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ADDICTOLOGY

Characteristics of patients who are initiated on long-acting buprenorphine (Buvidal®) in France: A retrospective cross-sectional study

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KEYWORDS

Buvidal® ;
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Summary

Aim. – The long-acting buprenorphine Buvidal® is a recent type of opioid agonist treatment (OAT) used for opioid use disorder (OUD). It was initially suggested to preferentially use Buvidal® for specific OUD populations, including people in prison, or patients in recovery and on sublingual

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buprenorphine. We conducted a national study to examine whether the profile of patients treated with Buvidal® in France matched these initial recommendations.

Methods. — A retrospective cross-sectional study was conducted in 13 national addiction centers (outside prison), using the individual medical records of patients initiated on Buvidal®. Baseline characteristics were collected and described, including sociodemographic features, comorbid medical conditions, concurrent substance use and prescription drug misuse, and OAT features before Buvidal® initiation, respectively.

Results. — In total 101 patients (72.3% males, mean age 43.9 ± 11.3 years) were identified, which corresponded to one sixth of all patients treated with Buvidal® in France at the time of the study. Of them, 36 (36.4%) of them were professionally active, 35 (35.4%) were durably inactive, and the rest in an intermediary situation. Furthermore, 90 (90.0%) patients had at least one medical comorbidity (all types), and 83 (83.0%) at least one psychiatric comorbidity. Most frequent non-psychiatric comorbidities were chronic pain ($n=20$, 20.0%) and chronic viral infection ($n=16$, 17.8%). Current use of psychoactive substances included cocaine and crack ($n=43$, 42.6%), heroin ($n=19$, 18.8%), but also misuse of prescription drugs ($n=20$, 20%), mainly opioid analgesics. Moreover, 99 (98.0%) patients had an OAT before Buvidal® initiation, including 7 (8.1%) patients on methadone.

Conclusion. — The profile of patients initiated on Buvidal® in France was extremely similar to that of patients treated for OUD in France, either in terms of social or clinical features. While initial recommendations essentially underlined the interest of Buvidal® for some niche populations, the on-the-ground practice reveals a more widespread use, including for unrecovered patients, or patients treated with methadone.

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Abbreviations

AAH	<i>allocation adulte handicapé</i> (allowance for disabled adults)
CNIL	<i>Commission nationale de l'informatique et libertés</i> (French National Commission for Information Technology and Liberties)
HBV	hepatitis B virus
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IQR	interquartile range
OAT	opioid agonist treatment
OUD	opioid use disorder
RSA	<i>revenu de solidarité active</i> (active solidarity income)
SD	standard deviation

Introduction

Opioids consist of a heterogeneous family of molecules which all share the ability to bind on receptors of the same name, i.e., the opioid receptors, in particular the μ opioid receptors [1]. μ -receptor agonist can restrain pain, but also trigger dose-related sedation, which may lead to coma and death [1,2]. Chronic exposure to opioids can induce addiction, that is, a state in which the individual is no longer able to stop or control opioid use, because of several biological

and social processes such as tolerance, withdrawal, or craving [1,2]. This state is also named opioid use disorder (OUD) [2].

Opioid agonist treatments (OATs) are opioids used for the treatment of OUD [2]. While they also activate the μ -receptor, they induce less processes of loss of control and craving, and thus allow to reduce craving, withdrawal, and to reduce the adverse consequences related to OUD [2,3]. Methadone and buprenorphine are the two main types of OAT. While methadone is a full μ -receptor agonist, buprenorphine is a partial μ -receptor agonist, which is thus more practical and safer to use, in the sense that it reduces the risk of overdose [2,3]. However, buprenorphine can be more easily diverted and misused, relative to methadone, and sublingual forms must be taken at least on a daily basis, which can be cumbersome for some patients [4].

