Fluanxol Depot

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fluanxol Depot 20 mg/ml solution for injection
Fluanxol Depot 100 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Flupentixol decanoate 20 mg/ml
Flupentixol decanoate 100 mg/ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

20 mg/ml: clear, colourless to slightly yellowish oil, practically free from particles
100 mg/ml: clear, yellowish to yellow oil, practically free from particles

4. CLINICAL DATA

4.1 Therapeutic indications

Indicated for the maintenance treatment of schizophrenia and other psychotic disorders, with symptoms mainly including hallucinations, delusions and thought disorders, accompanied by apathy, lack of energy, depression and withdrawal.

Fluanxol Depot is indicated in adults.

4.2 Dosage and method of administration

Dosage

Adults
The dosage and the interval between injections will be adjusted individually for each patient by the treating physician in order to obtain maximum suppression of psychotic symptoms with a minimum of side effects.

Flupentixol decanoate 20 mg/ml
The usual maintenance dose is 20-40 mg (1-2 ml) at intervals of 2 to 4 weeks, depending on response.
Some patients may require higher doses or shorter intervals. Flupentixol decanoate 20 mg/ml is not suitable for patients requiring sedation. Injection volumes greater than 2 ml should be divided between two injection sites.

If volumes higher than 2-3 ml of the 20 mg/ml solution are required, the more concentrated solution (flupentixol decanoate 100 mg/ml) is preferred.

During exacerbation or acute relapse of the disease, single injections of 400 mg every two weeks (or weekly for a short period in exceptional cases) may be required.

Flupentixol decanoate 100 mg/ml
The dosage ranges from 50 mg (0.5 ml) every 4 weeks to 300 mg (3 ml) every 2 weeks, but some patients may require up to 400 mg (4 ml) weekly.
Injection volumes greater than 2 ml should be divided between two injection sites.

Usually, adequate control of severe psychotic symptoms is achieved within 4 to 6 months with the concentrated injectables and may justify gradual tapering to a lower maintenance dose.

When switching from oral flupentixol treatment to maintenance treatment with flupentixol decanoate, the following guidelines apply:

x mg per os per day corresponds to 4x mg decanoate every 2 weeks.
x mg per os per day corresponds to 8x mg decanoate every 4 weeks.

During the first week after the first injection, flupentixol should be continued orally, but at a lower dose.

Patients switched from other depot preparations should receive a dose of 40 mg flupentixol decanoate which is equivalent to 25 mg fluphenazine decanoate, 200 mg zuclopenthixol decanoate or 50 mg haloperidol decanoate.

The subsequent doses of flupentixol decanoate and the interval between injections should be adjusted according to the patient's response.

Elderly
Elderly should be given doses that are as low as possible.

Reduced renal function
Flupentixol decanoate may be given at usual doses to patients with reduced renal function.

Reduced liver function.
Dose carefully and, if possible, a blood level determination is recommended.

Paediatric population
Due to a lack of clinical data, flupentixol decanoate is not indicated for use in children.

Method of administration

Flupentixol decanoate is injected intramuscularly into the upper outer quadrant of the gluteal region. Injection volumes exceeding 2 ml should be divided between two injection sites. Local tolerance is good.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Circulatory collapse, decreased level of consciousness regardless of cause (e.g. intoxication with alcohol, barbiturates or opiates), coma.

4.4 Special warnings and precautions for use

With any antipsychotic, there is a possibility of developing a neuroleptic malignant syndrome with symptoms: hyperthermia, muscle rigidity, unstable consciousness, unstable functioning of the autonomic nervous system. This risk is however greater with more potent neuroleptics. Patients with pre-existing brain insufficiency, with mental retardation, and with opiate and alcohol abuse are overrepresented among the fatal cases.

Treatment: Discontinue neuroleptic therapy. Treatment is symptomatic and involves general supportive measures. Administration of dantrolene and bromocirptine may be helpful. Symptoms may persist for a week or longer after discontinuation of oral neuroleptics; somewhat longer when associated with depot forms of the drug.

