

Morphine sulphate consumption by French drug users

Recent trends (2012-2013)

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Morphine sulphate is the active ingredient in a class of opioid medications indicated in the treatment of intense pain and/or pain uncontrolled by other analgesics. Although they do not have MAs (marketing authorisations) for use in treating opioid drug addiction, morphine sulphates are sometimes prescribed in this indication, either within the scope of the "Girard circular" (circulaire Girard)¹ of 27 June 1996 or outside of this framework. Moreover, morphine sulphate-based medications can be used for reasons other than substitution by drug users and be misappropriated for sale on the black market.

The main morphine medication that is misappropriated is Skenan[®] LP, a sustained-release formulation that exists in several dosages of microsphere-filled capsules. Moscontin[®] LP, another sustained-release formulation, sold in tablet form by a different company, and Actiskenan[®], a rapid-release formulation, are not very present on the black market and do not seem to be particularly sought-after. Medications containing morphine sulphate are classified as narcotics.

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1. Issued by the *Direction Générale de la Santé* (National Health Directorate), it authorises the use of morphine sulphate after approval by the physician advisor of the CPAM (French Local Social Security Office) when substitution treatments with marketing authorisation are ineffective or when these medications are contraindicated.

SUMMARY

The use of morphine sulphate outside of the scope of the therapeutic framework is not a new phenomenon. However, starting in 2000 and for a decade thereafter, such use appeared to be fairly controlled, geographically-contained and volatile over time. Since 2011 or so, there has been a rise in demand that is disparate, but geographically widespread. This surge in demand is increasingly accompanied by high pressure, especially on general practitioners, who are not always able to resist.

Two main reasons help to explain this phenomenon:

■ Firstly, there has been a heroin “shortage” in Europe since 2011, which was evidenced in France by a significant decrease in heroin purity², and especially the heroin purity/price ratio. For opioid users making choices on the market based on factors such as substance quality, accessibility and price, this situation has led them to shift to morphine sulphate, which they deem to be similar to heroin. This is obviously due more to the “high” that goes along with morphine sulphate use than with the substance’s “treatment” facet. It explains the geography of use in part. However, starting in 2013, there has been an apparent rise in heroin purity recorded.

■ The increase seems to be related to the search for a “different” type of substitution, especially among patients who are not satisfied with methadone or high dose buprenorphine (HDB). Morphine sulphate is considered as “injectable”³ (contrary to methadone) and the source of a “flash”⁴ or at least a perceived effect (contrary to HDB), two aspects that many illegal drug users receiving treatment cannot seem to give up.

Finally, the hypothesis that methadone is difficult to access in certain rural areas should be explored given the geographic differences in use among CAARUDs (low-threshold structures) clients.

This pertains to two main types of users.

■ Active users, who are fairly young (20-30 years of age) but who are getting older and familiar with the party scene and are in major social distress and engaging in polydrug use and injection, practices that do not really decline with age. They encounter morphine sulphate much earlier than their elders. The youngest of these users tend to seek out Skenan[®], while the oldest among them consume it when there is no heroin.

■ The oldest users being followed for substitution treatment, usually methadone, seek it when they are having difficulty with their treatment because they are still injecting drug users.

Moreover, this substance is highly accessible, and depending on the opioid supply, or even drug supply in general, there are opportunistic users. These users are not necessarily attached to Skenan[®].

The market is often supplied by a limited number of physicians who prescribe high quantities and are often identified by users who may come from distant geographic locations. Although discussed in the media, deliberate trafficking by physicians seems to be rare. Other professionals seem to be worn down by consistent and sometimes violent pressure exerted upon them. The problem of insufficient supply is also raised through practitioners likely to be overwhelmed by the influx of patients after prescribing once. There are also cases of physicians who, by themselves, are forced to treat a large (excessive) proportion of drug users from a sector due to reticence by their colleagues to do so.

Therefore, regardless of the vagaries of the heroin market, it seems that it is more generally the treatment of addiction that is called into question through this morphine sulphate use.

2. The mean purity of heroin was halved between 2010 and 2012 [7].

3. Most users do not consider methadone as injectable. HDB is considered an injectable, despite the local and general damage injecting it can cause, but it is not considered satisfactory for some users.

4. An effect that gives the impression of a “peak”, a “quick high”, a peak and then a more progressive “coming down”.

TREND SCHEME: METHODOLOGY

TREND (Emerging Trends and New Drugs) is a scheme established by the OFDT in 1999. TREND endeavours to detect emerging phenomena and trends in illegal drug use, including trends in substances, supply, routes of administration and user profiles. To fulfil its observation mission, TREND relies first and foremost on a network of seven local coordinating sites (Bordeaux, Marseille, Lille, Metz, Paris, Rennes, Toulouse) with a common information collection and analysis strategy.

The TREND scheme has been focusing on observing the French urban setting and the techno party scene. The French urban setting primarily refers to treatment centres (CSAPAs, or National Treatment and Prevention Centres for Addiction) and harm reduction facilities (CAARUDs, or low-threshold structures), squats and open spaces (e.g., the street, dealing sites and areas surrounding stations). Some of the people met in these settings are drug users living in highly precarious conditions. The party scene refers to places where events are organised around the “techno” music trend. They encompass the so-called “alternative” scene (free parties, «teknivals», alternative party areas within more general festivals) as well as commercial or more conventional locations (clubs, discotheques and even private parties) and now tend to cover the general party scene because of the spread/dilution of the techno movement into the more general population.