For a few years, new formulations of buprenorphine have been commercialized, which allow for a weekly, monthly, or six-month coverage of the treatment [5]. These so-called long-acting buprenorphine formulations comprise different types of systems, including depots or implants [5]. So far, the only long-acting buprenorphine depot formulation in Europe has been Buvidal® (Camurus), which offers either a weekly or a monthly injection of buprenorphine [5]. Buvidal® has been shown to be at least as efficacious a sublingual form of buprenorphine [6], with adequate level of safety [7], and enhanced patient satisfaction [8]. Initially, Buvidal® was intended to be specifically suited for some subpopulations of patients with OUD, particularly those in custodial settings

[5,9,10], those treated with sublingual buprenorphine and who were in recovery [10], or those who inject or snort sublingual buprenorphine [10]. In practice, however, Buvidal® has rapidly become the most-used OAT in some European countries, e.g., Finland [11], where it is proposed to any type of patient with OUD.

By contrast, among the European countries in which Buvidal® is available, France is one of the countries in which Buvidal® has been the least used, with an estimate, at the beginning of 2024, of only 600 patients treated on Buvidal®, which corresponds to less than 0.5% percent of all patients treated with buprenorphine [11]. In line with premarketing clinical guidelines [10], the use of Buvidal® in France has been prioritized by public authorities, for some subcategories of the OUD patients, in particular those in prison, and those with OAT misuse [12]. Moreover, because there has been no direct comparison between methadone and Buvidal®, and because it has been feared that the switch from methadone to Buvidal® may induce withdrawal [13], this switch is usually considered hazardous, and many clinicians are reluctant to propose Buvidal® to patients on methadone. Outside the context of custodial setting, Buvidal® has been recommended mainly for stabilized patients, i.e., those who do not use any opioids other than therapeutic prescriptions of buprenorphine, and even, those who do not use any psychoactive substance at all [10].

We conducted a retrospective examination of the clinical records of patients treated with Buvidal® since the marketing of the drug in France, with the aim to verify whether the sociodemographic and clinical characteristics of patients initiated on Buvidal® in France did actually correspond to those for whom Buvidal® had been initially prioritized.

Materials and methods

Centers and data collected

The medical records of all patients initiated on Buvidal® from July 2021 (i.e., the date of Buvidal® marketing in France) and August 2023 was searched and investigated in 13 different national addiction centers (outside prison). The list of the participating centers is available in [Supplemental Material 1](#).

The inclusion criteria comprised:

- being aged 18 years or more;
- having received at least one injection of Buvidal®.

All patients identified were notified by face-to-face discussion or postal mail about the anonymous extraction and use of their medical data for research purpose, and about their right to oppose this procedure by return mail or email. No such opposition was noted. The research protocol and data extraction procedure were declared to the *Commission nationale de l'informatique et libertés* (CNIL).

The following data were extracted:

- sociodemographic features, that is, gender (males or females), age (years), professional status, marital status;
- number and types of current comorbidities (including psychiatric comorbidities) and number and type of concurrent medications;

- number and type of current substance use, including prescription drug misuse, based on the dose, duration, and indication of use;
- type and treatment duration of previous OAT (if any).

Statistics

Only descriptive statistics are provided. Quantitative variables are described using the mean and standard deviation (SD) and the median and interquartile range (IQR). Qualitative variables are described using the number and percentage (n , %). Data were analyzed by the Contract Research Organization *KAPPA Santé* (<https://www.kappasante.com/>), using the SAS software (SAS Institute, version 9.4, North Carolina, USA).

Results

Sociodemographic features

One hundred and one (101) exploitable medical files were identified, which consisted of the data of 73 (72.3%) males, aged of a mean of 43.9 ± 11.3 (median = 46 [35–53]) years. Sociodemographic features of patients are displayed in [Table 1](#).

Overall, 41 (41.5%) of the patients were professionally active or students, 22 (22.2%) were job seeker, and 35 (35.4%) were inactive and one (1.0%) patient was retired. Regarding the 35 inactive patients, 28 (80%) of them received the allowance for disabled adults (*allocation adulte handicapé*, i.e., AAH), 3 (8.6%) were in durable unemployment with no specific allowance, two received the active solidarity income (*revenu de solidarité active*, i.e., RSA), and two (5.7%) were following an adult reinsertion program.

