slightly greater in recipients of CMU at 11 mg/d (Table 4).

Overall, in these two years, almost 9/10 of people received a mean daily dose of 16 mg/d or less, 10% received a dose of between 16 and 32 mg/d and approximately 2% (slightly less in 2007), received a dose of more than 32 mg/d. The maximum daily dose found in the whole patient group was 373.3 mg/d in 2006 and 224 mg/d in 2007 in Ile-de-France.

For methadone, whereas the recommended maintenance dose is between 60 and 100 mg/d, the mean doses found here were less than the minimum recommended dose (48.8 and 49.5 mg/d respectively [Table 4a]) and less than the dose found in 2002 (88 mg/d). Overall, only twenty five per cent of patients received a mean dose of between 60 and 100 mg/d, although almost two-thirds received a dose of between 20 and 70 mg per day; 6% received a mean daily dose of over 100 mg/d over the two years (with maximum doses of 200 and 240 mg/d respectively). The mean daily doses for those benefiting from CMU were, like HDB, higher than doses for the whole sample group (51.2 and 52.9 mg/d) respectively.

This fall in mean methadone doses can be explained by the gradual extension of its prescription which was initially reserved, for limited accessibility reasons, for people with the most long-standing or intense drug addiction habits. It could therefore be prescribed to younger people¹⁰ who are undoubtedly less dependent. The 2002 study also showed the beginning of a fall in mean daily doses in some sites between 2001 and 2002.

General features of the healthcare professionals

The people included in the sample consulted 5,887 prescribing physicians in 2006 and to 5,639 in 2007. Almost all of these practitioners were generalists (97%), the few specialists involved in OST prescribing being mostly psychiatrists (47% (n=79) in 2006 and 55% (n=92) in 2007). Approximately one quarter of the people (27%) were seen in these two years by hospital physicians or those working in treatment centres and were either managed exclusively in these structures or alternatively with the primary care physician (most probably in the event of relapse).

In 2007, the patients saw an average of two physicians, whether they received HDB or methadone (Table 2) and only a quarter of the patients saw at least three physicians during the year. The percentage of patients who had seen at least three physicians has fallen considerably compared to the figures of 32% amongst HDB recipients and 28.5% amongst methadone recipients in 2006. The maximum number of physicians seen per HDB patient also fell considerably (33 in 2007 versus 51 in 2006).

These patients also went to 5,756 pharmacies in 2006 and 5,504 in 2007. Whilst 20% of these patients went to three or more during the year, these were mostly patients receiving HDB (22.6% versus 8.2% of patients receiving methadone in 2007). The maximum number of pharmacies consulted during the year was 42 for a subject receiving HDB, again a fall compared to 2006 (n=67).

Treatment regularity

One of the major benefits of prescription data is that they make it possible to analyse the continuity and regularity of OST use. Patient "profiles" have therefore been esta-

blished depending on their length of actual treatment over the year and the intervals between two dispensing episodes.

An initial distinction was made between patients receiving regular treatment (see box below for definitions), who made up almost two-thirds of the samples (62.5% and 60.8% respectively) and the patients who were not receiving regular treatments (the remaining third). These results were consistent with the 2002 survey¹¹.

The patients receiving regular treatment were then classified as receiving "continuous" or "virtually continuous" treatment, depending on the time between two dispensing episodes. Treatment continuity does not in fact depend on its actual duration – as those receiving less than 300 days of treatment can be treated "continuously" – but on the time intervals between two dispensing episodes (< 35 days for HDB and < 15 days for methadone), slightly longer times than those set out in the regulations (28 days for HDB and 14 for methadone). In addition to the time interval, it is only possible to include a patient receiving less than 300 days' treatment in the regular treatment group if dispensing of the patient's last treatment takes place between 5th and 31st December, guaranteeing continuity of treatment at the end of the year in patients randomly selected the following January.

Subjects not falling in these "continuous" or "virtually continuous" treatment categories were defined as "irregular", indicating intermittent treatment.