The data collection tools used are mainly qualitative: continuous ethnographic observations conducted in urban areas and on the party scene, qualitative questionnaires administered to structures or associations in contact with drug users (CAARUDs), and focus groups (“health”, “law enforcement”) that aim to rapidly establish overviews of the situation with professionals in the field.

Note

The TREND scheme mainly reports on morphine sulphate use trends that do not comply with current regulations or treatment standards. Even though the sites also observe patients receiving morphine sulphate as part of opioid addiction treatment (off-label prescription), the clients of these treatments are often seen in the TREND scheme, either because they inject or because they sell some of their treatment, or because they obtain the drug on the black market or by pressuring prescribers, or because they use other substances.

Since the TREND scheme was first implemented, the misuse of morphine sulphates has been an often volatile and geographically localised phenomenon, seemingly closely related to whether or not prescribing physicians are locally present. Overall, the TREND sites have always reported significant reticence by physicians to prescribe morphine sulphates to drug users. During the 2000s, the TREND sites reported that Skenan[®] was primarily available in Rennes, and especially in Paris, before the National Health Insurance Fund (*Assurance Maladie*) in Brittany (2006) reprimanded prescribers and a Subutex[®] and Skenan[®] distribution network (physicians/chemists) was dismantled in Paris (2007), seriously reducing Skenan[®] availability. In 2008 and 2009, while the Parisian market began a new upswing, although it did not reach its previous high, an increase in availability was reported in Metz, while morphine sulphate misuse remained invisible or marginal at other TREND sites [1]. Subsequently, Skenan[®] availability has experienced local fluctuations without any clear-cut trends on a national level.

Since 2011-2012 [2-3], this relative national stability has given way to a more or less marked rise in demand at all TREND sites, with the exception of the Lille site and in the Nord-Pas-de-Calais department in general, where trafficking exists but remains marginal or localised. This phenomenon was observed in Lorraine, Nancy until 2012 and Metz until 2013. Over the course of this year, the phenomenon was especially noticeable in the south-west of France, in Bordeaux (likewise in the Landes department) and in Toulouse as well as, to a lesser extent, in Paris. This encouraged the local authorities in these areas to take action.

TREND NETWORK OBSERVATIONS IN 2012 AND 2013

MARKET

The most sought-after formulation is the Skenan[®] LP 100 mg or 200 mg capsule, depending on the site. Lower doses (30 mg, 60 mg) can be negotiated when better cannot be found, as can Moscontin[®] LP⁵ or Actiskenan[®]⁶.

The accessibility by prescription, as well as the availability and accessibility on the black market, seem to be inconsistent from site to site and region to region (Table 1).

High pressure of demand on several sites

With the exception of the Lille site, where opioid users seem to be unfamiliar with morphine sulphate use⁷, starting in 2012 several TREND sites observed a marked rise in demand for this substance, and this demand was even more intense in 2013. This phenomenon seemed to be most pronounced in Bordeaux and Metz, but was also visible in Marseille and was just starting in Toulouse. This increase was evidenced through consultations at CAARUDs, by frequent requests for prescriptions in CSAPAs and from general practitioners, and high, sometimes violent pressure on these GPs (Bordeaux, Toulouse, Metz, Marseille). At the same time, Skenan[®] is becoming more popular among users and observers are identifying new users of this product.

One of the characteristics of demand is that users no longer hesitate to travel to obtain Skenan[®] prescriptions in a region where it seems to be accessible. Therefore, in Marseille, some precarious, transient users organised their travels to coastal cities (such as Nice and Montpellier) according to their ability to obtain Skenan[®] prescriptions, while others travelled as far as Spain to procure the product. In Rennes, users who cannot obtain prescriptions locally travelled to other cities in Brittany or neighbouring regions (especially Normandy), or even to Paris. Some even migrated. At the same time, Metz reported users coming from Marseille in search of prescriptions, while the CAARUDs of Bordeaux identified users coming from other regions for the same reasons. In the Nord-Pas-de-Calais region, identified Skenan[®] users seeking to procure the product were rarely local consumers, the latter knowing little about the product.

Therefore, geographic areas considered to be zones of “accessibility” underwent pressure not only from local users for their own use, but also by users coming from other regions who either sought direct prescriptions or resorted to the black market, eliciting dealing behaviours from other users.

Prescription, a determinant of accessibility

In 2013, Skenan[®] was considered to be very easily accessible by prescription in Bordeaux, and had been in Metz into that year; it was reputed to be more difficult to obtain prescriptions for this drug in Rennes and Toulouse due to strategies that rarely include morphine sulphate in opioid addiction treatment; access was also limited in Marseille.

The data from site reports help schematically differentiate several prescription frameworks. Although the elements provided by the scheme do not enable these situations to be quantified, it appears that the market is usually supplied by a limited number of physicians who prescribe heavily. The «therapeutic framework» is very likely, and by far, the most frequent. There were a few “overloaded” physicians per site, and deliberately trafficking physicians were the exception.

5. Moscontin[®] LP is allegedly more difficult to prepare for injection than Skenan[®] LP.

6. Due to its rapid onset, but short-lived action, Actiskenan[®] is not indicated in the treatment of chronic pain except when such pain begins or when used as an opioid substitution treatment. Therefore, it is infrequently prescribed to drug users. Furthermore, drug users who inject Skenan[®] unpackage and prepare it (see “routes of administration”) to extract the morphine sulphate and circumvent the sustained release profile of the product. Finally, Actiskenan[®] exists in doses that do not exceed 30 mg while unit doses in sustained release formulations are as high as 200 mg.