Of the identified patients, 52 (52.0%) were single, 26 (26.0%) were in couple, 20 (20.0%) were separated or divorced, and two (2.0%) were widowed, while information was missing for one (1.0%) patient. Forty-four (44.9%) of the patients had children, and 66 (66.0%) of them reported having a stable housing, while 25 (25.0%) patients were in unstable housing and 5 were homeless. Another situation was reported for 4 patients and concerns prison sentence adjustment measures. Regarding the level of education, 6 (6.3%) patients reached the primary school, 67 (70.5%) the secondary school, and 22 (23.2%) reached higher (“*post-baccalauréat*”) education, respectively.

Current comorbidities and other prescribed medications

Current comorbidities and associated prescribed medications are displayed in [Table 2](#). Among the 101 medical records explored, 90 (90.0%) patients were identified with at least one current medical comorbidity. The mean number of current medical comorbidities was 1.8 ± 1.1 , and the median [IQR] was 2 [1–3]. Only 10 (10.0%) patients were found with no current medical comorbidity. Among patients with at least one comorbidity (all types combined) were mood or anxiety disorder ($n = 70$ 77.8%), personality disorder ($n = 28$, 31.1%), psychotic disorder ($n = 17$, 18.9%), chronic

Table 1 Description of sociodemographic characteristics of patients initiated on Buvidal® in France.

Gender <i>n</i> = 101	Males	73 (72.3%)
	Females	28 (27.7%)
Age (years) <i>n</i> = 101	Mean ± SD	43.9 (± 11.3)
	Median [IQR]	46 [35–53]
Professional status <i>n</i> = 99	Student	5 (5.1%)
	In post	36 (36.4%)
	Job seeker	22 (22.2%)
	Retired	1 (1.0%)
	Other	35 (35.4%)
	If "other"	
Specification <i>n</i> = 35	AAH - allowance for disabled adults	28 (80.0%)
	Sustained unemployment	3 (8.6%)
	RSA - Active solidarity income	2 (5.7%)
	Adult Reinsertion program	2 (5.7%)
Marital status <i>n</i> = 100	Single	52 (52.0%)
	In couple	26 (26.0%)
	Separated or divorced	20 (20.0%)
	Widowed	2 (2.0%)
Children <i>n</i> = 98	Yes	44 (44.9%)
	No	54 (55.1%)
Main housing place <i>n</i> = 100	Stable housing	66 (66.0%)
	Unstable housing	25 (25.0%)
	Homeless	5 (5.0%)
	Other	4 (4.0%)
Level of education <i>n</i> = 95	Primary school	6 (6.3%)
	Secondary	67 (70.5%)
	Higher education (i.e., <i>post-baccalauréat</i>)	22 (23.2%)

AAH: *allocation adulte handicapé*, allowance for disabled adults, which guarantees a minimum income to people with chronic and fixed disabilities; IQR: interquartile range; RSA: *revenu de solidarité active*, i.e., active solidarity Income, which provides a minimum level of income for people without resources which varies according to the composition of their household; SD: standard deviation

pain (*n* = 20, 20.0%), and chronic infection by hepatitis C virus (HCV) hepatitis B virus (HBV), or human immunodeficiency virus (HIV) (*n* = 16, 17.8%).

Regarding concurrent psychiatric comorbidities only, 17 (17.0%) patients had no identified psychiatric comorbidity, while 54 (54.0%) had one reported psychiatric comorbidity, 26 (26.0%) had two psychiatric comorbidities, and 3 (3.0%) had three identified psychiatric comorbidities, respectively. Information was missing for one patient. No concurrent medication was found in the record of 12 (12.0%) patients, 1 or 2 concurrent medications were found in 40 (40.0%) of them, 3 or 4 concurrent medications were found in the in 25 (25.0%) of them, and 5 concurrent medications or more were found in the record of 23 (23.0%) patients. Information was missing for one patient. The list of the 15 most prescribed concurrent medications is provided in Table 2. The five most prescribed concurrent medications were diazepam (*n* = 25, 28.4%), oxazepam (*n* = 13, 14.8%), zopiclone (*n* = 12, 13.6%), paroxetine (*n* = 10, 11.4%), and cyamemazine and mirtazapine (*n* = 9, 10.2%), respectively.

