HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

OPINION

21 October 2009

Examination of the dossier of medicinal products included on the reimbursement list for a period of 5 years from 5 October 2004 (*Journal Officiel* of October 29th, 2004).

TAMIFLU 12 mg/ml, powder for oral suspension
One bottle of 30 g (CIP: 359 963-5)

TAMIFLU 75 mg, capsule
Pack of 10 capsules (CIP: 359 962-9)

TAMIFLU 30 mg, capsule
Pack of 10 (CIP: 382 015-2)

TAMIFLU 45 mg, capsule
Pack of 10 (CIP: 382 016-9)

Applicant: ROCHE REGISTRATION LTD

Oseltamivir phosphate

List I
ATC Code: J05AH02

Date of Marketing Authorisation:
TAMIFLU 12 mg/ml, powder for oral suspension and 75 mg capsule: 20/06/2002
TAMIFLU 30 mg and 45mg capsule: 19/09/2007

Reason for request: Renewal of inclusion on the list of reimbursable medicinal products.

Medical and Economic Evaluation and Public Health Directorate

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

Oseltamivir phosphate

1.2. Indication

"*Treatment of influenza* in adults and children one year of age and older who present with typical symptoms of influenza, when influenza virus is circulating in the community. Efficacy has been demonstrated when treatment is initiated within two days of first onset of symptoms. This indication is based on clinical studies of naturally occurring influenza in which the predominant infection was influenza A.

- *Prevention of influenza* Post-exposure prevention: in adults and children one year of age and older following contact with a clinically diagnosed influenza case when influenza virus is circulating in the community.
- The appropriate use of TAMIFLU for prevention of influenza should be determined on a casebycase basis by the circumstances and the population requiring protection. In exceptional situations (e.g., in case of a mismatch between the antigens of the circulating and vaccine virus strains or a pandemic situation), seasonal prophylaxis may be considered in adults and children from one year of age.

TAMIFLU is not a substitute for influenza vaccination.

The use of antivirals for the treatment and prophylaxis of influenza should take into consideration official recommendations, variability in the epidemiology, and the impact of the disease in different geographical areas and patient populations."

1.3. Dosage

Treatment of influenza:
Treatment should be initiated as soon as possible within the first two days of onset of influenza symptoms.
For adolescents (13 to 17 years of age) and adults: the recommended oral dose is 75 mg oseltamivir twice daily for 5 days.

For infants older than 1 year of age and for children 2 to 12 years of age: TAMIFLU 30 mg and 45 mg capsules and oral suspension are available.

The following weight-adjusted dosages are recommended:

Body weight	Recommended dose for 5 days
≤ 15 kg	30 mg twice daily
> 15 kg to 23 kg	45 mg twice daily
> 23 kg to 40 kg	60 mg twice daily
> 40 kg	75 mg twice daily

Children weighing over 40 kg who are able to swallow capsules may receive treatment with the adult dosage of 75 mg capsules twice daily for 5 days as an alternative to the recommended dosage of TAMIFLU suspension.

Prevention of influenza Post-exposure prophylaxis: For adolescents (13 to 17 years) and adults: the recommended dose of oseltamivir for influenza prophylaxis after close contact with an infected person, is 75 mg once daily for 10 days. Therapy should begin as soon as possible and within two days of contact with an infected subject.
For infants older than 1 year of age and for children 2 to 12 years of age: TAMIFLU 30 mg and 45 mg capsules and oral suspension are available.

The recommended post-exposure dose of TAMIFLU is:

Body weight	Recommended dose for 10 days
≤ 15 kg	30 mg once daily
> 15 kg to 23 kg	45 mg once daily
> 23 kg to 40 kg	60 mg once daily
> 40 kg	75 mg once daily

Children weighing over 40 kg and who are able to swallow capsules may receive preventive treatment with a 75 mg capsule once daily for 10 days as an alternative to the recommended dosage of TAMIFLU suspension.

Prevention during an influenza epidemic: The recommended dose for prevention of influenza during an epidemic is 75 mg oseltamivir once daily for up to 6 weeks.

Specific populations:

- Hepatic impairment: no dose adjustment is required either for treatment or for prevention in patients with impaired hepatic function.
- Impaired renalfunction: adjust the dose from a creatinine clearance of 30 ml/min or less. Not recommended for a clearance of less than 10 ml/min and for dialysed patients.
- Elderly subject: no dosage adjustment is necessary, except in the case of severe renal impairment.