Regular treatment

- "Continuous treatment" regardless of duration (= 300 days or < 300 days) with the correct time between two dispensing episodes (= 35 days for HDB and = 15 days for methadone) and a last dispensing date between 5th and 31st December for treatment < 300 days.
- "Virtually continuous treatment" regardless of treatment duration (= 300 days or < 300 days) with the correct time between two dispensing episodes (= 45 days for HDB and = 25 days for methadone) and a maximum of 3 episodes during the year for which the time period may be between 36 and 45 days for HDB and between 16 and 25 days for methadone. A last dispensing date between 5th and 31st December is essential for treatment < 300 days.

Irregular treatment

All of the other patients receiving less than 300 days' treatment or more but not falling into the above categories

Table 2 - Percentage of physicians and pharmacies seen per patient depending on type of OST prescribed or dispensed in 2007

Physicians per patient	HDB (n=3 711)	Methadone (n=896)	Total (n=4 607)
1	1 662 (44.8 %)	370 (41.3 %)	2 032 (44.1 %)
2	1 139 (30.7 %)	296 (33 %)	1 435 (31.1 %)
3 à 5	782 (21 %)	221 (24.7 %)	1 003 (21.8 %)
6 à 10	102 (2.7 %)	9 (1 %)	111 (2.4 %)
>10	26 (0.8 %)	0	26 (0.6 %)
Mean number per patient	2,1	2	
Maximum number per patient	33	8	

Pharmacies per patient	HDB (n=3 711)	Methadone (n=896)	Total (n=4 607)
1	1 991 (53.6 %)	640 (71.4 %)	2631 (57.1 %)
2	882 (23.8 %)	182 (20.3 %)	1064 (23.1 %)
3 à 5	672 (18.1 %)	72 (8 %)	744 (16.1 %)
6 à 10	128 (3.5 %)	2 (0.3 %)	130 (2.8 %)
>10	38 (1 %)	0	38 (0.8 %)
Mean number per patient	2.1	1.4	
Maximum number per patient	42	6	

Source : CNAMTS data in 2006-2007, OFDT estimates

9. In 2006 in Ile-de-France, Alsace and PACA respectively: 19.6, 10.3 and 10.1 mg/d, and in 2007: 13.6, 11.4 and 10.9 mg/d.

10. 35.1 years old for methadone versus 34.5 for HDB (Table 1). The 2002 study found a mean age of 35.9 versus 34.4 years old.

11. The study found that 65% of people were included in a treatment system probably corresponding in this case to the regular treatment category.

Table 3 - Distribution of OST recipients by regularity of treatment

	2006			2007		
	HDB	Methadone	Total	HDB	Methadone	Total
Patients receiving "regular treatment"	2 574 (66 %)	388 (45.5 %)	2 962 (62.5 %)	2 418 (65 %)	384 (42.8 %)	2 802 (60.8 %)
<i>Of which:</i>						
- Continuous treatment	2 059 (80 %)	189 (49 %)	2 248 (76 %)	1 900 (78.5 %)	184 (48 %)	2 084 (74.4 %)
- Virtually continuous treatment	515 (20 %)	199 (51 %)	714 (24 %)	518 (21.5 %)	200 (52 %)	718 (25.6 %)
Patients receiving "irregular treatment"	1 310 (34 %)	464 (54.5 %)	1 774 (37.5 %)	1 293 (35 %)	512 (57.2 %)	1 805 (39.2 %)
All patients	3 884	852	4 736	3 711	896	4 607

Source : CNAMTS data 2006-2007, OFDT estimates

According to these definitions, 80% of patients receiving HDB as regular treatment over the two years were receiving continuous treatment (Table 3) compared to half of those who were receiving methadone. This difference can undoubtedly be explained by more intermittent management in the methadone patients because of alternating follow up between primary care and the treatment centre which may result from the use of this substance.