7. “And I heard of something new, and I saw it in Lille, about a week ago, I was in treatment no less, and it's Skenan[®]! From what I saw, it was morphine tablets, but they were shooting up with it! And in Paris, it's all the rage”, stated a user from Lille [4.]

- The therapeutic framework

Some physicians prescribe within the scope of following addiction therapy, in compliance with the terms of the “Girard circular” or otherwise. The Brittany site specified that this seemed to be less and less frequently recognised by the National Health Insurance Fund, and that it was becoming increasingly difficult for prescribers to obtain the agreement of the insurance fund, even within this framework. For prescribers, this could mean combining substitution treatment with pain treatment, choosing morphine sulphate as opioid substitution treatment or even providing temporary support for an injecting Skenan[®] user transitioning to methadone⁸. In contrast, many physicians are hesitant to prescribe morphine sulphate for fear of future misuse or because they do not want to prescribe a frequently-injected drug within an unclear regulatory framework⁹ or because the National Health Insurance Fund performs strict surveillance. It should be noted that, as illustrated through example, given the calling into question of physicians and pharmacists of the Pas-de-Calais department since 2011, the prescription framework has not always been easy to describe and what appears to be “therapeutic” to one prescriber may be considered abusive by CPAMs or professional bodies.

- The “overloaded” therapeutic framework

Some physicians are overloaded with demand and fall outside of the therapeutic framework. There are two major underlying factors for these slips.

■ A local shortage of physicians following drug users: some physicians agree to treat drug users in areas where no prescriber sees them, and where certain stable methadone patients can no longer find prescribers. Under these conditions, physicians agreeing to prescribe experience an influx of drug users and can quickly be overwhelmed (Rennes and Toulouse are examples).

■ Requests for prescriptions can sometimes be very aggressive. Prescriptions obtained through pressure by users have been reported in Bordeaux, Metz, Marseille, and to a lesser extent, Toulouse. Some physicians prescribe out of fear and such information can spread rapidly. Similarly, any physician fragility, including for personal reasons, can be exploited. For example, the Lorraine site reports the case of a physician close to Nancy who allegedly moved to avoid pressure by users seeking HDB and Skenan[®], a case of a colleague who defended himself by shooting rubber bullets and even one who hired a guard. In Marseille, a user with several National Health Insurance cards allegedly forced a physician to provide several prescriptions at a time.

- Deliberate prescriber trafficking

Finally, there is a very small number of prescribers who can be more clearly involved in lucrative trafficking, as was the case in Paris in 2008. In Metz, three physicians, who were investigated in 2013, were suspected of having abusively prescribed Subutex[®] and Skenan[®] during fictitious consults as part of an illegal trafficking of National Health Insurance cards.

Prescriptions are regulated by the National Health Insurance Fund, which can, if appropriate, take action among users, physicians or pharmacists.

In Rennes, even under protocol, prescriptions seem to be regulated by the National Health Insurance Fund through the summoning of users when doses are deemed too high and the refusal to authorise pharmacy dispensing if users do not respond to summonses. In Bordeaux, the CPAM also employed patient control strategies by discontinuing reimbursements.

Consumers adapt to these measures in different ways, either by resorting to heroin use or by seeking out opioid substitution medications from primary care physicians or by joining a protocol. The Rennes site mentioned that some users anticipated stricter conditions for obtaining Skenan[®] by voluntarily reducing their doses and offsetting this dose reduction by using other opioids (such as tramadol).

8. This will require the gradual lowering of doses of morphine sulphate while methadone doses increase.

9. Prescribing morphine sulphate as substitution treatment remains “regulated” by a simple, 18-year-old circular.

The black market

- Trafficking

When it is limited in scope, trafficking is generally through users who engage in small-scale dealing. Some of them are being treated through a protocol, which enables them to sell some of their substance, either because they succeeded in obtaining a prescription that covers more than what they need or because they are diminishing their use. These practices appear to be increasingly rare in areas where prescriptions are few and well-controlled. Bordeaux also has small-time dealers who supply a certain group or area, such as a squat. In contrast, certain patients in a treatment protocol allegedly remain very discreet to avoid pressure by people seeking the substance.

A portion of the users also obtain multiple prescriptions and supply the black market by consulting several physicians. These users include, once again, certain users following a protocol (Rennes). Like for HDB, obtaining multiple prescriptions can involve procuring them outside of the department or region either to avoid being identified or when access appears to be «saturated» or when the relationship of trust with the prescriber is broken.

As was previously mentioned, some users or even small-time dealers¹⁰ (Bordeaux, Marseille) resort to National Health Insurance card trafficking and threats.

Finally, in Bordeaux, there appears to be a network overseen by people from Eastern Europe and the Caucasus organising traffic bound for their countries of origin¹¹. This trafficking represents the lion's share of misused substance.

According to the OPPIDUM 2012 survey (Observation of Illegal Drugs and Misuse of Psychotropic Medications) conducted by the ANSM (National Agency for Medicines and Health Products Safety) and the CEIP (Centre for Evaluation and Information on Pharmacodependence) mainly in drug treatment centres, 76 % of people who stated taking morphine sulphate reported having obtained it illegally [5].

- Availability

Skenan[®] is only available in urban settings (see the TREND methodology box), except in Marseille, where in 2013 it could be found on the alternative party scene.

Skenan[®], the morphine sulphate form most frequently seen on the black market, is used in inter-user bartering and “as spare supply” between users helping each other out. Markets like this limit the accessibility of Skenan[®] to people who already know each other. In 2013, it was still only on the Bordeaux market that Skenan[®] became accessible through easy-to-obtain prescriptions. In contrast, in Rennes, prescriptions were very limited, and the logic of “spare supply” between users to help each other out was the norm because users receiving treatment tended to keep their prescriptions.

