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TRANSPARENCY COMMITTEE

Opinion
20 November 2013

STRUCTOFLEX 625 mg, hard capsule

Box of 60 hard capsules (CIP: 34009 346 919 2)

Applicant: PIERRE FABRE MEDICAMENT

INN	Glucosamine (hydrochloride)
ATC code (2012)	M01AX05 (other non-steroidal anti-rheumatic anti-inflammatory drugs)
Reason for the review	Re-assessment of the actual benefit pursuant to the findings of the Transparency Committee in its opinion of 30 June 2010.
List(s) concerned	National Health Insurance (French Social Security Code L.162-17) Hospital use (French Public Health Code L.5123-2)
Indication(s) concerned	"Relief of symptoms in mild to moderate osteoarthritis of the knee."

Actual Benefit	Insufficient Actual Benefit
Therapeutic Use	Due to the very modest efficacy on pain and functional disability on the one hand, and the absence of a demonstrated impact in terms of reduced consumption of NSAIDs on the other hand, STRUCTOFLEX has no place in the treatment of mild to moderate osteoarthritis of the knee.

01 ADMINISTRATIVE AND REGULATORY INFORMATION

Marketing Authorisation (procedure)	02/04/2010 (under the name GLUCOSAMINE VENIPHARM 625 mg, national procedure) amendment of 02/09/2010 and 08/03/2010 (name change)
Prescribing and dispensing conditions / special status	List II

ATC Classification	2012	
	M	Musculo-skeletal system
	M01	Anti-inflammatory and anti-rheumatic drugs
	M01A	Non-steroidal anti-inflammatory and anti-rheumatic drugs
	M01AX	Other non-steroidal anti-rheumatic and anti-inflammatory drugs
	M01AX05	glucosamine

02 BACKGROUND

During the application for inclusion on the national health insurance and hospital use lists for STRUCTOFLEX, the Committee found that its AB was low and gave a favourable opinion for inclusion, on the condition that a study was set up and conducted within two years of marketing (deadline of 30 June 2013) to show the impact of STRUCTOFLEX prescription in terms of reducing NSAID consumption (opinion of 30 June 2010).

On 26 November 2008, a similar opinion was rendered for the medicinal products: ART 50 mg and ZONDAR 50 mg (diacerein), CHONDROSULF (chondroitin sulfate) and PIASCLEDINE (unsaponifiable components of avocado and soybean oils). In its opinions of 9 January 2013, the Committee evaluated the results of a study (PEGASE) that did not show reduction in NSAID consumption related to the prescription of these four medicinal products; it therefore concluded insufficient actual benefit.

Due to the late arrival on the market of proprietary medicinal products based on glucosamine, the Committee re-assessed the AB for STRUCTOFLEX, after the 2-year period set, on the basis of the results of the PEGASE study, in response to the Committee's request in its 2010 opinion.

03 THERAPEUTIC INDICATIONS

"Relief of symptoms in mild to moderate osteoarthritis of the knee."

04 DOSAGE

"2 hard capsules (1250 mg of glucosamine) once daily for relief of symptoms.

Glucosamine is not indicated for the treatment of acute pain. Relief of symptoms (especially pain relief) may not be experienced until after several weeks of treatment and in some cases even longer. If no relief of symptoms is experienced after 2-3 months of treatment, continued treatment with glucosamine should be re-assessed.

The capsules must be swallowed with plenty of water.

The capsules may be taken with or without food.

Additional information for special populations:

Children and adolescents

STRUCTOFLEX should not be used in children and adolescents below age 18 due to the lack of data on safety and efficiency.

Elderly

No specific study has been conducted in the elderly, but from clinical experience, no dosage adjustment is necessary when treating elderly patients otherwise in good health.

Renal or hepatic impairment:

No study has been conducted in the population of patients with renal and/or hepatic impairment, so no dosage recommendation can be made."

05 THERAPEUTIC NEED

The first steps to take in treating osteoarthritis symptoms of the lower members are hygiene and dietary rules (weight loss, regular physical activity except during flare-ups of pain or congestion where reduced activity is necessary) and non-pharmacological (physical therapy, wearing orthotics, using canes, etc.).

Treatment must be individualised and include risks factors related to the knee (obesity, mechanical stress, physical activity) and general risk factors (age, multiple medications, etc.), the intensity of the pain and the disability that it causes, the presence of inflammatory signs (effusion), and the degree of structural impairment.