Concurrent substance use and information on previous OAT are provided in Table 3. Overall, current substance use was reported for 84 (83.2%) patients. After excluding tobacco, the average number of current substance use was 1.8 (± 1.5), while the median [IQR] number of substances was 2 [1–3]. More specifically, current use was reported

in 51 (50.5%) patients for alcohol, 49 (48.5%) patients for cannabis, 43 (42.6%) patients for cocaine/crack, and 19 (18.8%) patients for heroin, respectively. The misuse of drugs other than OAT was reported in the records of 20 (20.0%) patients, mainly concerning tramadol (*n* = 12, 60.0%). Taken together, 32 (32.0%) patients used either heroin and/or misused opioid medicines. Misuse of OAT concerned 17 (17.2%) patients.

Buvidal® was initiated after switching from previous OAT in 99 (98.0%) patients. This previous OAT was buprenorphine in 92 (92.9%) patients, methadone in seven (7.2%) patients. The mean duration of previous OAT was 10.4 (± 7.7) years and the median [IQR] duration was 10 [4–15] years.

Discussion

This study aimed to depict the profile of patients treated with Buvidal® in France, using a retrospective exploration of the medical records of 101 patients among 13 addiction centers that were homogeneously distributed on the mainland national territory. As the total number of patients initiated on Buvidal® in France was estimated to reach 600 at the time of the study [11], the sample encompassed approximately one sixth of all patients treated with Buvidal® ever,

Table 2 Description of the current comorbidities and concurrent medications in patients initiated on Buvidal® in France.

At least one current medical comorbidity <i>n</i> = 100	Yes	90 (90.0%)	
	No	10 (10.0%)	
Number of current medical comorbidities (quantitative variable) <i>n</i> = 100	Mean ± SD	1.8 (± 1.1)	
	Median	2	
	Q1-Q3	1–3	
	Min-Max	0–5	
	None	10 (10.0%)	
Number of current medical comorbidities (categorical variable) <i>n</i> = 100	1 current medical comorbidity	31 (31.0%)	
	2 current medical comorbidities	33 (33.0%)	
	3 current medical comorbidities	21 (21.0%)	
	4 current medical comorbidities	4 (4.0%)	
	5 current medical comorbidities	1 (1.0%)	
If at least one current medical comorbidity, specification (<i>n</i> = 90)	Mood or anxiety disorder	70 (77.8%)	
	Personality disorder	28 (31.1%)	
	Psychotic disorder	17 (18.9%)	
	Chronic pain	20 (22.2%)	
	HCV, HBV, HIV	16 (17.8%)	
	Other	30 (33.3%)	
If other, specification (<i>n</i> = 90)	Neurodevelopmental disorder	8 (26.7%)	
	Liver disease	5 (16.7%)	
	COPD	3 (10.0%)	
	Diabetes	2 (6.7%)	
	Crohn's disease	2 (7.4%)	
	Chronic pancreatitis	2 (7.4%)	
At least one current psychiatric comorbidity <i>n</i> = 100	Yes	83 (83.0%)	
	No	17 (17.0%)	
Number of current psychiatric comorbidities (quantitative variable) <i>n</i> = 100	Mean ± SD	1.2 (± 0.7)	
	Median	1	
Number of current psychiatric comorbidities (categorical variable) <i>n</i> = 100	None	17 (17.0%)	
	1 current psychiatric comorbidity	54 (54.0%)	
	2 current psychiatric comorbidities	26 (26.0%)	
	3 current psychiatric comorbidities	3 (3.0%)	
At least one concurrent medication (<i>n</i> = 100)	Yes	88 (88.0%)	
	No	12 (12.0%)	
Number of concurrent medications (quantitative variable) <i>n</i> = 100	Mean ± SD	2.9 (± 2.1)	
	Median	2	
	Q1-Q3	1–4	
	Min-Max	0–8	
	None	12 (12.0%)	
Number of concurrent medications (categorical variable) <i>n</i> = 100	1 or 2 concurrent medications	40 (40.0%)	
	3 or 4 concurrent medications	25 (25.0%)	
	5 or more concurrent medications	23 (23.0%)	
List of the 15 most used concurrent medications <i>n</i> = 88	DIAZEPAM	25 (28.4%)	
	OXAZEPAM	13 (14.8%)	
	ZOPICLONE	12 (13.6%)	
	OPIOID PAINKILLERS	20 (22.8%)	
	<i>Of which with misuse/diversion</i>	14 (15.9%)	
	PAROXETINE	10 (11.4%)	
	CYAMEMAZINE	9 (10.2%)	
	MIRTAZAPINE	9 (10.2%)	