Like other neuroleptics, flupentixol decanoate should be used with caution in patients with cerebral insufficiency, seizure disorders or with pronounced liver disease.

Flupentixol decanoate at low doses is not recommended for excited or “overactive” patients, as it may further exacerbate these characteristics.

As described with other psychotropic drugs, flupentixol decanoate may alter insulin and blood glucose levels, requiring adjustment of antidiabetic therapy in diabetics.

During long-term treatment, especially at high doses, it is advisable to closely monitor the patient and evaluate periodically with a view to reducing the maintenance dose.

As with other drugs belonging to the therapeutic class of antipsychotics, flupentixol decanoate may cause QT prolongation. Persistent QT interval prolongation may increase the risk of malignant arrhythmias. Therefore, flupentixol decanoate should be used with caution in susceptible individuals (hypokalaemia, hypomagnesia or genetic predisposition) and in patients with a history of cardiovascular disorder, e.g. QT prolongation, significant bradycardia (< 50 beats per minute), recent acute myocardial infarction, uncompensated heart failure, or cardiac arrhythmias. In addition, flupentixol should be used with caution in patients with a family history of QT prolongation. Concomitant treatment with other antipsychotics should be avoided (see section 4.5).

Suicide/suicidal thoughts or clinical worsening
Depression is associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk persists until significant remission occurs. Because improvement may not be seen during the first few weeks or more of treatment, patients should be closely monitored until improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

Other psychiatric conditions for which Fluanxol Depot is prescribed may also be associated with an increased risk of suicide-related events. In addition, these conditions may be comorbid with major depressive disorder. Therefore, the same precautions that apply to patients with major depressive disorder should be observed for patients with other psychiatric conditions.

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressant drugs in adults with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old. These patients, and in particular those at high risk, should receive close monitoring during treatment, particularly in early treatment and following dose changes.
Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Some cases of venous thromboembolism (VTE) have been reported with antipsychotics. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with Fluanxol Depot and preventive measures undertaken.

Leukopenia, neutropenia and agranulocytosis have been reported with antipsychotics, including flupentixol decanoate.
Long-acting depot antipsychotics should be used with caution in combination with other drugs known to have myelosuppressive potential, as these may not be rapidly cleared from the body in cases where this might be necessary.

Elderly

Cerebrovascular
In randomised placebo controlled clinical trials in a dementia population, a three-fold increased risk of cerebrovascular adverse events has been seen with some atypical antipsychotics. The mechanism for this increased risk is unknown. An increased risk cannot be excluded with other antipsychotics or in other patient populations. Flupentixol decanoate should be used with caution in patients with risk factors for cerebral vascular accident (CVA).

Increased mortality in older people with dementia
Data from two large observational studies suggest a slightly increased risk of mortality in older people with dementia treated with antipsychotics compared to older people who do not receive treatment. At present, there are insufficient data to accurately estimate the precise magnitude of the risk. The cause of the increased risk is still unknown.

Fluanxol Depot is not approved for the treatment of dementia-related behavioural disturbances.

4.5 Interaction with other medicinal products and other forms of interaction

Combinations requiring caution in use
Flupentixol decanoate may enhance the sedative effects of alcohol, barbiturates and other drugs that cause central nervous system depression.

Neuroleptics may enhance or antagonize the blood pressure lowering effect of antihypertensives; the antihypertensive effect of guanfacine and similar substances is antagonized.
Concomitant use of neuroleptics and lithium increases the risk of neurotoxicity. Tricyclic antidepressants and neuroleptics may inhibit each other's metabolism.
Flupentixol decanoate may reduce the effect of levodopa and adrenergic agents.
Concomitant use of metoclopramide or piperazine increases the risk of extrapyramidal disorder.