Whilst receiving irregular treatment suggests episodic follow up associated with greater vulnerability or even misuse, regular treatment and, to an even greater extent, "continuous treatment" conversely implies that the management is sustained over time in patients who have consulted regularly and submitted all of their treatment units for reimbursement.

Specific case of patients receiving both OST

In addition to examining the levels of use within the different groups of patients who received HDB or methadone, a separate study was made of profiles of patients who were prescribed both substances during each year, defined as "mixed treatment". These patients had initially been excluded from the two sample populations (see box "methodological information"), and represent less than 5% of the groups, totalling 153 patients in 2006 and 176 the following year, approximately half of whom had received more than three prescriptions of HDB and methadone during the year. This co-existence of prescriptions usually represents a switch from HDB to me-

thadone (66% in 2006 versus 73% in 2007) or more rarely, from methadone to HDB (10% in both years). Only 23% and 16% of the patients respectively alternated between the substances.

Patients' "behaviours"

An analysis conducted from possible indicators of misuse attempted to identify the intended use of treatment (therapeutic or otherwise) in these patients (Tables 4 and 4a). Examining some of the medical prescriptions which these patients may also have received during the year is also informative (Table 5).

Indicators of misuse

Some indicators which have already been established from a large panel of studies conducted in OST (and specifically for HDB) can be used to understand the patients' type of use [3-5-6]. A mean daily dose of more than 32 mg/d of HDB in particular, but also medical (5 or more prescribers) and/or pharmacy (5 or more pharmacies) nomadism are thresholds above which a strong presumption of misuse of the substance can be made, particularly if these factors co-exist.

According to the 2002 study, 6% of patients receiving HDB were given a mean daily dose of 32 mg/d or more during the second half-year and the same number of patients had received prescriptions from at least five physicians over this period. Some sites such as Paris, the North Paris suburb area and Marseilles showed particular evidence of misuse. Although this study may have slightly

overestimated the actual situation nationally¹², the 2006 and 2007 results show a large fall in doses over 32 mg/d, which were found in only 2% (n=84) of all of the patients in 2006, followed by 1.6% the next year (n=61). Moreover, the proportions of amounts reimbursed for HDB in these patients represented 10.8% of the whole sample in 2006 and fell in the following year (6.9%).

As previously observed, whilst almost a third of patients saw three or more physicians in 2006, slightly fewer than 10% saw five or more physicians and 8% went to five or more pharmacies. These rates fell in 2007, a quarter seeing three or more physicians and 6% seeing five or more (similar figure to the 2002 survey).

There was also a positive correlation for these two years between the mean daily dose of HDB and the number of prescribers seen (the higher the daily dose the greater the number of physicians consulted), particularly for 2006 ($r=0.58$, $p < 0.0001$).

In terms of patients benefiting from CMU, higher rates of these indicators of misuse were seen than in the whole population with a mean daily dose above 32 mg/d in 3% and 3.5% respectively and larger numbers of healthcare professions seen in 2006 (2.5 times more patients seeing five or more physicians and twice as many patients going to five or more pharmacies than in the whole sample). A clear fall in these practices was seen between 2006 and 2007 (Table 4), which is very probably explained by the strengthening of the National Health Insurance monitoring plan, but also the dismantling of the dealing network in Ile-de-France in 2007 [7].

The study report to be published shortly will provide further details concerning this study of the misuse indicators in the different patient groups described above, particularly those considered to be receiving irregular treatment.