While only Paris and Marseille already had well-established Skenan[®] street markets in the prior decade, in 2013 a street market appeared in Toulouse¹² (2013).

However, after an increase in activity in 2011 and the majority of 2012, the Paris¹³ Skenan[®] market, which was located around the *Gare du Nord* train station, also experienced shortages, sometimes with weeks at a time where there was no Skenan[®]. This had not happened since 2008 and led users to barter Moscontin[®], which no longer appeared on the Paris market. The decrease in availability continued in 2013 with the establishment of a priority safety zone in the 18th arrondissement of Paris. This led to violence and tension between law enforcement services and users or dealers.

10. They are not necessarily users themselves.

11. Sources: National Health Insurance Fund, prison workers

12. It is possible that the Metz site also had a street market from 2010 to 2013. It was not visible in 2013.

13. The Parisian Skenan[®] market was part of the medication market that mainly covered the 18th arrondissement and the *Gare du Nord* area. However, Skenan[®] sales mainly took place at the *Gare du Nord*, since the black market for the 18th arrondissement was dominated by HDB.

Finally, in the Nord-Pas-de-Calais region (Lille site), although there was almost no market in Lille, one city in the Pas-de-Calais had a small market before the prescriptions halted following a series of CPAM investigations.

Table 1- Standard Skenan® prices and accessibility, 2013

Sites	Skenan® LP capsules	Standard prices	Changes in prices 2012-2013	Mode of access	Availability on the black market
Bordeaux	200 mg	€3-5	↘	- Prescription +++ - Small supply networks	Increasing
Lille				- Prescriptions - No discernible market	Almost none
Marseille	100 ou 200 mg	€10	→	- Prescription + - Street market - User network - Occasional sales on the alternative party scene	Constant but insufficient compared to the demand
Metz	200 mg	€10-15	↗	- Prescription ++ discontinued - Exchange and « spare supply » between users	Down in Metz (end 2013) and Nancy (2013) but up in the Vosges
Paris	100 mg	€5-7	→	- Prescription + - Street market	Down
Rennes	100 mg	€7-10	→	- Prescription +/- - Very localised street market - Closed user network	Constant
Toulouse	200 mg	€15	→	- Prescription – - User networks - Emergence in 2013 of a street market	Increasing

Source : TREND/OFDT

- Prices

The prices vary considerably with the site (Table 1). The lowest price of 100 mg is currently in Bordeaux (€3-5 per 200 mg capsule)¹⁴ and the highest is in Toulouse (€15 for the same quantity), thereby illustrating the existence of local markets.

Regardless of the site, as for the entire street medication market, prices vary depending on the time of day and the day of the week (going for up to twice the price on weekends and in the evening). Sales by the box help decrease the price per capsule, in Metz for example, where a box of 14 Skenan® LP 200 mg capsules goes for €40 to €80; the same box runs about €70 in Bordeaux.

Subsequently, in Metz, where availability dropped sharply in 2013, the price per capsule rose from €5 to €10 in 2012 and to €10 to €15 in 2013, while in Bordeaux, the reverse trend was seen: on average, €15 in 2010, €5 in 2012, and less than €5 in 2013. In Paris, market tensions are mainly seen through more volatile pricing, leading for example, to a 100 mg tablet price of up to €15 on the weekends (unusual price for Paris).

Finally, when a transaction takes place on the open market, it can take the form of bartering (for example in Metz, users can trade one Skenan® capsule for three ecstasy tablets).

14. In 2013, a blister pack of 14 capsules of Skenan® LP 100 mg cost €26.20 (or €1.20 per capsule) and that of Skenan® LP 200 mg, €46.93 (or €3.50 per capsule). Of course, when it is reimbursed, it does not cost the patient anything. Subutex® tablets cost €2.50 to €5.00 on average, depending on the site (2012-2013), but it can be less expensive when purchased in higher quantities. Heroin is dealt at about €40 per gram (2 to 10 injections, depending on user tolerance and expected purity).