In association with antipsychotic treatment, QT interval prolongation may be exacerbated by concomitant administration of other drugs known to significantly prolong the QT interval. Concomitant administration of such drugs should be avoided.
Classes of drugs involved include:

- Class Ia and III antiarrhythmic drugs (e.g. quinidine, amiodarone, sotalol, dofetilide)
- Some antipsychotics (e.g. thioridazide)
- Some macrolides (e.g. erythromycin)
- Some antihistamines (e.g. terfenadine, astemizole)
- Some quinolone antibiotics (e.g. gatifloxacin, moxifloxacin)

This list is not exhaustive and other specific drugs known to significantly prolong the QT interval (e.g. cisapride, lithium) should be avoided.

Flupentixol should be used with caution with medicinal products known to cause electrolyte imbalance such as thiazide diuretics (hypokalaemia) and with medicinal products known to increase the plasma concentration of flupentixol decanoate, as these may increase the risk of QT prolongation and malignant arrhythmias (see section 4.4).

4.6 Fertility, pregnancy and breastfeeding

Pregnancy
Fluanxol decanoate should only be administered during pregnancy if the therapeutic benefit to the patient is greater than the theoretical risk to the fetus.

Newborns born to mothers treated with neuroleptics at the end of pregnancy or during labour may show signs of intoxication such as lethargy, tremor and hyperexcitability and have a lower Apgar score.

Neonates exposed to antipsychotics (including flupentixol decanoate) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or discontinuation symptoms that may vary in severity and duration following delivery. Agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorders have been reported. Consequently, neonates should be monitored carefully.

Studies in animals have shown reproductive toxicity (see section 5.3).

Breastfeeding
Given the low concentrations of flupentixol found in breast milk, it is unlikely that, at therapeutic doses, it will affect the infant. The dose ingested by the neonate is less than 0.5% of the daily dose ingested by the mother (in mg/kg). If clinical importance prevails, breast-feeding may be continued during flupentixol decanoate therapy, but observation of the neonate, especially during the first 4 weeks after birth, is recommended.

Fertility
There are no clinical trial data available on the effect of the active substance flupentixol on fertility.

In humans, adverse reactions such as hyperprolactinemia, galactorrhoea, amenorrhea, decreased libido, erectile dysfunction and ejaculation failure have been reported (see section 4.8). These adverse reactions may have a negative impact on female and/or male sexual function and fertility.

If clinically significant hyperprolactinemia, galactorrhoea, amenorrhea or sexual dysfunction occur, a dose reduction (if possible) or discontinuation of therapy should be considered. The adverse effects are reversible upon discontinuation of therapy.

In preclinical fertility studies in rats, flupentixol slightly affected the pregnancy rate in female rats. The effects were seen at doses well above those used clinically.

4.7 Effects on ability to drive and use machines

Flupentixol decanoate in low to moderate doses (up to 100 mg every 2 weeks) is not sedating which may have minor to moderate influence on the ability to drive and use machines.
However, patients prescribed psychotropic drugs may be expected to have minor impairment of general attention and concentration. Therefore, caution is advised when driving or using machines.

4.8 Side effects

Summary of the safety profile
Adverse effects are largely dependent on the administered dose. Frequency and severity are most pronounced in the early stages of treatment and decrease as treatment continues.

Extrapyramidal reactions may occur, especially during the first few days after injection and during the initial phase of treatment. In most cases, these adverse effects can be adequately controlled by dose reduction and/or administration of antiparkinsonian agents. Routine use of antiparkinsonian agents as prophylaxis is not recommended.
Antiparkinsonian agents do not alleviate the symptoms of tardive dyskinesia and may even worsen them. Dose reduction or, if possible, discontinuation of flupentixol treatment is recommended.
In persistent akathisia, administration of a benzodiazepine or propranolol may be useful.