During symptomatic phases, treatment mainly includes analgesics, starting with paracetamol, and during acute flares, short courses of oral NSAIDS at the minimum effective dose in patients who do not respond to paracetamol.

Local analgesic treatments, especially topical NSAIDS and intra-articular corticosteroid injections, can also be used, especially during congestive phases.

Medicines based on chondroitin sulfate, unsaponifiable components of avocado and soybean oil, diacerein and glucosamine have minimal effects only on pain and functional disability. It has not been demonstrated that they reduce NSAID consumption, which causes very notable and often serious adverse effects, in particular in the elderly. Consequently, they have no therapeutic use. The risk/benefit ratio for diacerein was deemed unfavourable by the MA Committee (July 2012).

Surgery (arthroplasty, prosthesis implant) is reserved for radiologically advanced osteoarthritis that is painful and disabling and resistant to the usual therapeutic measures.

There is therefore currently no primary treatment that can change the progression of osteoarthritis.

06 CLINICALLY RELEVANT COMPARATORS

06.1 Medicinal products

Active ingredient	Proprietary medicinal product	Company	Presentation	Indication	AB	Date of opinion	Reimbursement
Glucosamine (hydrochloride)	FLEXEA 625 mg	Expanscience	tablet	Delayed-effect symptomatic treatment of hip and knee osteoarthritis	Insufficient	22 July 2009	yes
	VOLTAFLEX 625 mg	Novartis Santé Familiale S.A.S.	tablet			10 March 2010	
Glucosamine (sulfate)	OSAFLEXAN 1178 mg	Rottapharm S.A.R.L.	oral powder for solution in single dose sachets			10 March 2010	
	DOLENIO 1178 mg	Biocodex	tablet			13 January 2010	
Chondroitin (sulfate)	CHONDROSULF 400 mg	Genévrier	hard capsule and oral granulate for solution in sachet			09 January 2013	
Diacerein	ART 50 mg	Negma-Lerads	hard capsule			09 January 2013	
	ZONDAR 50 mg	Pharma 2000	hard capsule	09 January 2013			
Unsaponifiable components of avocado and soybean oil	PIASCLEDINE 300 mg	Expanscience	hard capsule	09 January 2013			

06.2 Other health technologies

Not applicable

► Conclusion

The most relevant comparators are other glucosamine-based proprietary medicinal products.

07 INTERNATIONAL INFORMATION ON THE MEDICINAL PRODUCT

STRUCTOFLEX does not have a marketing authorisation for sale abroad.

08 SUMMARY OF PREVIOUS ASSESSMENTS

Date of opinion	30 June 2010 (Inclusion) under the name GLUCOSAMINE VENIPHARM 625 mg, hard capsules
Indication	"Relief of symptoms in mild to moderate osteoarthritis of the knee."
AB	<p><i>Symptomatic osteoarthritis of the knee is characterised by pain and functional disability that can become chronic. It may eventually require surgical treatment with a prosthesis implant.</i></p> <p><i>This proprietary medicinal product is intended for symptomatic treatment.</i></p> <p><i>GLUCOSAMINE VENIPHARM 625 mg is not expected to benefit public health.</i></p> <p><i>This proprietary medicinal product is not very effective in relieving knee osteoarthritis symptoms. The efficacy/adverse effects ratio is modest.</i></p> <p>Treatment of osteoarthritis of the lower members relies above all on hygiene and dietary rules (weight loss, regular physical exercise) and non-pharmacological measures (physical therapy, wearing orthotics, using canes, etc.). Symptomatic treatment mainly relies on oral analgesics and NSAIDs. This proprietary medicinal product has a limited place in the symptomatic treatment of mild to moderate knee osteoarthritis.</p> <p>Due to its modest efficacy and limited role in therapeutic use, the actual benefit of GLUCOSAMINE VENIPHARM 625 mg, hard capsules, is low.</p>
Improvement Actual Benefit	in GLUCOSAMINE VENIPHARM 625 mg, hard capsule, does not provide improved actual benefit (IAB V) with regard to other slow-acting osteoarthritis drugs.
Studies requested	A favourable opinion for inclusion on the list of medicines refundable by national health insurance and on the list of medicines approved for hospital use and various public services in the indications and at the dosage in the MA, on the condition that a study is conducted within two years to show the impact of GLUCOSAMINE VENIPHARM 625 mg prescription in terms of reduced NSAID consumption.