Table 2 (Continued)

QUETIAPINE	8 (9.1%)
HYDROXYZINE	7 (8.0%)
OLANZAPINE	7 (8.0%)
NICOTINIC SUBSTITUTES	7 (8.0%)
ARIPIPIRAZOLE	5 (5.7%)
ALPRAZOLAM	5 (5.7%)
SERTRALINE	5 (5.7%)
VENLAFAXINE	5 (5.7%)
PRAZEPAM	4 (4.5%)

COPD: chronic obstructive pulmonary disease; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; Q1: quartile #1; Q3: quartile #3; SD: standard deviation.

Table 3 Description of current substance use and previous OAT in patient initiated on Buvidal® in France.

At least one current substance use <i>n</i> = 101	Yes	84 (83.2%)
	No	17 (16.8%)
Number of substances currently used (expect from tobacco) <i>n</i> = 101	Mean ± SD	1.8 (± 1.5)
	Median [IQR]	2 [1–3]
Current use tobacco <i>n</i> = 101	Yes	76 (75.2%)
	No	25 (24.8%)
Current use of alcohol <i>n</i> = 101	Yes	51 (50.5%)
	No	50 (49.5%)
Current use of cannabis <i>n</i> = 101	Yes	49 (48.5%)
	No	52 (51.5%)
Current use of cocaine/crack <i>n</i> = 101	Yes	43 (42.6%)
	No	58 (57.4%)
Current use of other psychostimulants <i>n</i> = 101	Yes	8 (7.9%)
	No	93 (92.1%)
Current use of heroin <i>n</i> = 101	Yes	19 (18.8%)
	No	82 (81.2%)
Current use of unprescribed or misused medications (Except from prescribed OAT) <i>n</i> = 100	Yes	20 (20.0%)
	No	80 (80.0%)
If yes, specification <i>n</i> = 20	Tramadol-codeine	12 (60.0%)
	Other opioid	3 (15.0%)
	Benzodiazepines	5 (25.0%)
Current use of heroin or misused opioid <i>n</i> = 101	Yes	32 (31.7%)
	No	69 (88.3%)
Former OAT at Buvidal initiation <i>n</i> = 101	Yes	99 (98.0%)
	No	2 (2.0%)
Mean duration of first OAT (years) <i>n</i> = 94	Mean ± SD	10.4 (± 7.7)
	Median [IQR]	10 [4–15]
If yes. type of OAT <i>n</i> = 99	Buprenorphine	92 (92.9%)
	Methadone	7 (7.1%)
If yes. misuse of OAT <i>n</i> = 99	Yes	17 (17.2%)
	No	82 (82.8%)

IQR: interquartile range; OAT: opioid agonist treatment; SD: standard deviation.

which we believe to be a reasonable size for ensuring representativeness.

Overall, we found that the profile of patients initiated on Buvidal® mostly consisted of male individuals, aged between 35 and 55 years, frequently unemployed and single. Moreover, clinical data revealed that the patients initi-

ated on Buvidal® displayed frequent medical comorbidities other than OUD, in particular very frequent psychiatric comorbidities, as well as very frequent persistent substance use, including persistent use of heroin or other opioids. These findings suggest that a majority of patients initiated on Buvidal® were not in recovery, either on a social or

clinical standpoint, even if a large part of them had received an OAT for many years. Overall, this profile is very similar to that found in outpatient French addiction centers at the same time as the study [14]. Consequently, no specific profile emerged from our data, regarding the profile of patients treated with Buvidal® in France (outside from the context of prison).