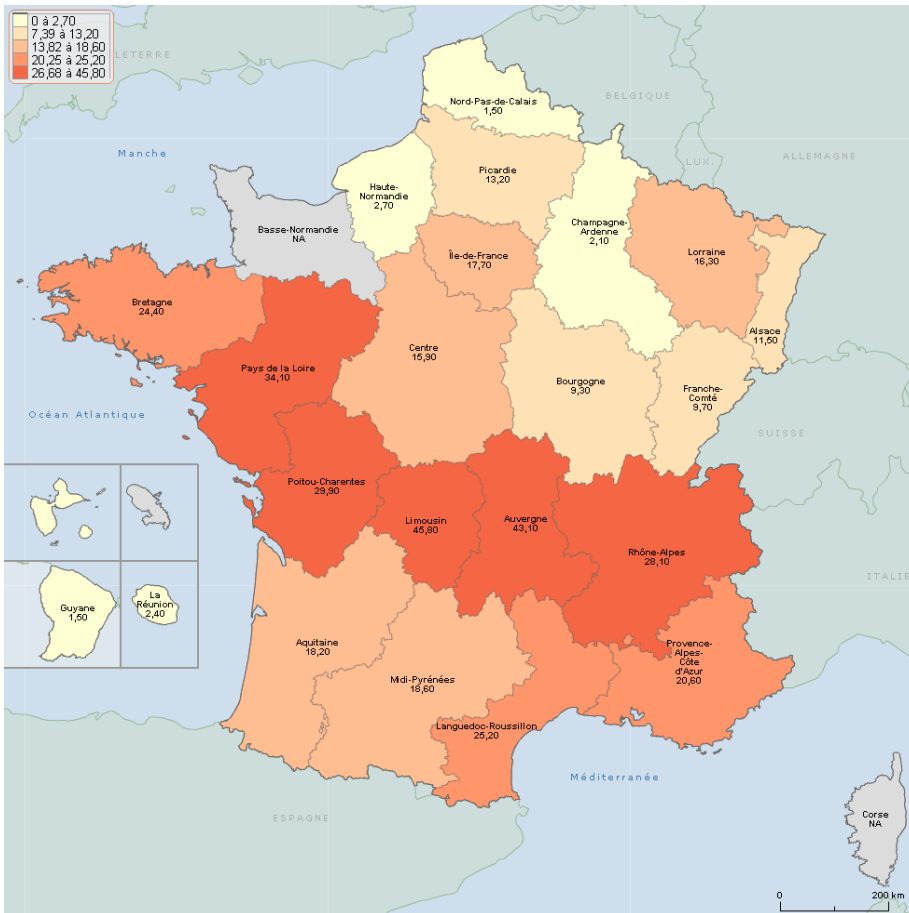
Regional data

In the month preceding the ENa-CAARUD survey in 2012, 17% of CAARUD clients consumed morphine sulphates¹⁵ (versus 15% in 2008 and in 2010)¹⁶.

This national prevalence masks wide geographic disparity. The map of prevalence by region demonstrates that, overall, prevalence declines from north-east/south-west; more specifically, there is a swathe of overconsumption crossing France from Brittany to the Rhône-Alps, centred on the Auvergne and Limousin regions. In the latter regions, four to five in ten CAARUD clients had taken Skenan® in the month preceding the 2012 survey.

In the absence of qualitative TREND data on the majority of this area - data that would better describe the phenomenon - it can be hypothesised that this area, which is far from both the north-eastern and the Spanish borders of France, where heroin transits, represents an area where heroin is difficult to access or the purity/price relationship is unfavourable.

Figure1 - Prevalence of stated last-month morphine sulphate use (%) by CAARUD clients, 2012



Source : ENa-CAARUD 2012, OFDT/DGS

15. Measured consumption included all types of use, whether as substitution treatment or otherwise. Experience shows that it is very difficult for CAARUD users to distinguish between use and misuse.

16. Difference is significant for a risk of 5%

Table 2 - Prevalence of last-month morphine sulphate use by CAARUD clients by regional group, 2012

Inter-regional zones ¹⁷	Proportion of last-month morphine sulphate users	Proportion of morphine sulphate users among opioid users*
Northwest	3.3 %	4.8 %
East	12.2 %	13.7 %
IDF (Ile-de-France region)	17.7 %	28.8 %
West	29.5 %	33.7 %
Centre	27.8 %	30.5 %
Rhône-Alpes (region located on south-eastern border of France)	28.1 %	32.6 %
Southwest	21.5 %	28.6 %
PACA (or Provence-Alpes-Côte d'Azur, a region in south-eastern France) and Corsica	19.7 %	25.9 %
DOM (Overseas departments)	1.5 %	11.0 %
France-wide	17.2 %	23.7 %

* The proportion of opioid users who recently consumed morphine sulphate provides a more specific estimate of the development of Skenan[®] use among its potential « population ».

Source : ENa-CAARUD 2012, OFDT

Factors promoting use

Like for substitution treatments, Skenan[®] can, depending on the user, schematically have the same role as that of a «drug», have a self-substitution function, or be part of a therapeutic framework like substitution treatment for opioid addiction or treatment for pain. Several sites also insist on the fact that Skenan[®] is consumed by users to self-treat pain.

The interest in using Skenan[®] is measured against other opioids. Regardless of the context of use, it has a very positive image.

- A very positive image for a drug

Within the scope of its “drug” function, Skenan[®] is mainly compared with heroin, which has similar effects, despite its different kinetic profile¹⁸.

The oldest heroin users continue to prefer heroin to morphine sulphate and generally take it by default (see below).

In contrast, the following generation (now 25 to 30 years of age) has a particularly positive view: “Skenan[®] is the perfect drug” stated an opioid user [6]. Its status as a medication reassures users: compared with heroin, morphine sulphate has an image of a reliable substance without unpredictable cutting products, and is even considered to be “hygienic” (people know how it is transported). Its price, whether in pharmacies or on the black market, is clearly competitive. In Bordeaux, rumour has it that morphine sulphate is being transformed into heroin (“if you filter it twice with the wheel [filter], you’ll get heroin”) [6].

It is essentially used for its own effects. Only the Marseille site reports the use of Skenan[®] to help drug users “come down” off stimulant highs on the party scene (punk rock scene), and the Paris site reports use to “come down” off of crack.

In addition to psychoactive effects, the effects of Skenan[®] on the skin (mainly itching, skin rash, flushing) represent, for many users, a necessary evil along with the expected effects.

17. The groups are explained in the appendix.

18. According to users, when it is used orally, the peak occurs approximately one hour after intake and the effect lasts for about 12 hours. When injected, the peak occurs more quickly and more violently than for heroin and the effects are shorter-lived (approximately three hours).