Date of opinion	21 September 2011 (re-assessment of the actual benefit following the referral to the Transparency Committee of 16 June 2011 by the Social Security Directorate pursuant to Article R 163-19/6° of the French Social Security Code).
Indication	"Relief of symptoms in mild to moderate osteoarthritis of the knee."
AB	<p>Symptomatic osteoarthritis of the knee is characterised by pain and functional disability that can become chronic. It may eventually require surgical treatment with a prosthesis implant.</p> <p>This proprietary medicinal product is intended for symptomatic treatment.</p> <p><u>Public health benefit:</u></p> <p>The public health burden of osteoarthritis of the knee is moderate. The reduction in functional limitations and disability induced by osteoarthritis, as well as the improvement in quality of life in people who suffer from it, represent a public health need. The response to this need is not only drug-based.</p> <p>The available data regarding pain and algofunctional indexes do not permit concluding the existence of an impact of glucosamine on improving quality of life and reducing functional limitations: no quality of life data, little effect on symptoms.</p> <p>The theoretical benefit, in public health terms, of slow-acting osteoarthritis drugs resides in reducing NSAID consumption, which reduces the frequency of adverse digestive effects that are particularly detrimental in the elderly. For glucosamine, this benefit has not been proven by evidence. Consequently, STRUCTOFLEX 625 mg is not expected to benefit public health.</p> <p>This proprietary medicinal product is not very effective in relieving knee osteoarthritis symptoms. The efficacy/adverse effects ratio is modest.</p> <p>Treatment of osteoarthritis of the lower extremities relies above all on diet and lifestyle measures (weight loss, regular physical exercise) and non-pharmacological measures (physical therapy, wearing orthotics, using canes, etc.). Symptomatic treatment mainly relies on oral analgesics and NSAIDs. This proprietary medicinal product has a limited place in the symptomatic treatment of mild to moderate knee osteoarthritis.</p> <p>Due to its modest efficacy and limited role in therapeutic use, the actual benefit of STRUCTOFLEX 625 mg, hard capsules, remains low in the MA indications.</p>
Studies requested	A favourable opinion for continued inclusion on the list of medicines refundable by national health insurance in the indications and at the dosages in the MA, while awaiting the results of the 3A-PEGASE study.

09 ANALYSIS OF AVAILABLE DATA

09.1 Efficacy

The company has not provided any new clinical efficacy data.

09.2 Safety/Adverse effects

The company has provided new safety data: PSUR covering the period from 29 October 2010 to 31 May 2011. These data are not likely to change the known profile of glucosamine.

09.3 Usage/prescription data

Observational study

Since 2008, the Transparency Committee has re-assessed all delayed-effect symptomatic treatments for hip and knee osteoarthritis included on the list of reimbursable medicinal products (ART 50, ZONDAR, CHONDROSULF and PIASCLEDINE) and, in 2010, examined the various applications for inclusion of glucosamine-based proprietary medicinal products and other delayed-effect symptomatic treatments with a similar indication (relief of symptoms related to mild to moderate osteoarthritis of the knee): DOLENIO, FLEXEA, OSAFLEXAN, STRUCTOFLEX and VOLTAFLEX. Due to their low efficacy on pain and joint function, the Committee believed that the potential benefit of these treatments, in particular glucosamine-based medicines, would reside in a possible reduction of NSAID consumption.

Its favourable opinion for continued listing or inclusion of these proprietary medicinal products depended on setting up and conducting a study, within two years after marketing (deadline of 30 June 2013), to show their impact in terms of reducing NSAID consumption.

To meet the Transparency Committee's request dated on 13 January 2010, Pierre Fabre Médicaments participated in the PEGASE study.

As a reminder, PEGASE is a cohort study of patients with knee or hip arthritis, treated or not treated by delayed-effect symptomatic osteoarthritis medicines including glucosamine-based medicines, which aimed to measure their impact on NSAID use and describe their usage profile during follow-up.

During this study, a total of 940 patients had STRUCTOFLEX prescribed at least once, but the company did not wish to file the results of the study concerning its proprietary medicinal product in the absence of agreement on the definition of exposure and on the choice of time units for non-exposure used in the primary analysis.

The Committee believes that since the PEGASE study has been concluded and the results regarding STRUCTOFLEX are available, they should have been submitted to the Committee in accordance with the company's commitments.