2 PREVIOUS COMMITTEE OPINIONS AND LISTING CONDITIONS

Post-exposure influenza prophylaxis

Opinion of February 11th, 2004

In subjects aged from 13 to 64 years without comorbidity, the actual benefit is insufficient to justify reimbursement.
In high-riskpatients : adolescents and adults from 13 to 64 years with comorbidity, adults over 65 years, the Committee considers the actual benefit to be not important. It is qualified as low.
In the specific case of subjects at risk (institutionalised patients, contraindication to the vaccine, immunocompromised subjects (in particular AIDS subjects, transplant recipients and patients receiving immunosuppressive drugs), incomplete vaccine protection compared to the circulating strain) : The Committee considers that actual benefit to be moderate.

Improvement in actual benefit III relative to Mantadix

Opinion of June 21st, 2006 (extension of indication to children from 1 year of age)

Same formulation for the actual benefit as 11 February 2004, in the extension of indication to children older than 1 year.
IAB V in the management of post-exposure prophylaxis in children from 1 to 12 years.

Opinion of January 3rd, 2007 (extension of reimbursement)

Low actual benefit in the following populations unable to undergo influenza vaccination for medical reasons:

- Patients with asthma and COPD,
- Persons staying in medium or long-term stay facilities of whatever age,
- Children and adolescents (from 1 to 18 years) whose health status requires prolonged treatment by acetylsalicylic acid.

Opinion of December 5th, 2007 (listing of 30-mg and 45-mg capsules)

In adults and children

In subjects without comorbidity, the actual benefit is insufficient to justify reimbursement.

In high-risk patients: children from 1 year of age and adults from 13 to 64 years with comorbidity and adults over 65 years, the actual benefit is low.

In the specific case of subjects at risk:

- Subjects living in institutions (institutionalised patients),
- Subjects with a contraindication to the vaccine,
- Immunocompromised subjects (in particular AIDS subjects, transplant recipients or patients receiving immunosuppressive drugs),
- Situations in which the vaccine only provides limited protection against from the circulating strain: the actual benefit is moderate.

Opinion of April 16th, 2008 (reassessment of actual benefit)

Population without risk for complications: the actual benefit in influenza prophylaxis in subjects without comorbidity is insufficient.

Population at high risk for complications: the actual benefit for post-exposure prevention in high risk populations is low.

In addition, the actual benefit of TAMIFLU for post-exposure prophylaxis is moderate in subjects at risk, in the following specific cases:

- Subjects living in institutions (institutionalised patients),
- Subjects with a contraindication to the vaccine,
- Immunocompromised subjects (in particular subjects with AIDS, transplant recipients or patients receiving immunosuppressive drugs),
- Situations in which the vaccine only provides partial protection from the circulating strain.

Curative treatment of influenza

Opinion of February 11th, 2004, confirmed on June 21st, 2006 and April 16th, 2008

Children

The actual benefit of TAMIFLU is insufficient to justify reimbursement.

Adults from 13 to 64 years of age with or without comorbidity:

The actual benefit of TAMIFLU is insufficient to justify reimbursement.

Adults over 65 years old

The actual benefit of TAMIFLU is insufficient to justify reimbursement.

December 5th, 2007 (listing of 30-mg and 45-mg capsules)

The actual benefit of TAMIFLU is insufficient to justify reimbursement.

3 SIMILAR MEDICINAL PRODUCTS

3.1. ATC Classification (2009)

J : anti-infectives for systemic use
J05 : antivirals for systemic use
J05A : direct-acting antiviral agents
J05AH : neuraminidase inhibitors
J05AH02 : oseltamivir

3.2. Medicines in the same therapeutic category

Comparator drug
Neuraminidase inhibitor antiviral agents:
RELENZA 5 mg/dose, (zanamivir) inhalation powder, in single-dose container

3.3. Medicines with a similar therapeutic aim

Influenza prevention:

- influenza vaccines,
- another antiviral, MANTADIX 100 mg capsule (amantadine), is indicated for prophylaxis of influenza exclusively due to influenza virus A.

Treatment of influenza:
Non-specific symptomatic medications: analgesics and antipyretics.