- A rather unattractive heroin market

In addition to this excellent image, Skenan® currently is of economic interest due to the poor “quality” of heroin (2011-2012) following its “return” in the late 2000s. In 2011 and 2012, heroin experienced a decline in quality that had not been seen in recent years (from 13% to 8% purity), making its quality/price ratio rather unattractive for users, especially in the west and south-west regions of France [7]. “*Smack is too expensive and of bad quality, so sken is used*” [8]. These comparisons were reported at the Rennes, Bordeaux, Marseille and Paris sites. They continued in 2013 in the field, while the mean purity of seized heroin for the full year 2013 was 13%¹⁹.

The differences observed between the price/purity ratio of heroin at France’s north-eastern border, which are much smaller than those reported in Rennes, Toulouse and Bordeaux, support this hypothesis [7].

Furthermore, in certain geographic areas (such as in inner Paris), morphine sulphate is more available than heroin.

- A very positive image as treatment

Within the scope of substitution treatment, morphine sulphate is compared with other OSTs. Some even mention it in the list of possible OSTs.

Compared with HDB, whose effects are considered to be rather unattractive or non-existent, Skenan® is considered to have a more satisfying effect. Moreover, users mention fewer skin and venous complications with Skenan® injections than with HDB injections.

More often compared with methadone by users, they believe Skenan® has an advantage in being injectable. In fact, even within the scope of a substitution protocol, many users observed by the TREND scheme do not wish to give up injection, or feel incapable of doing so, or seek a significant effect at the moment of intake.

Several sites report “unofficial” transitions from methadone treatment to the methadone/morphine sulphate combination; methadone is still taken as part of daily substitution, while the combination is more often injected as an addition. Other users supposedly abandon their substitution treatment for Skenan®, considering that it will be easier to “quit”.

USERS

There are two main Skenan® user profiles:

Traditional users, who tend to use it for substitution

The older and best-known Skenan® user profile is comprised of older users (35 to 40 years of age) who have a long history of opioid addiction and injection.

Some socially-integrated drug users receive Skenan® as part of a therapeutic protocol. It seems that they represent a high proportion of the Skenan® users observed by the Rennes and Nancy sites, and the only type of profile observed after the decrease in prescriptions. The majority of them are not visible in the TREND scheme.

People seen within TREND are most often drug users who are still active or who are unstable with their substitution treatment, even if such treatment is being received within the framework of a protocol.

19. The difference between purity perceived by users and the purity of seized product can be related to the fact that samples seized that do not contain heroin or only contain traces are not included in the seizure statistics, while in fact they are purchased and consumed by users, as the SINTES heroin study 2011 demonstrated [7].

At all TREND sites, with the exception of Rennes, visible Skenan[®] users are often marginalised users in unstable living conditions whose use is mainly medication-based (Subutex[®], benzodiazepines). For example, the Paris site reports a relationship with crack use and a partial overlap in populations, while Marseille reports a relationship with Ritalin[®] use²⁰; both these types of use locally involve rather unstable individuals living on the streets or in squats and often suffering from psychiatric disorders. In this context, Skenan[®] plays a role similar to that of Subutex[®], acting both to provide substitution and a high to varying extents [1].

Wandering youth and “nomadic” users, more clearly involved in drug use

Younger and appearing more recently than the previous group, wandering or nomadic users [9] somewhat represented “the new Skenan[®] users” (early in the current decade). Wandering youth²¹ (some of whom are starting to age) were mainly mentioned in the south-west of France (Bordeaux, Toulouse) and in Paris, while nomadic users²² who used Skenan[®] were more often seen in the south-east, in Marseille, and seemed to move to places where they believed they could source. These users, who are often referred to as “punks with dogs”, mainly used to get high rather than for substitution treatment. Of these young users, some allegedly began their opioid use with Skenan[®]. Several sites mentioned young women who started using drugs with Skenan[®].

Only the Paris site also observed an extension of the use of Skenan[®] to Eastern European groups living in extremely difficult conditions²³.

Opportunistic users

Finally, other than traditional users and wandering young users, there is a population of opportunistic users that take advantage of local accessibility when it is on the rise. This seemed to be the case in Bordeaux in 2012 and 2013, when there appeared to be a larger population evidenced through a diversification in routes of administration, both in Toulouse and in Lorraine, where Nancy revealed more treatment-centred user profiles when the medication became less available.

MORPHINE SULPHATE USERS IN CAARUDs, 2012

The 497 recent morphine sulphate users were compared with users of opioids other than morphine sulphate (N=1,595). The morphine sulphate users were slightly younger overall than other opioid users (34.3 years of age versus 35.8 years of age) because there were proportionately fewer people over the age of 35 (47.5% vs. 53.9%). However, very few of these users were under the age of 25²⁴ (11.9%). The percentage of women in both groups was similar (21.4% vs. 19.0%). Their mean level of instability was not significantly different than that of users of other opioids (32.8% were very unstable whereas 25.8% were without official income).

The description of the population of recent morphine sulphate users frequenting CAARUDs²⁵, which combines various users profiles, nevertheless helps identify several characteristics of the groups seen at TREND sites.

Recent Skenan[®] users more often appeared to be polydrug users than recent users of other opioids (a mean of 5.9 different substances used in the last month versus 4.2) and this polydrug use does not really seem to diminish with age. This confirms the more intense difficulties encountered by these users over the course of their addiction than other users (6.2 substances for the under-25 set, 5.6 for the 35-and-over set) (Table 3, see the Appendices).

They are characterised by a higher proportion of «party» users, as defined by CAARUDs, which includes wandering young users and party-going users: half of users under the age of 35 and one third of users 35 and over (vs. 23.4% of other opioid users).

20. Skenan[®] and Ritalin[®] can be used in combination and injected or used sequentially in the same day.

21. Marginal boys and girls (20-25 years of age) characterised by profound health and social problems representing the end stage of a process of isolation.