Instead, to answer the Committee's question, the company conducted another study on the basis of data from the IMS Health Disease Analyser, a database for longitudinal follow-up of patient care. This database collects computer data regarding daily consultation and prescription from around 1200 French generalist physicians or specialists practising in metropolitan France. The nationwide representativeness of the panel of physicians is verified by the following criteria: age, sex, geographic location, volume of business and type of practice.

OBJECTIVES AND METHOD

This cohort study aimed to evaluate decreased NSAID use in osteoarthritis patients as a result of taking STRUCTOFLEX in a population of patients treated with STRUCTOFLEX compared with a group of patients not treated by any delayed-effect symptomatic osteoarthritis treatment throughout the study period.

In this study, the exposed patients were included as soon as a diagnosis of knee osteoarthritis (CIM10 M17) associated with starting STRUCTOFLEX treatment between 1 October 2010 and 30 September 2012 was identified in the database.

Patients had to have a minimum history in the database of at least one year and must not have been treated by a medicinal product with indications similar to STRUCTOFLEX in the past 12 months preceding the initial prescription. They had to have at least one consultation during the six months following the start of STRUCTOFLEX treatment and must not have been treated by another medicine having indications similar to STRUCTOFLEX during the follow-up period.

Non-exposed patients were defined as any patient with a minimum history in the database of at least one year, who had a diagnosis during this history of knee osteoarthritis (CIM10 M17), polyosteoarthritis (CIM10 M15), or osteoarthritis, not otherwise specified (CIM10 M199), and were not treated by a medicine with indications similar to STRUCTOFLEX during the year preceding the inclusion period or during the six-month follow-up period.

The control group was matched to the patients of the STRUCTOFLEX group in terms of age, sex, age of the diagnosis in the database, and whether or not NSAIDs had been previously prescribed.

The follow-up period was one year.

The primary analysis aimed to compare NSAID consumption (excluding prescription at inclusion) in patients exposed to STRUCTOFLEX (whether combined with another compound or not) with patients not exposed to any SYSADOA.

Secondary analyses aimed to compare the impact of treatment with STRUCTOFLEX on analgesic and PPI use and on the number of general practice visits.

There was no hypothesis set beforehand to calculate the necessary number of subjects.

Description of the cohort

The number of physicians who participated in the study is not provided.

A total of 2241 patients treated with STRUCTOFLEX was identified in the database, of whom 1160 were treated for knee osteoarthritis and 1081 were treated for another osteoarthritis location. Among the former, 581 had not received a prescription for a medicine with an indication similar to STRUCTOFLEX in the previous year and 436 received a minimum of one year of follow-up in the database.

Accordingly, of the 2241 patients treated with STRUCTOFLEX in the analysis period considered, only 436 patients (or 19.43%) strictly meeting the inclusion and non-inclusion criteria were included.

In all, 11,336 patients not treated by any medicine with indications similar to STRUCTOFLEX were identified in the database.

The screening process for non-exposed patients is not discussed in detail.

One out of 26 patients could be matched.

The main characteristics of patients exposed to STRUCTOFLEX at inclusion (n = 436) were the following:

- 67.6% of patients were female;
- the majority of patients (58.7%) were between 50 and 65 years old, 21.8% were between 66 and 75 years old and 19.5% were older than 76 years old;
- the history of osteoarthritis was less than one year for approximately half the patients (51.6%);

- nearly 49% of patients were not treated by NSAIDs¹ in the previous year;
- STRUCTOFLEX prescription is associated with an NSAID in 23.2% of patients.

Due to the matching, the main characteristics of patients exposed to STRUCTOFLEX do not differ from those of patients never exposed to any medicine with indications similar to STRUCTOFLEX during the follow-up.

However, there is no information available on the degree of severity of the disease, the patients' primary co-morbidities at inclusion and the primary analgesic prescriptions at inclusion.

RESULTS

During the follow-up periods (excluding initial prescription), 192/436 patients exposed to STRUCTOFLEX (44.0%) were treated with an NSAID *versus* 4997/11,336 (44.1%) in the non-exposed group.

During follow-up, 25.5% of patients from the group exposed to STRUCTOFLEX who did not have an NSAID prescription before inclusion had one the following year, *versus* 27.7% in the non-exposed group.

Furthermore, 38.4% of patients from the group exposed to STRUCTOFLEX who had an NSAID prescription before inclusion did not have one the following year, *versus* 40.50% in the non-exposed group.