Incidentally, the data reveal that seven patients were switched from methadone to Buvidal®, which is generally considered as tricky, given the theoretical risk of withdrawal [13], and even though previous reports found that it seemed safer and easier than previously believed [15]. Moreover, it is important to note the substantial amount of patients in whom associated use of full opioid agonists were noted before Buvidal® initiation was found, as concurrent use of heroin was reported in almost one fifth of the sample, and concurrent use of either heroin or misused opioids was reported in more almost one third of the sample.

Possibly in line with this, chronic pain was identified in 20 individuals (19.8% of the study population), among whom 7 (35.0%) were treated using opioid painkillers. In parallel, 13 individuals used painkillers but did not report chronic pain. Most opioid medications used by these patients were not prescribed, and thus probably resulted from purchases on black market. A recent meta-analysis found that chronic pain could reach more than 40% of patients on OAT [16]. Here, the prevalence of chronic pain was lower. This could be related to the fact that the use of a long-acting form of buprenorphine in patients with chronic pain is inappropriate because buprenorphine is a partial mu-receptor agonist which blocks the action of other opioids, which can theoretically increase pain [17]. In practice however, it seems that long-acting buprenorphine, including Buvidal®, can be effective on patients with chronic pain [17], even if the European Medicines Agency has still requested more data to approve such use [18]. In practice, however, chronic pain was not a complete barrier to initiate Buvidal® in the French practice. More longitudinal data are required to appraise whether this treatment is beneficial to OUD patients with chronic pain.

Our study has limitations that should be acknowledge. The retrospective nature of the investigation, in particular using medical records that can be incomplete, is an obvious source of possible bias. However, this type of bias essentially tends to omit data, and less to generate erroneous information. In the case of the present study, we found many more comorbidities and associated substance use than we could expect to find, given the fact that patients in recovery were one of the main target population of the initial recommendations of Buvidal®. Consequently, if the study design may have generated some over-detection bias, this would have only lowered our main findings. We also have to acknowledge that some variables had relatively unprecise definitions. For example, the collection of information about prescription drug misuse could have varied, according to the investigator, as the definition given for this variable was wide, and could include both prescribed or un-prescribed medications, as well as parameters such as doses or indications. Despite this, our study has also some strengths, including the fact that this data collection was undertaken in a limited range of time on a large proportion of patients who have been initiated on Buvidal® in France.

In conclusion, even if Buvidal® use remains extremely limited in France, when compared to some other European countries, in the centers that use it, the target population and clinical indications are extremely diversified, and does not correspond to the niche categories of patients that were initially identified as the most fitted for this treatment, including people in prison, patients in recovery with no longer substance use and with a stabilized social environment, and excluding patients treated with methadone. By contrast, given the frequency of comorbid psychiatric disorders and associated substance use in the treated population, Buvidal® initiation appeared to correspond to a need for a more effective treatment, which should be investigated using longitudinal analyses.

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Disclosure of interest

Over the past 5 years, Alice Deschenau has been paid as speaker, consultant and advisory board member for Camurus AB, as speaker for Bouchara Recordati and Ethypharm. She received specific fees from Camurus for coordinating the OPALÉ 2 study. Georges Brousse received fees for lectures and consultancy from Camurus, Individior, Recordati, Ethypharm, Accord Health and AbbVie. Margaux Kosim and Benjamin Touchon are employees at Camurus, France. Benjamin Rolland received fees for lectures and consultancy from Camurus, Individior, Recordati, Ethypharm, Accord Health, HAC Pharma, Biocodex, PileJe, Zentiva, Janssen, Gilead and AbbVie. He received specific fees from Camurus for writing the manuscript. The other authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.j.therap.2024.09.003>.

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