22. Often older than young wanderers, nomadic users tend to choose to live in an alternative social situation and have more control over their condition. This enables them to move between regions, and even between countries.

23. In Bordeaux, this population seemed to be involved in Skenan[®] trafficking, although they did not necessarily use the product.

24. This should be considered with the understanding that young drug users tend to avoid voluntarily consulting CAARUDs, in contrast with older precarious users.

25. In other words, they had engaged in last month use of a substance representative of the techno music party scene: stimulants other than cocaine or hallucinogens.

There was a high proportion of injectors, regardless of the age (89.7% in the last 30 days vs. 52.0 %) (Table 3, see the Appendices).

They more frequently received methadone substitution treatments: of recent morphine users, 38% stated having received methadone treatment versus 27% for other opioid users, and the relationship was the reverse for HDB (13.4% vs. 49.6%) and only 22.2% stated receiving Skenan[®] as substitution treatment. This proportion pertained to nearly one quarter of users aged 25 and over, while only one in ten users under the age of 24 was concerned, thereby confirming the different substance functions for each age group.

Skenan[®] is only considered the primary drug by 7.3% of all CAARUD clients (in fifth place after alcohol, HDB, heroin and cocaine), but it is the primary drug for 36.2 % of its own recent users. Skenan[®] is then in second place after HDB and before crack.

ROUTES OF ADMINISTRATION

Morphine sulphate is prescribed for oral intake. Testimonials demonstrated that it is taken orally by a number of patients. The large majority of users who frequent CAARUDs and precarious users inject (out of habit, because they have mastered the behaviour, or because it is economical). Snorting has also been observed (among first-time users, among people who engage in occasional use)²⁶. The Bordeaux site reported smoking after freebasing the substance among young users. Some users did not know that it was possible to take the drug orally because it was so closely associated with injection.

In CAARUDs, 84.3% of 2012 recent morphine sulphate users had injected the substance, 15.9% had taken it orally, 10.1% had snorted, and finally, only 1.1% had smoked.

Morphine sulphate remained the first-ever injected substance for 4.7% of CAARUD clients who stated lifetime use, but this proportion was higher - one in ten - among the youngest users, i.e., users under the age of 25²⁷.

In the OPPIDUM 2011 survey (ANSM and CEIP) conducted mainly in drug treatment centres, 71% of morphine sulphate users stated injecting this substance [10].

It seems that increasing the number of injections per day by dividing the doses of the substance is a widespread practice that increases injection-related risks. There was a reported case of a user injecting Skenan[®] up to ten times a day in addition to their oral methadone use. In Bordeaux, some users allegedly injected the substance in three doses six hours apart, like they would in a prescription.

Few consumers use the filters provided by structures, abandoning the *Sterifilt*[®] because they deemed the procedure involved to be too long or the expected adverse effects (scratching, for example) insufficient to warrant the filtering, or they did not master the wheel filter use technique. Some resorted to using cigarette filters, and others do not filter at all.

There are many ways to prepare a Skenan[®] injection. The coordination efforts of the TREND Metz [11] and Paris [12] sites provided a precise description of the different possibilities. The 2012 Paris report therefore explained:

Several more or less complex steps are needed to obtain a morphine sulphate solution. Each of these steps carries different risks, which vary depending on the user.

Reduce into powder form?

Some crush the Skenan[®] capsule microspheres to obtain a powder and facilitate solubility. To crush the microspheres, consumers place the contents of one (or more) capsules on a piece of paper, fold the paper and crush the contents. Others pour the microspheres directly into the recipient (such as a *Stericup*[®]) to crush them with the end of a syringe¹.

26. However, the microspheres are reportedly difficult to crush to obtain a powder.

27. However, this phenomenon did not specifically pertain to morphine sulphate, but rather was part of the more general trend towards a diversification of substances used during initial injection.

Dilute?

Nearly everyone uses the water for injection contained in the Steribox®. Some dilute in 1 ml, while others opt for larger volumes (2 ml or even 5 ml).

Heat?

Many users heat the Skenan® despite the harm reduction messages on the subject distributed among this population². Users may have borrowed this habit from brown heroin users, and some may be persuaded that «heating» is necessary to obtain a solution that produces a «high» and/or the stinging sought when using Skenan® intravenously. Some heat the water + Skenan® (crushed or uncrushed) before mixing. Others do not heat before mixing. Some (especially Russian-speaking users) heat uncrushed Skenan® microspheres (even before they add water). In fact, users call this preparation technique «Russian». Some heat water before adding it to the crushed or uncrushed Skenan®. When Skenan® is heated, the alcohol pad is often used as a torch and lit using a lighter.

Filter?

Once the heated or unheated mixture has been obtained, filtering takes place.

The cotton filter contained in sterile injection kits, cigarette filters, Sterifilt® filters and, to a lesser extent, wheel filters are used.

Each filter has its strengths and weaknesses in terms of filtration, sought effect and risks run.

- Cigarette filters (with cotton) are probably what are most frequently used. The filter is often torn with the teeth, which introduces the risk of contamination through the saliva.
- Wheel filters are almost never used by Skenan® consumers (soaks up too much liquid, get clogged too easily).
- Since Skenan® solutions are often sludgy, filters that clog quickly (Sterifilt®, wheel filters) are often criticised by users.
- Double filtration (cotton or cigarette filter + Sterifilt®) help prevent clogging while doing a relatively good job of filtering the solution. However, this practice is still rarely observed because it is complex.

Which syringe?