For methadone, which is misused far less often than HDB, both in 2006 and in 2007 slightly more than a quarter of the patients saw at least three physicians during the year and 4% saw five or more (Table 4a). It must be noted, however, that switching from primary care management to treatment centre management for methadone treatment tends to increase the number of physicians potentially consulted. On the other hand, consulting five or more pharmacies was very rare

Table 4 - Mean daily dose and indicators of misuse in patients receiving HDB

HDB	2006		2007	
	All patients (n=3884)	Patients CMU+ (n=893)	All patients (n=3711)	Patients CMU+ (n=793)
Mean Daily Dose (MDD)	9.5	11	8.9	11.1
MDD ≤ 16 mg/l	87 %	83 %	87.2 %	82 %
16 < MDD ≤ 32 mg/l	11 %	14 %	11.2 %	14.5 %
MDD > 32 mg/l	2 %	3 %	1.6 %	3.5 %
≥ 3 prescribers	32.3 %	36 %	24.5 %	28.1 %
≥ 5 prescribers	9.7 %	23.5 %	6.3 %	9.3 %
≥ 3 pharmacies	24.3 %	30 %	22.6 %	26.5 %
≥ 5 pharmacies	8 %	18 %	6.9 %	10.2 %

Source : CNAMTS data 2006-2007, OFDT estimates

12. Areas were found in which dealing was most intense amongst the 13 départements included in the study. However, to qualify this assertion, it should be noted that the study included urban metropolitan areas which contain a large proportion of the opiate users in France.

13. Unlike HDB, methadone is a narcotic. Prescription is limited to 14 days (versus 28 days for HDB) and it is dispensed in 7-day fractions except if accompanied by the instruction "dispense as a single dose" (idem for HDB). Its initial prescription is restricted to addiction, support and prevention treatment centres (the general practitioner becoming involved for maintenance treatment) whereas any physician can prescribe HDB.

(0.3% in 2006 and 0.9% in 2007). This may be explained firstly by the fewer number of opportunities for misusing this substance in view of the ways in which it is prescribed¹³ but also by reduced accessibility in pharmacies compared to HDB. As for HDB, patients benefiting from CMU, however, had slightly higher levels of use compared to the whole sample in 2006 (10% between 100 and 300 mg/d versus 6%) and twice as many saw five or more physicians (8% versus 4%). This difference was no longer present in 2007.

Profiles of patients receiving more than 32 mg/d of HDB

The very great majority of these patients were male (84% in 2006 and 88% in 2007) and were significantly older than those receiving 32 mg/d or less (36.1 years old in 2006, and 38.6 years old in 2007). More of these patients also benefited from CMU (42% and 56%).

As in the previous studies, a marked geographical localisation of misuse was found. These problem dosages were found in 2006 in 10 regions, with a clear predominance in Ile-de-France which made up 70% of all cases (n=59) followed by the PACA and Alsace regions (8% in each case). Whilst problem dosages were found in more regions in 2007 (n=14¹⁴) the same regional ranking was seen, 47% being found in Ile-de-France, 14.7% in the PACA region and 9.8% in Alsace. The drug dispensed to patients who were receiving a high mean daily dose was usually the primary substance (72% in 2006 although only 49% in 2007): alternation between primary molecules and generics increased from 28% in 2006 to almost 50% in 2007. Generics alone were only prescribed in a single patient in 2007.

Table 4a - Mean daily dose and indicators of misuse in patients receiving methadone

Methadone	2006		2007	
	All patients (n=852)	Patients "CMU+" (n=147)	All patients (n=896)	Patients "CMU+" (n=167)
Mean Daily Dose (MDD)	48.8	51.2	49.5	52.9
MDD ≤ 100 mg/J	94 %	90 %	94 %	93 %
100 <MDD ≤ 300 mg/J	6 %	10 %	6 %	7 %
MDD > 300 mg/J	0	0	0	0
≥ 3 prescribers	28.5 %	25.2 %	26 %	27.5 %
≥ 5 prescribers	4.1 %	8.2 %	3.8 %	4 %
≥ 3 pharmacies	7.4 %	7.5 %	8.2 %	9 %
≥ 5 pharmacies	0.3 %	2 %	0.9 %	2.4 %

Source : CNAMTS data 2006-2007, OFDT estimates

Therapeutic associations

In addition to OST, these patients received other therapeutic substances, particularly psychotropic drugs, usually taken for therapeutic purposes, although occasionally these were misused¹⁵. Although it is not possible here to determine whether these prescriptions were made on the same prescription as the OST or to give further information about the context in which they were used, the fact that some classes of medicines are involved is however informative.