Tabulated list of adverse reactions
The reported frequencies are taken from the literature and also come from spontaneous reporting. Frequencies are defined as:
very common (1/10); common (1/100 to < 1/10); uncommon (1/1,000 to < 1/100); rare (1/10,000 to < 1/1,000); very rare (< 10,000); not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System organ class	Frequency	Preferred term
Blood and lymphatic system disorders	Seldom	Thrombocytopenia, neutropenia, leukopenia, agranulocytosis
Immune system disorders	Seldom	Hypersensitivity, anaphylactic reaction
Endocrine disorders	Seldom	Hyperprolactinemia
Nutritional and metabolic disorders	Often	Increased appetite, weight gain
	Sometimes	Decreased appetite
	Seldom	Hyperglycemia, impaired glucose tolerance
Mental disorders	Often	Insomnia, depression, nervousness, agitation, decreased libido
	Sometimes	Confusion
	Not known	Suicidal thoughts, suicidal behavior [1]
Nervous system disorders	Very often	Somnolence, akathisia, hyperkinesia, hypokinesia
	Often	Tremor, dystonia, dizziness, headache
	Sometimes to rarely	Tardive dyskinesias, dyskinesia, parkinsonism, speech disorder, convulsions
	Very rarely	Neuroleptic malignant syndrome
Eye disorders	Often	Accommodation disorders, abnormal vision
	Sometimes	Oculogyric crisis

Heart disease	Often	Tachycardia, palpitations
	Seldom	Electrocardiogram prolonged QT
Blood vessel disorders	Sometimes	Hypotension, hot flushes
	Very rarely	Venous thromboembolism
Respiratory, thoracic and mediastinal disorders	Often	Dyspnoea
Gastrointestinal disorders	Very often	Dry mouth
	Often	Excessive salivation, constipation, vomiting, dyspepsia, diarrhea
	Sometimes	Abdominal pain, nausea, flatulence
Liver and biliary disorders	Sometimes	Impaired liver function tests
	Very rarely	Jaundice
Skin and subcutaneous tissue disorders	Often	Hyperhidrosis, pruritus
	Sometimes	Rash, photosensitivity reaction, dermatitis
Musculoskeletal and connective tissue disorders	Often	Myalgia
	Sometimes	Muscle rigidity
Kidney and urinary tract disorders	Often	Micturition disorder, urinary retention
Pregnancy, perinatal period and puerperium	Not known	Discontinuation syndrome in newborns (see section 4.6)
Reproductive system and breast disorders	Sometimes	Ejaculation disorder, erectile dysfunction,
	Seldom	Gynecomastia, galactorrhea, amenorrhea
General disorders and administration site conditions	Often	Asthenia, fatigue
	Sometimes	Injection site reaction

[1] Cases of suicidal ideation and suicidal behaviour have been reported during flupentixol therapy or early after treatment discontinuation (see section 4.4)

Description of selected adverse reactions
As with other drugs belonging to the therapeutic class of antipsychotics, rare cases of QT prolongation, ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia, Torsades de Pointes, cardiac arrest and sudden death have been reported with flupentixol (see section 4.4).

Abrupt discontinuation of flupentixol decanoate may be associated with withdrawal symptoms. The most commonly observed symptoms are nausea, vomiting, anorexia, diarrhea, rhinorrhea, sweating, myalgia, paresthesias, insomnia, restlessness, anxiety, and agitation. Patients may also experience vertigo, alternating hot and cold sensations, and tremor. Symptoms generally occur 1 to 4 days after discontinuation of treatment and subside after 7 to 14 days.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Belgium
Federal Agency for Medicines and Health Products
www.fagg.be
Vigilance Department:
Website: www.eenbijwerkingmelden.be
e-mail: adr@fagg-afmps.be

4.9 Overdose

Given the form of administration, it is unlikely that overdose symptoms will occur.

Symptoms
Drowsiness, coma, movement disorders, convulsions, shock, hyperthermia or hypothermia.
When taken in overdose with drugs known to affect the heart, ECG changes, QT prolongation, Torsades de Pointes, cardiac arrest and ventricular arrhythmias have been reported.