➤ Primary analysis

The mean number of days of NSAID treatment expressed as defined daily dose² (DDD) is 45.1 days (standard deviation: 49.0) during the first year, excluding prescription at inclusion, in the STRUCTOFLEX group and 53.0 days (standard deviation: 71.1) in the non-exposed group, or an absolute difference of **8 days** ($p = 0.033$). The medians are, respectively, 29 and 30 days and the ranges are, respectively [1.33 - 300 days] and [0.5 - 780 days].

The mean cumulative duration of NSAID prescription (excluding any initial co-prescription) during the year of follow-up is 30.4 days (standard deviation: 38.6) in the group exposed to STRUCTOFLEX and 37.8 days (standard deviation: 54.6) in the non-exposed group.

➤ Secondary analyses

Results on analgesic and PPI use:

During follow-up, 53.0% of patients from the group exposed to STRUCTOFLEX who did not have an analgesic prescription before inclusion had one the following year, *versus* 49.5% in the non-exposed group.

Furthermore, 13.0% of patients from the group exposed to STRUCTOFLEX who had an analgesic prescription before inclusion did not have one the following year, *versus* 13.9% in the non-exposed group.

During follow-up, 21.3% of patients from the group exposed to STRUCTOFLEX who did not have a PPI prescription before inclusion had one the following year, *versus* 22.4% in the non-exposed group.

Furthermore, 30.9% of patients from the group exposed to STRUCTOFLEX who had a PPI prescription before inclusion did not have one the following year, *versus* 27.5% in the non-exposed group.

Although these analyses were specified in the study protocol, the number of days of treatment expressed in DDD for analgesics and PPIs were not compared between the two groups.

¹ The exact definition applied for NSAID exposure is not specified in the company's report.

² Measurement unit defined by the WHO as the assumed average maintenance dose per day for a medicinal product used for its main indication in adults. http://www.whocc.no/atc_ddd_index/

Results on general practice visits:

The mean number of general practice consultations during the study follow-up year was 7.0 (standard deviation: 4.3) in the STRUCTOFLEX group and 7.3 (standard deviation: 4.4) in the non-exposed group, or an absolute difference of 0.3 consultations (NS).

CONCLUSION

The Committee believes that the results of the PEGASE study concerning STRUCTOFLEX should have been submitted in compliance with the company's commitments.

The report presented for the study conducted on the Disease Analyser database is brief and has substantial methodological limits that make the results of this study difficult to interpret given:

- The representativeness of the population studied is not ensured. In particular, attrition bias can not be ruled out, given:
 - on the one hand, that the screening procedure for patients treated with STRUCTOFLEX according to its MA (inclusion only of patients with knee osteoarthritis) led to non-inclusion of half the population identified as receiving a STRUCTOFLEX prescription;
 - and, on the other hand, that the non-inclusion of patients treated by another delayed-effect symptomatic osteoarthritis treatment during the follow-up period led to non-inclusion of half the population with knee osteoarthritis identified as receiving a STRUCTOFLEX prescription.
- The hypotheses chosen for comparative analysis between the patient groups were not clearly formulated and, in particular, specified neither the date selected as the index date for the subjects of the non-exposed group, nor the test statistics (given the non-independence of the groups).
- The definition selected for NSAID prescription (in a given period) is not specified.
- The number of days of treatment is based on the prescriptions of generalist physicians and does not reflect actual patient exposure. In fact, the PEGASE study indicated that for this medicinal class, a significant number of patients did not take their prescribed delayed-effect symptomatic osteoarthritis treatment.
- The definition of non-exposed patients in terms of disease studied (CIM10 M17, M15, M199) was not strictly similar to the one applied for exposed patients (CIM 10 M17 only). Furthermore, there is no information available on the degree of severity of the disease, the primary co-morbidities and the primary analgesic prescriptions at inclusion. This could alter the comparability of the groups at inclusion and limit the interpretation of results.
- The extent of the distribution of treatment days appears questionable.
- The clinical relevance of reducing NSAID consumption by 8 days out of one year of follow-up, especially in terms of reducing digestive complications, is unknown.
- Finally, the data analysis does not include information on or take into account whether or not the STRUCTOFLEX treatment was maintained during the one-year follow-up period. The Committee actually has no information on the duration of STRUCTOFLEX treatment during the follow-up, which limits the evaluation of the impact attributable to STRUCTOFLEX regarding reduction in NSAID use.