Prescribing levels of several potentially misused psychotropic drugs such as some benzodiazepines¹⁶ (anxiolytics or hypnotics), Artane® (a synthetic anti-Parkinsonian agent occasionally taken for its psychotropic effects), or other substances which are markers of potential misuse such as Fucidine® (a local antibiotic commonly used for skin abscesses and

therefore a potential marker of intravenous use) or even "occupational" trafficking such as Cytotec® (a gastric antisecretory agent misused and exported as a pro-abortion substance) are shown in Table 5. These associations were found throughout the whole patient group but also in those benefiting from CMU and/or a mean daily dose of HDB of over 32 mg/d. Prescribing levels were relatively similar over the two years and only the 2007 results are shown here.

Three profiles of patients receiving HDB appear to emerge from these observations:

■ the "all patients" group (98% of whom receive up to 32 mg/d of HDB): slightly under half of whom (40%) were using benzodiazepines (Lexomil® and hypnotics in particular) with the number of prescriptions of substances suspected of being misused (Artane® and Cytotec®) being almost zero. These patients

Table 5 - Prevalence of use of non-opiate drugs amongst different groups of patients receiving substitution treatment in 2007

	HDB "all patients" (n=3711)	HDB "CMU+" (n=793)	HDB > 32mg/j (n=61)	Methadone "all patients" (n=896)	Methadone "CMU+" (n=167)
PSYCHOTROPIC DRUGS					
Benzodiazepines :					
Anxiolytics					
Tranxene®	3.9 %	6.2 %	4.9 %	3.2 %	7.2 %
Lexomil®	14.9 %	18.5 %	29.5 %	14.9 %	20.3 %
Valium 10 mg®	6.3 %	10.6 %	21.3 %	8.5 %	12.6 %
Seresta®	8.3 %	10.3 %	22.9 %	8.3 %	7.2 %
Rivotril®	4.8 %	6.9 %	37.7 %	4.7 %	6.6 %
Rohypnol®	3.7 %	6.3 %	49.2 %	3 %	4.2 %
Benzodiazepines :					
Hypnotics					
Imovane®	11.1 %	17.1 %	26.2 %	12 %	15.6 %
Stilnox®	13.5 %	16.6 %	26.2 %	13.4 %	11.3 %
At least one of these Benzodiazepines prescribes					
	40 %	53 %	85 %	44 %	54 %
Neuroleptics					
Tercian®	8.2 %	10.3 %	18 %	7 %	5.9 %
SUSPECTED MISUSED MEDICINES					
Artane®	0.3 % (n=12)	0.5 % (n=4)	3.3 % (n=2)	0.2 % (n=2)	0
Cytotec®	0.4 % (n=14)	0.7 % (n=6)	14.8 % (n=9)	0.3 % (n=3)	0.6 % (n=1)
Fucidine®	8 % (n=301)	13 % (n=103)	14.8 % (n=9)	7.8 % (n=70)	12 % (n=20)

Source : CNAMTS data 2006-2007, OFDT estimates

14. In addition to the 10 regions already involved (Alsace, Bourgogne, Centre, Ile-de-France, Languedoc-Roussillon, Lorraine, Nord-Pas-de-Calais, Picardie, Poitou-Charente and PACA), some regions witnessed a few cases of misuse in 2007. This applies to the three southern regions (Aquitaine, Midi-Pyrénées and Rhône-Alpes) and Haute-Normandie (a total of 5 cases).

15. Not all uses of a psychotropic drug in a drug user or ex-user are systematically synonymous with the desire to "get high", as the high prevalence of psychiatric comorbidities in users is often associated with anxiety symptoms, leading to either legitimate or illegitimate use of these agents.