4 DRUG USAGE DATA

According to data extracted from the IMS/Dorema database (CMA May 09), 130,000 prescriptions of TAMIFLU were made between June 2008 and May 2009. In 93% of cases, the reason for prescription was influenza. The mean duration of prescription was 5.3 days and the usual dosage was 2.0 tablets per day. These data suggest that TAMIFLU is mainly prescribed for curative treatment.

5 UPDATING WITH DATA OBTAINED SINCE THE PREVIOUS OPINION

Roche submitted data from 6 new studies:

- Two observational studies about the management of an influenza epidemic occurring in institution,
- Four American retrospective studies on high risk populations in which TAMIFLU was used for curative treatment of influenza.

5.1. Post-exposure prophylaxis and curative treatment

- Gaillat[1] study in a home for the elderly in Annecy

This was an observational study performed during an influenza epidemic occurring in August 2005 in a home for the elderly. Viral propagation was facilitated by confinement in air-conditioned rooms during a heat wave. The mean age of residents was 88 years old. A flu-like syndrome was reported in 32/81 residents and 6/48 staff members. After identification of the virus by a rapid diagnostic test, the following measures were taken: isolation, wearing of face masks, curative treatment by TAMIFLU for 19 symptomatic residents out of 32, and 5 symptomatic staff members out of 6.
Prophylactic treatment was given to 47 non-symptomatic residents and 42 staff members. The epidemic was completed in 48 hours. Five deaths occurred, including 2 treated with oseltamivir.

5.2. Post-exposure prophylaxis

- Study of Vu[2]: safety follow-up during an epidemic in an allograft recipients home.

This was a retrospective study describing a cohort of patients who had undergone or were on the waiting list for a haematopoietic stem cell transplant staying in specialised home in the United States. They were given a prophylactic treatment by TAMIFLU during the 2002 winter influenza epidemic.
The epidemic was declared after 4 cases of influenza virologically confirmed. 45 patients were given prophylactic treatment. No new case of influenza was diagnosed and no death occurred.
No adverse events difference was observed between patients who received TAMIFLU and a control group of patients untreated during previous influenza epidemics.

5.3. Curative treatment

- Children at high risk[3]

In the American Thomson Reuters MarketScan database, TAMIFLU was prescribed to 1,634 children with influenza and at risk of complications (diabetes, cancer, asthma, neurological and neuromuscular diseases, renal impairment, organ transplantation, HIV, etc.) during 6 successive flu seasons. Thechildren were compared to 3,721 other children at risk of the same complications and who had not been treated by an antiviral for influenza
TAMIFLU was associated with a significant reduction in the risk of respiratory diseases other that pneumonia, hospitalisations and otitis media at 14 days.

Reduction in the relative risk of the influenza-related complications and hospitalisations with TAMIFLU occurrence in patients and adolescents at risk

[1] Gaillat J, Dennetière G, Raffin-Bru E, Valette M, and Blanc M.C. Summer inflenza outbreak in a home for the elderly: application of preventive measures. Journal Hospital Infection 2008 ; 70 : 272-277
[2] Vu D, Peck A.J, Nichols W.G, Varley C, Englund J.A, L. Corey, and Boeckh M. Safety and tolerability of oseltamivir prophylaxis in hematopoietic stem cell transplant recipients: a retrospective case-control study. Infectious Diseases Society of America 2007; 45:187-93.
[3] Pedro A et al. Effects of Oseltamivir on Influenza-Related Complications in Children With Chronic Medical Conditions. Pediatrics 2009 ; 124 : 170-178.

Complications	HR at 14 days [95% CI]	HR at 30 days [95% CI]
Respiratory diseases other than pneumonia	0.74 [0.63 ; 0,87]	0.87 [0.77 ; 0.97]
Otitis media and its complications	0.69 [0.48 ; 0.99]	0.70 [0.53 ; 0.92]
Hospitalisation for all causes	0.33 [0.13 ; 0.83]	0.49 [0.27 ; 0.89]

- Elderly over 65 years old and not institutionalised[4]

This was a retrospective study performed in the United States which evaluated the impact of TAMIFLU curative treatment on the occurrence of stroke or transient form
TAMIFLU was prescribed to 1,190 influenza patients aged over 65 years. They were compared to 7,392 influenza patients over 65 years not treated by antiviral. TAMIFLU was associated with a significant reduction in the relative risk of stroke of 51% at 1 month (RR=0.49 - 95%CI: 0.27 ; 0.91).