Treatment
Treatment is symptomatic and supportive. Measures should be taken to support the respiratory and cardiovascular systems. Epinephrine (adrenaline) will not be administered, as further reduction in blood pressure may occur. Convulsions can be treated with diazepam and extrapyramidal symptoms with biperiden.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: neuroleptics (antipsychotics); ATC code: N05AF01.

Mechanism of action
Flupentixol is a neuroleptic belonging to the thioxanthenes group.
The antipsychotic effect of a neuroleptic is linked to the antagonism of dopaminergic receptors, but 5-HT (5-hydroxidetryptamine) receptor blockade may also play a role. *In vitro* and *in vivo,* flupentixol has a high affinity for both dopamine D_1 and D_2 receptors, while fluphenazine is almost D_2 selective *in vivo* . The atypical antipsychotic, clozapine, shows – like flupentixol – a similar affinity for D_1 and D_2 receptors, both *in vitro* and *in vivo* .

Flupentixol has a high affinity for α_1 -adrenoceptors and 5-HT_2 receptors (but lower than that of chlorprothixene, high doses of phenothizines and clozapine), but no affinity for cholinergic muscarinic receptors. It has only mild antihistaminic properties and no α_2 -adrenoceptor blockade activity.

Flupentixol was found to be a potent neuroleptic in all behavioural studies on neuroleptic action (dopamine receptor blockade). Correlation was found in *in vivo* test models, the affinity for dopamine D_2 binding sites *in vitro* and the average daily oral antipsychotic doses.
Perioral movements in rats are dependent on D_1 receptor stimulation or blockade of the D_2 receptor population. The movements can be prevented by flupentixol. Similarly, results from monkey studies show that oral hyperkinesia is more related to D_1 receptor stimulation and to a lesser extent to D_2 receptor hypersensitivity. This leads to the assumption that D_1 activation is responsible for similar effects in humans, e.g. dyskinesia. Therefore, blockade of D_1 receptors might be of benefit.

Like most neuroleptics, flupentixol increases serum prolactin levels in a dose-dependent manner.

Pharmacological studies have clearly shown that the oil solution of flupentixol decanoate has a prolonged neuroleptic effect and that the amount of drug required to maintain a certain effect over a longer period is considerably less with the depot preparations than with daily oral administration of flupentixol. Only at very high doses could a very moderate and short-lived potentiation of the duration of sleep induced by barbiturates be demonstrated in mice. Hence it is unlikely that any significant interference with anaesthetics could occur in patients receiving depot drugs.

Clinical efficacy and safety
In clinical use, flupentixol decanoate is indicated for maintenance treatment of chronically psychotic patients. The antipsychotic effect increases with increasing dose. Flupentixol decanoate is non-sedating at low to moderate doses (up to 100 mg/2 weeks), whereas some non-specific sedation may be expected when higher doses are administered.
Flupentixol decanoate is particularly useful for the treatment of apathetic, withdrawn, depressed and poorly motivated patients.
Flupentixol decanoate allows uninterrupted treatment, especially for those patients who are not reliable in taking their prescribed oral medication.
Flupentixol decanoate thus prevents frequent relapses for patients who are not compliant with oral medication.

Pediatric patients
No data available

5.2 Pharmacokinetic properties

Absorption
By esterifying flupentixol with decanoic acid, a highly lipophilic substance is obtained, flupentixol decanoate. Dissolved in vegetable oil and injected intramuscularly, this substance diffuses rather slowly into the interstitial fluid where it is enzymatically hydrolysed and the active substance flupentixol is released.

Peak serum concentrations are generally reached after a period of 3 to 7 days after intramuscular injection. The half-life is estimated at 3 weeks (which reflects the release from the depot); steady-state conditions are reached after approximately 3 months on repeated administration.

Distribution
The fictitious volume of distribution (V_d)$_\beta$ is approximately 14.1 l/kg. Serum protein binding is approximately 99%.