16. The study of therapeutic associations was based on the main benzodiazepines used and occasionally misused (already analysed in the 2002 study). The category "prescription of at least one of these benzodiazepines" provides a global view of the level of prescribing of these substances through the anxiolytics and hypnotics selected for the different population groups defined.

were probably not dealing and had similar use profiles to the patients receiving methadone.

■ patients benefiting from CMU with a slightly higher level of benzodiazepine prescription than the previous group (53%), a strong likelihood of higher psychiatric comorbidity (10.3% versus 8.2% receiving at least one prescription of Tercian®) and more frequent use of Fucidine® (13% versus 8%). These findings point towards more prevalent injection practices in these more vulnerable, fragile patients who were however very little involved in dealing (only 0.7% were receiving Cytotec®).

■ patients receiving more than 32 mg/d: 85% of whom were receiving a different profile of benzodiazepines (Rivotril® and Rohypnol® for most of them¹⁷) and a high level of Cytotec® prescriptions (15% of this group). This suggests a group of patients very likely to be involved in dealing or at least suspected misuse and having greater difficulties (use of Tercian® by almost 20 per cent of them in addition to benzodiazepines, but also Artane®¹⁸ by 3%).

Fucidine®, a probable marker of injection, was found in the same ranking but with smaller differences between the three groups, suggesting that this practice affects all patients, even those receiving methadone, and thus proving that it probably was not exclusively the substitution treatment which was injected.

Conclusion and future perspectives

This study conducted in two samples of patients representative of the population receiving substitution treatment in 2006 and 2007 provides a more detailed categorisation than the previous studies of the types of patient treatment as a function of their actual length of treatment during the year and the interval between two dispensing episodes. Although, according to the analysis conducted here, almost two-thirds of the patients in these samples are considered to be receiving regular treatment and therefore a priori included in a treatment system, not all of the other people are necessarily outside of the care system. Some who are considered to be receiving irregular treatment may for example receive episodic medical follow-up in addition to their prescriptions – particularly those receiving HDB – through procurement on the black market for self-substitution and/or misuse purposes.

This analysis also provides details on some populations, particularly those benefiting from CMU, which are more vulnerable than the whole population studied and have more problematic prescriptions in terms of mean

daily OST doses and therapeutic associations and populations receiving more than 32 mg/d of HDB with more intensive use profiles.

Finally, the study of HDB misuse has shown a clear fall between the previous estimate in which 6% of people were receiving 32 mg/d of HDB or more, and this one which only mentioned 2% of the population in 2006 followed by 1.6% the following year. This effect is a direct result of the National Health Insurance monitoring plan which has been implemented since 2004 for insured members suspected of misuse or dealing of OST based on different types of actions depending on the cases (the defining of a treatment protocol between the prescribing physicians and the patient, suspension of some services which are not medically justified or even legal action).

Whilst the findings on HDB misuse can be compared to existing data, those on levels of use in the different patient groups identified here do not allow any conclusions to be drawn about trends in use or behaviour because of the duration of the study, limited to two consecutive years. Continuation of this cooperation between CNAMTS and the OFDT may however allow trends in use to be identified and even determine courses of use over longer periods if it is possible to ensure follow-up of individuals from one year to the next.

The complete study report to be published here at the end of 2009 will provide a more detailed analysis of user behaviour and, in particular, dealing in the different patient groups defined above. Broadening the availability of HDB on the market in 2006 will also be an opportunity to identify different methods of use depending on the type of substance dispensed (primary molecule or generic) if these exist.

17. Rohypnol®, prescription of which has been controlled since 2001 because of its misuse in recent years, is still, however, misused in a socially very marginalised population, as is Rivotril®, for which the “getting high” effect appears to be less pronounced.

18. Misuse of Artane® is mostly found in an extremely marginalised population often suffering from psychiatric disorders, which uses it for its hallucinogenic effects and the effect of invincibility which it produces (enabling them to face up to street life).

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