Consequently, given the above-mentioned limits, the Committee believes that it has not been proven by evidence that STRUCTOFLEX contributes to reducing NSAID consumption in osteoarthritis patients.

09.4 Summary & discussion

No new clinical efficacy data were submitted.

The updated safety data (PSUR) are not likely to change the known safety profile of glucosamine.

In its opinion of 10 June 2010, the Transparency Committee made its favourable opinion for inclusion on the list for reimbursement, given a low AB, dependent on setting up and conducting, within two years, a study to show the impact of STRUCTOFLEX (formerly Glucosamine Venipharm) prescription in terms of reducing NSAID consumption.

The main results of the study presented are:

- a similar consumption rate between the group exposed to STRUCTOFLEX (44.0%) *versus* the non-exposed group (44.1%);
- a number of treatment days expressed in DDD of 45.1 days (standard deviation: 49.0) in the STRUCTOFLEX group and 53.0 days (standard deviation: 71.1) in the non-exposed group, or an absolute difference of 8 days of treatment over the year ($p = 0.033$). However, the medians are, respectively, 29 and 30 days.

Nevertheless, these results are difficult to interpret given the significant methodological limits of the study conducted and, in particular, related to:

- attrition bias, which could not be ruled out given the patient screening procedure that led to non-inclusion of 74% of patients identified as receiving a STRUCTOFLEX prescription;
- lack of precision related to the methodology applied for the study;
- the absence of information regarding the duration of STRUCTOFLEX treatment in the group of exposed patients, limiting the evaluation of the impact attributable to delayed-effect symptomatic osteoarthritis treatment on reducing NSAID use during the follow-up.

As a result, STRUCTOFLEX has not been proven by evidence to contribute to reducing NSAID consumption in osteoarthritis patients.

010 THERAPEUTIC USE

Due to the very modest efficacy on pain and functional disability on the one hand, and the absence of a demonstrated impact in terms of reduced consumption of NSAIDs on the other hand, STRUCTOFLEX has no place in the treatment of mild to moderate osteoarthritis of the knee.

011 TRANSPARENCY COMMITTEE CONCLUSIONS

In view of all the above information, and following the debate and vote, the Committee's opinion is as follows:

011.1 Actual benefit

► Symptomatic osteoarthritis of the knee is characterised by pain and functional disability that can become chronic. It may eventually require surgical treatment with a prosthesis implant.

► This medicinal product is a symptomatic treatment

► Public health benefit:

The public health burden of osteoarthritis of the knee is moderate.

Reduction of functional limitations and disabilities induced by osteoarthritis, as well as improvement in the quality of life of people affected with it, represent a public health need included in the priorities established in the public health policy act of 9 August 2004 (objective 85). However, the response to this need is not limited to drug treatment.

The available data regarding pain and algofunctional indexes do not permit concluding the existence of an impact of glucosamine-based proprietary medicinal products on improving quality of life and reducing functional limitations: no quality of life data, little effect on functional disability.

The theoretical benefit, in public health terms, of medicines indicated in the treatment of osteoarthritis symptoms resides in reducing NSAID consumption, which would likely reduce the frequency of adverse digestive effects that are particularly detrimental in the elderly. This usefulness of STRUCTOFLEX has not been proven by evidence from the observational study conducted on the database.

Consequently, STRUCTOFLEX does not benefit public health.

► This proprietary medicinal product is not very effective in relieving knee osteoarthritis symptoms. The efficacy/adverse effects ratio is modest.

► Treatment of osteoarthritis of the lower extremities relies above all on diet and lifestyle measures (weight loss, regular physical exercise) and non-pharmacological measures (physical therapy, wearing orthotics, using canes, etc.). Symptomatic treatment mainly relies on oral analgesics and NSAIDs. Glucosamine-based proprietary medicinal products, including STRUCTOFLEX, are not very effective on pain and functional disability and it has not been proven that they reduce NSAID use. Consequently, STRUCTOFLEX has no role in the treatment of mild to moderate osteoarthritis of the knee.

Taking account of these points, the Committee considers that the actual benefit of STRUCTOFLEX 625 mg, tablets is insufficient in the relief of symptoms of mild to moderate osteoarthritis of the knee for reimbursement by National Health Insurance.

The Committee renders an unfavourable opinion for continued inclusion on the list of medicines refundable by National Health Insurance and on the list of medicines approved for hospital use in the indication "Relief of symptoms in mild to moderate osteoarthritis of the knee" and at the dosages in the Marketing Authorisation.