- Patients with a history of cardiovascular disease[5]

This study performed in the United States evaluated the incidence of cardiovascular events in influenza patients with a past medical history of chronic heart disease. These were data from the US military health system database for a military population.
TAMIFLU was prescribed to 6,771 adults with influenza. They were compared with 30,711 influenza patients not treated by antiviral. The rate of cardiovascular events occurrence was significantly lower (8.5%) in the TAMIFLU group than the control group (21.2%) ($p<0.005$).

- Diabetic patients[6]

This study performed in the United States in diabetic adult patients with influenza evaluated the incidence of influenza-related complications.
Data were obtained from the Thomson Reuters MarketScan database for 6 successive influenza seasons. TAMIFLU was prescribed to 2,919 patients and 6,171 patients at risk of complications.
Fourteen days after the start of treatment, TAMIFLU was associated with a significant reduction in the risk of respiratory infection other than pneumonia (RR 0.83; 95% CI: 0.73 ; 0.93) and hospitalisations (all causes except pneumonia) (RR 0.70; 95% CI: 0.52 ; 0.94).

5.4. Tolerance

According to the new pharmacovigilance data, the tolerance data in the application have remained unchanged since the previous Committee evaluation.

The SPC was modified on October 31st, 2008.The Committee had already been notified about this change.
In addition, oseltamivir must only be used during pregnancy if the benefit for the mother outweighs the potential risk for the foetus.

5.5. Resistance to oseltamivir in humans

As already noted by the Transparency Committee in its opinion of May 13th, 2009, the SPC mentions that “the extent of reduction in susceptibility to oseltamivir and the prevalence of such viruses appear to vary seasonally and geographically”.

[4] Madjid M, Curkendall S, and Blumentals W.A. The influence of oseltamivir treatment on the risk of stroke after influenza infection. Cardiology 2009;113:98–107
[5] Ward Casscells S, Granger E, Kress A.M, Linton A, Madjid M and Cottrell L. Use of Oseltamivir After Influenza Infection Is Associated With Reduced Incidence of Recurrent Adverse Cardiovascular Outcomes Among Military Health System Beneficiaries With Prior Cardiovascular Diseases. Circ Cardiovasc Qual Outcomes 2009;2;108-115.
[6] E.A. Orzeck, N. Shi, and W.A. Blumentals. Oseltamivir and the Risk of Influenza-Related Complications and hospitalizations in patients with diabetes. Clinical Therapeutics. 2007, 29,

5.6. Conclusion

For prophylaxis, the observational study of Gaillatt[7] showed that the value of a complete management during an influenza epidemic occurred in August in a home for the elderly. It is impossible to determine the specific contribution of oseltamivir in comparison with the other measures such as isolation and wearing masks.

During the Vu study, no serious adverse reaction to oseltamivir was detected in 45 treated patients at high risk of complications.

Within the framework of curative treatment, retrospective cohort studies demonstrated the association of a reduction in certain complications of influenza in patients at risk treated by oseltamivir. However, these studies, with only a low level of evidence, were performed in the United States in selected populations, and cannot therefore be used to evaluate the reduction in seasonal influenza-related complications and/or hospitalisations in France in high risk populations.

6 TRANSPARENCY COMMITTEE CONCLUSIONS

6.1. Reassessment of Actual Benefit

The actual benefit level of TAMIFLU is not modified by the new data submitted by the applicant.

Influenza is a highly contagious, acute viral disease which, in most cases, is not serious and spontaneously resolves in about 1 week. However, in certain subjects, influenza complications may be serious and life-threatening.

In children, the clinical aspect of influenza is more subtle when children are young. Children are the first to be affected during an epidemic.
The influenza complications are particularly serious in infants aged less than 1 year and children with a comorbid disease (asthma in particular).
There are usually no serious complications in healthy children over 1 year of age. The most frequent complications are respiratory and ENT disorders, otitis in particular. The incidence of these complications decreases with age.

[7] Gaillat J, Dennetière G, Raffin-Bru E, Valette M, and Blanc M.C. Summer inflenza outbreak in a home for the elderly: application of preventive measures. Journal Hospital Infection 2008 ; 70 : 272-277

Vaccination against influenza is the cornerstone of management of this disease. It is particularly recommended in subjects at high risk of complications[8] and in health care professionals.