Many intravenous Skenan® users employ a wider-gauge syringe than what is provided in sterile injection kits. These syringes are called «2 cc» (or even «5 cc») syringes by users in reference to their volume in cubic centimetres (millilitres). Since large-volume syringes (greater than 1 ml) are not pre-assembled, users select the diameter (gauge) of their needle based on several parameters, such as the injection site and the type of vein they want to use).

1. As a reminder, syringe covers are not sterile, while the extremity of the piston, which is protected by a cap, is sterile. Many users know this and consider this element to reduce the risks related to their injection practices.

2. When heated, Skenan® diluted in water forms a sort of paste, making it unfit for use by injection.

The reported doses vary. In Bordeaux, users consume a mean of 600 mg per day in several doses, but doses ranging from 100 mg to 500 mg are also frequently mentioned. Some users mention 100 mg as a large quantity for one dose, especially when injecting.

RISKS MENTIONED

The most frequently reported risks are:

■ destabilised treatment, observed in Metz and Bordeaux This is related to giving up treatment, mainly methadone, and taking Skenan®, or Skenan® plus methadone, instead. Some physicians suspend prescriptions understanding that their patients are also taking Skenan®.

■ Overdoses (ODs): there seems to be a real risk of overdose. They are encouraged by frequently reported rapid increases in daily dosages through the concomitant use of several opioids or by dosage errors based on the concept that one capsule represents one dose. Several reports by users, including heroin users, mention the surprise, and sometimes major concern felt given the powerful effects experienced during their first dose. In Bordeaux especially, repeated ODs were mentioned by Emergency Rooms that experienced an increase in the number of ER visits for ODs in 2013.

- Tolerance: caregivers and some users insisted on the need to rapidly increase doses to continue to feel an «effect», which leads users to seek increasingly higher quantities.
- Addiction: it is rarely anticipated by users who nevertheless experienced the rapid development of a «need» for Skenan®, especially among injectors. Therefore, as reported by the Metz site, CSAPAs receive requests for methadone treatment to remedy the situation.
- Finally, according to users and CAARUD professionals, venous complications arising from injection are less frequent than those related to HDB injection, but more harmful injection practices and conditions (poor hygiene, reused equipment) expose injectors to serious complications (abscesses, septicaemia).

CONCLUSION

Like for other psychotropic medicines, there are several issues related to morphine sulphate consumption by drug users.

One issue is morphine sulphate's use as opioid substitution treatment; the off-label and marginally-tolerated use of morphine sulphate in reference to an old, and sometimes unknown, circular has not been officially and collectively readdressed since a section on "substitution" was implemented in harm reduction policy in the mid 1990s [13]. This lack of an updated framework is causing a significant disparity in the practice of physicians.

Another issue is the use of substitution treatments as drugs. Improved access to opioids is almost mechanically accompanied by misappropriation for non-therapeutic use, but such misuse can be limited through controlled prescriptions. Against this background, this medication is compared by users to other available substances depending on the relationship between its benefits (quality and predictability of effects, accessibility) and its cost or associated level of danger. Therefore, from 2011 through part of 2013, the fairly low or even non-existent average purity of circulating heroin in France clearly encouraged the «drug» use of morphine sulphate.

There is also a more general question raised regarding the treatment of urban drug users. Morphine sulphates shed light on the difficulties encountered by some isolated practitioners in ensuring treatment of drug users under good conditions.

Finally, even though the geographic distribution of morphine sulphate use among CAARUD clients suggests an association with the heroin market, the assumption of a relationship with methadone accessibility in rural areas warrants exploration.

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APPENDICES

Table 3 - Injection practices and use among recent opioid users according to whether or not they used morphine sulphate

	Recent morphine sulphate users	Recent users of opioids other than morphine sulphate
Substances used in the last 30 days	%	%
Heroin	41.2	42.7
HDB	22.7	59.9*
Methadone	55.9	31.3*
Codeine	12.9	8.1*
Cocaine and/or crack	58.6	46.1*
Freebase cocaine	34.0	24.2*
MDMA	21.1	12.5*
Amphetamines	22.9	12.5*
Ritalin®	4.4	1.7*
Ketamine	18.1	8.1*
Benzodiazepines	46.3	33.7*
Injection	%	%
Lifetime injection	94.3	74.7*
Last-month injection	89.7	52.0*
Injected heroin (among heroin users)	69.4	52.3*
Injected morphine	84.3	
Injected cocaine (among cocaine users)	78.4	50.5*
Injected amphetamines (among amphetamine users)	55.8	26.1*

* $p < 0,01$

Source : ENa-CAARUD 2012, OFDT

Table 4 - Composition of the inter-regional zones used in Table 2

Grouping	Population	% National	Included regions
Northwest	398	13.7	Nord-Pas-de-Calais, Haute-Normandie, Basse-Normandie, Picardie
West	238	8.2	Bretagne, Pays de la Loire, Poitou-Charentes
Ile-de-France	691	23.8	Ile de France
East	373	12.8	Alsace, Lorraine, Champagne-Ardenne, Franche-Comté
Centre	169	5.8	Centre, Bourgogne, Auvergne, Limousin
Rhône-Alpes	154	5.3	Rhône-Alpes (region located on south-eastern border of France)
PACA and Corsica	232	8	Provence-Alpes-Côte d'Azur (a region in south-eastern France) and Corsica
Southwest	517	17.8	Aquitaine, Languedoc-Roussillon, Midi-Pyrénées
DOM (Overseas departments)	133	4.6	(French) Guiana, Guadeloupe, Réunion

Source : ENa-CAARUD 2012 / OFDT

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