Biotransformation
Flupentixol metabolism follows three main pathways: sulfoxidation, N-dealkylation of the lateral chain, and glucuronidation. The metabolites have no pharmacological activity. Flupentixol is present in higher abundance than its metabolites in the brain and other tissues.

Elimination
The elimination half-life ($T_{½\beta}$) of flupentixol is approximately 35 hours and the mean systemic clearance (Cl_s) is approximately 0.29 l/min.
Flupentixol is excreted mainly in the faeces, but also to some extent in the urine. In humans, after administration of tritium-labelled flupentixol, faecal excretion was 4 times that in urine.
Flupentixol is excreted in breast milk in small quantities. The ratio of milk to serum concentrations averages 1.3.

Linearity
The kinetics are linear. The mean steady-state serum level of flupentixol for injection corresponding to a dose of 40 mg flupentixol decanoate every 2 weeks is approximately 6 nmol/l.

Elderly
Pharmacokinetic studies have not been performed in elderly. For the similar drug belonging to the thioxanthene group, zuclopenthixol, the pharmacokinetic parameters are largely independent of the age of the patient.

Impaired renal function
Based on the above features of elimination, it is reasonable to assume that impaired renal function is unlikely to have much influence on the serum levels of the parent drug.

Reduced liver function
No data available

Pharmacokinetic/pharmacodynamic relationship
A pre-injection plasma concentration of 1-3 ng/ml (2-8 nmol/l) and a max./min. fluctuation < 2.5 have been suggested as a guideline for maintenance treatment in patients with mild to moderate schizophrenia. Pharmacokinetically, a dose of 40 mg/2 weeks of flupentixol decanoate is equivalent to a daily oral dose of 10 mg flupentixol.

Pediatric patients
No data available

5.3 Preclinical safety data

Acute toxicity
Flupentixol has weak acute toxicity.

Chronic toxicity
In chronic toxicity studies there were no concerning findings for the therapeutic use of flupentixol.

Reproductive toxicity
In fertility studies in rats, flupentixol slightly affected the pregnancy rate in female rats. The effects were seen at doses well above those used clinically.

Reproductive studies in mice, rats and rabbits have not shown a teratogenic effect. Embryotoxic effects in terms of increased post-implantation loss/increased absorption rate or occasional abortions were seen in rats and rabbits at doses associated with maternal toxicity.

Carcinogenicity
Flupentixol has no carcinogenic potential.

Local toxicity
Local tolerance is good. Local muscle damage was observed after injection of neuroleptics in aqueous solutions. After intramuscular injection of flupentixol decanoate oil solution in rabbits, only slight haemorrhage and oedema were observed.

6. PHARMACEUTICAL DATA

6.1 List of excipients

Medium chain, saturated triglycerides.

6.2 Instances of incompatibility

Do not mix flupentixol decanoate with other depot preparations containing sesame oil as a vehicle, as this will drastically alter the pharmacokinetic properties of the preparations involved.

6.3 Shelf life

4 years

6.4 Special precautions for storage

Store in the original package in order to protect from light.

6.5 Nature and contents of packaging

20 mg/ml:
Colourless glass (type I glass) ampoules of 1 ml.
Boxes of 1 x 1 ml, 10 x 1 ml
100 mg/ml:
Colourless glass (type I glass) ampoules of 1 ml.
Boxes of 1 x 1 ml or 10 x 1 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Lundbeck NV
Stephanie Square Center
Avenue Louise 65/11
1050 Brussels

8. MARKETING AUTHORISATION NUMBERS

20 mg/ml: BE015337
100 mg/ml: BE099565

9. DATE OF FIRST LICENSE GRANT / RENEWAL OF LICENSE

Date of first grant of the permit :

Fluanxol 20 mg/ml solution for injection : 01/04/1971
Fluanxol 100 mg/ml solution for injection : 01/02/1976

Date of last renewal : 19/01/2007

10. DATE OF REVISION OF THE TEXT

Date of approval of the text: 11/2024
Date of revision of the text: 10/2024