TAMIFLU is an antiviral treatment intended for curative treatment and prevention (post-exposure prophylaxis).

Curative treatment with oseltamivir only has a limited benefit for the following reasons:

- The probabilistic nature of influenza diagnosis in particular when the subject is young,
- The need to administer treatment within 48 hours of the first symptoms for it to be effective. Data show that problems with health care organisation make this objective difficult to achieve in practice.

Public health benefit of TAMIFLU for treatment of influenza

Influenza is a common, contagious disease which may be serious in certain patients categories (comorbidity and/or age over 65 years in particular). It constitutes a moderate public health burden.

Reducing the morbidity and mortality of influenza during epidemics is a public health need. This need is generally covered by vaccination. However, an additional means of therapy may be useful in high risk subjects (comorbidity and/or age over 65 years in particular) who contract influenza despite vaccination.

The expected impact of this product in terms of morbidity and mortality cannot be quantified from the clinical study data as there is no mortality data and because the effect on morbidity criteria is only limited.

Moreover, it is difficult to extrapolate the results of these studies as they are dependent on healthcare organisation (real vaccine coverage, time before initiation of treatment in real-life practice).

TAMIFLU does not therefore specifically address an identified public health need.

Consequently, TAMIFLU is not expected to benefit public health in this indication.

Public health benefit of TAMIFLU for post-exposure prophylaxis

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[8] Subjects “at high risk” are defined as subjects aged over 65 years or subjects belonging to the one of 11 categories below (9 long-term conditions and 3 other categories) entitled to reimbursement of influenza vaccine:

- Insulin-dependent diabetes mellitus, non-insulin-dependent diabetes mellitus not controlled by dietary measures alone
- Invalidating stroke
- Severe chronic renal disease and primary nephrotic syndrome
- Severe neuromuscular disorders (including myopathy)
- Cystic fibrosis
- congenital heart disease, severe cardiac insufficiency or heart failure, severe heart valve defects
- Serious chronic respiratory disease (including asthma on the long-term condition list)
- Serious primary immune deficiency disorder requiring prolonged treatment, infection by human immunodeficiency virus (for HIV-infected subjects the most recent studies show that vaccination may cause a transient increase in viral load so that vaccination should not be systematically recommended)
- Homozygous sickle cell anaemia (congenital haemolytic anaemia due to haemoglobinopathy);
- Patients with asthma and COPD,
- Persons staying in medium or long-term stay facilities of whatever age,
- Children and adolescents (aged from 1 to 18 years) whose condition requires prolonged treatment by acetylsalicylic acid.

The burden of influenza in children aged over 1 year and adults may be considered to be moderate. However, taking into consideration the flu vaccine coverage and the relatively small number of patients concerned by the indication (prophylaxis after contact with a clinically diagnosed case), the burden is low.

Reducing the morbidity and mortality of influenza during epidemy, in particular in high-risk patients, is a public health need.

Considering the data obtained during clinical studies and despite the lack of data on mortality, this proprietary medicine is expected to have a moderate impact in terms of morbidity and mortality. However, it is difficult to extrapolate the results of these studies as they are dependent on healthcare organisation (real vaccine coverage, time before initiation of treatment in real-life practice etc.).Moreover, there is a risk of a negative effect on public health and morbidity and mortality by reducing vaccine coverage after its marketing.

Taking into account these reservations, TAMIFLU should provide an additional response (after vaccination and non-medical measures) to an identified public health need.

Consequently,TAMIFLU is expected to benefit public health in this indication. This benefit is low.

Actual benefit in curative treatment of influenza

- Children (≥1) and adults (< 65 years) not belonging to high risk populations:

The new data submitted are not sufficient to change the committee's previous opinion. The actual benefit of TAMIFLU for curative treatment in children (≥ 1 year) and adults (< 65 years) remains insufficient.

- Children (≥1) and adults (< 65 years) with comorbidity:

The epidemiological studies provided do not show a significant reduction in mortality or length of hospital stay under real-life conditions of use.
The actual benefit of TAMIFLU for curative treatment in children (≥ 1 year) and adults (< 65 years) with comorbid disease is still considered insufficient.

- Elderly (> 65 years) :

The actual benefit of TAMIFLU for curative treatment in the elderly (>65 years) is still considered insufficient.

Actual benefit in post-exposure prophylaxis in adults and children from 1 year

TAMIFLU may be used for influenza prophylaxis from 1 year after close contact with a clinically diagnosed case in the household. Prevention must begin as soon as possible, within 48 hours of the onset of symptoms. Protection only lasts for the duration of treatment.

- Population without risk for complications:

The new data submitted are not sufficient to change the committee's previous opinion.
Taking into account the fact that, in this population, influenza is usually benign and vaccine efficacy high, the actual benefit of TAMIFLU for influenza prophylaxis in subjects without comorbid diseases is insufficient.

- Population at high risk for complications:

The new data submitted are not sufficient to change the committee's previous opinion.
Taking into account:

- The risk of serious complications in these populations,
- The lower efficacy of the vaccine in adults aged over 65 years,

the actual benefit of TAMIFLU for post-exposure prophylaxis in high risk populations remains low.

In addition, the actual benefit of TAMIFLU in post-exposure prophylaxis remains moderate in subjects at risk, in the following specific cases:

- Subjects living in institutions (institutionalised patients)
- Subjects with a contraindication to the vaccine.
- Immunocompromised subjects (in particular subjects with AIDS, transplant recipients or patients receiving immunosuppressive drugs)
- Situations in which the vaccine only provides partial protection from the circulating strain.

Taking into account the risk of potentially serious complications in these populations, the committee considers that TAMIFLU may benefit public health in these subjects.

6.2. Therapeutic use

Because of epidemiological evidence suggesting a reduction in influenza complications, hospital admissions and deaths of vaccinated subjects compared to unvaccinated subjects, influenza vaccination is the reference strategy for the management of influenza in high-risk groups.

In patients with flu-like syndrome, the reference symptomatic treatment is non-specific and is based on a combination of antipyretics and analgesics.
Antiviral agents (oseltamivir and zanamivir) only have a limited place in the symptomatic treatment of influenza in a normal epidemic situation.

During an epidemic, anti-influenza viral agents (oseltamivir and zanamivir) may be used after contact with a subject with flu-like syndrome. Treatment must be initiated as soon as possible after exposure and not later than 48 hours after the first symptoms in subjects with influenza symptoms. The protective effect lasts for the duration of treatment.

Prophylactic treatment is short lasting (maximum 6 weeks for oseltamivir and 4 weeks for zanamivir). Late vaccination is therefore still recommended during an epidemic.

In this setting, after contact with a subject with flu-like syndrome, the prophylactic use of zanamivir or oseltamivir is particularly recommended in subjects at high risk for complications who are only partially protected or not protected by the vaccine:

- Subjects aged over 65 years,
- Subjects vaccinated for less than 15 days,
- Subjects in whom vaccination is contra-indicated,
- When there is a mismatch between the vaccine strain and the circulating viral strain.

The following recommendations[9] should be respected when an epidemic occurs while influenza virus is circulating in the community and has been documented in institutions including healthcare facilities caring for high-risk subjects:

- Post-exposure prophylaxis should be initiated within 48 hours of contact with a person presenting influenza symptoms in all high-risk subjects aged from 1 year, whether they have been vaccinated or not,
- This treatment should be prescribed for up to 7 days after the onset of symptoms in the last case.

The choice of antiviral agent must take into account the pharmaceutical form: capsule or inhalation.

[9] According to the opinion of French Higher Council of Public Health on prophylaxis in persons at risk during an influenza outbreak in an institution when the virus is circulating in the community. Session of January 16th, 2004

6.3. Transparency Committee recommendations

The transparency committee recommends the inclusion of TAMIFLU on the list of medicines reimbursed by National Insurance in the indication “post-exposure prophylaxis for subjects at risk aged from 1 year”, in the indications and dosages of the marketing authorisation and in the following populations:

- Subjects aged from 1 to 65 years with one of the 9 long-term conditions qualifying for reimbursement of influenza vaccine,
- Subjects aged over 65 years,
- Subjects living in institutions (institutionalised patients)
- Immunocompromised subjects
- Subjects at risk when the vaccine only provides partial protection from the circulating strain.
- subjects with a contraindication to influenza vaccine, in particular in the following cases:
    - Patients with asthma and COPD,
    - Persons staying in medium or long-term stay facilities of whatever age,
    - Children and adolescents (from 1 to 18 years) whose health status requires prolonged treatment by acetylsalicylic acid.

Packaging: Appropriate to the conditions of prescription

Reimbursement rate: 35 %