SUMMARY OF DECISIONS FROM THE SPANISH INTERMINISTERIAL MEDICINAL PRODUCTS PRICING COMMITTEE (CIPM)

SESSION 205 OF OCTOBER 14TH, 2020

November 26th, 2020

INFORMATIVE NOTE FROM THE SPANISH INTERMINISTERIAL MEDICINAL PRODUCTS PRINCING COMMITTEE MEETING

SESSION 205 OF OCTOBER 14th, 2020

For information purposes, this note summarises the **main agreements** established by the Spanish Interministerial Medicinal Products Pricing Committee (CIPM), a collegial body competent in setting the maximum industrial price, gathered on October 14th, 2020.

It is specified that these agreements are not definitive since, prior to the Resolution by the Directorate-General for Basic Portfolio of Services of the National Health System and Pharmacy, the processing of allegations to the Project Resolution is at the disposition of the company, according to the administrative procedure.

The agreements taken in this Committee of September 2020 will not be effective until the corresponding final Resolution is issued by the Directorate-General for Basic Portfolio of Services of the National Health System and Pharmacy and the changes generated by these agreements are included in the corresponding billing Nomenclator.

The agreements differ into two **blocks**: agreements with pricing and reimbursement (approvals) and rejected agreements.

Each block is divided into the following **sections**:

A. New medicinal products: This section includes the agreements related to the inclusion or non-inclusion in the pharmaceutical provision of the National Health System (NHS) of **medicines with new active ingredients or combinations (A.1) and other medicines (A.2)** (this subsection includes, for example, the first generics, first biosimilars and first copies, among others).

B. New indications: This section includes the agreements regarding the inclusion or non-inclusion in the pharmaceutical provision of the NHS of **new indications of medicines that are already included in the pharmaceutical provision of the NHS.**

C. Modifications to the pharmaceutical offering: This section includes the agreements related to alterations in the offer, i.e., to the **modification of reimbursement and price conditions** (price raises or reductions, conditions of prescription and dispensation, exclusion of the provision) of medicines included in the pharmaceutical provision of the NHS.

D. Allegations: This section includes the agreements related to the records (may be new drugs, new indications or alterations of the offer) that have obtained an agreement of acceptance or non-acceptance of the allegations presented by the medicine's laboratory holder object of record.

In case that the medicines' laboratory holders included in sections A (new medicinal products), B (new indications) and C (modifications to the pharmaceutical offering) do not present allegations and accept the draft resolution or submit the allegations and these are accepted, a reimbursement resolution will be issued.

In case that the medicines' laboratory holders included in sections A (new medicinal products), B (new indications) and C (modifications to the pharmaceutical offering) present allegations and these are not accepted, an specific resolution of non-reimbursement will be issued.

It should be noted that in sections A (new medicinal products), B (new indications) and D (allegations) are included, both in the text of the agreement and in the table that is included in record, the reasons for reimbursement / non-reimbursement, these being those established in article 92 of Royal Legislative Decree 1/2015, of July 24th, where the revised text of the Law on guarantees and rational use of medicines and medical devices through (*Ley 29/2006, de 26 de julio, de garantías y uso racional de los medicamentos y productos sanitarios*) is approved and by which medicinal products are financed:

Article 92

a) *Severity, duration, and sequelae of the different pathologies for which they are indicated.*
b) *Specific needs of certain groups.*
c) *Therapeutic and social value of the medicinal product and its incremental clinical benefit, taking into account its cost-effectiveness ratio.*
d) *Rationalisation of public expenditure for pharmaceutical provision and budget impact in the National Health System.*
e) *Existence of medicinal products or other therapeutic alternatives for the same conditions at a lower price or lower treatment cost.*
f) *Degree of innovation of the medicinal product.*

In section C (modifications to the pharmaceutical offering) the criteria for decision-making are those established in articles 93 and 96 of the above-mentioned Law.

1. P&R APPROVALS

A. NEW MEDICINAL PRODUCTS

A.1. NEW MEDICINAL PRODUCTS

○ RINVOQ®

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
ABBVIE SPAIN S.L.	RINVOQ 15 MG S	28 prolonged-release tablets	727711	940,8€	c) and d)

Active substance: L04AA44 - Upadacitinib

Authorised therapeutic indication:

RINVOQ is indicated for the treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs (DMARDs). RINVOQ may be used as monotherapy or in combination with methotrexate.

Prescription and dispensation conditions: Medical prescription. Hospital diagnosis.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Set the price** of the cited medicine, which is listed in the table above.
- **Establishment for this medicine of special dispensation conditions** within the scope of the NHS, consistent with limiting its dispensation, without the need for a visa, to patients not hospitalised in the Hospital Pharmacy Services.
- **Annual revision of sales and prices now set**, to ensure that they are within the legally established parameters, and if not, proceed to their adaptation through the corresponding price reduction.
- The monitoring and control of the expense generated will be carried out through the **SEGUIMED computer process** and / or any other available. The laboratory will be obliged to register in the aforementioned application and to communicate on a monthly basis to the NHS the appropriate information regarding the sales of the medicine.

A.2 OTHER MEDICINAL PRODUCTS

○ RIVAROXABÁN 10 MG EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
REDDY PHARMA IBERIA SA	RIVAROXABAN DR REDDYS 10 MG EFG	10 film-coated tablets	726263	11,64	d)
REDDY PHARMA IBERIA SA	RIVAROXABAN DR REDDYS 10 MG EFG	30 film-coated tablets	726264	34,92	d)
KRKA FARMACEUTICA SL	RIVAROXABAN TAD 10 MG EFG	30 film-coated tablets	728412	34,92	d)

Active substance: B01AF01- Rivaroxaban

Therapeutic indication:

Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Prescription and dispensation conditions: Medical prescription. Differentiated seal coupon (CPD) per indication.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Set the price** of the cited medicine, which is listed in the table above.
- **Restrict funding with a visa for the indication**: "Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.".
- **No financing of the indication**: "Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.".

○ RIVAROXABÁN 15 and 20 MG EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
REDDY PHARMA IBERIA SA	RIVAROXABAN DR REDDYS 15 MG EFG	28 film-coated tablets	726277	32,59	d)
REDDY PHARMA IBERIA SA	RIVAROXABAN DR REDDYS 15 MG EFG	42 film-coated tablets	726278	40,74	d)
KRKA FARMACEUTICA SL	RIVAROXABAN TAD 15 MG EFG	28 film-coated tablets	728414	32,59	d)
REDDY PHARMA IBERIA SA	RIVAROXABAN DR REDDYS 20 MG EFG	28 film-coated tablets	726258	32,59	d)
KRKA FARMACEUTICA SL	RIVAROXABAN TAD 20 MG EFG	28 film-coated tablets	728416	32,59	d)

Active substance: B01AF01- Rivaroxaban

Therapeutic indication:

Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation, with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack.

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Prescription and dispensation conditions: Medical prescription. Differentiated seal coupon (CPD) per indication.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Set the price** of the cited medicine, which is listed in the table above.
- **Restrict funding with a visa for the indication**: "Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation, with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack".
- **No financing of the indication**: “Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.”.

○ IMBRUVICA®

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
JANSSEN CILAG SA	IMBRUVICA 420 MG	30 film-coated tablets	726956	6.583,13	c)
JANSSEN CILAG SA	IMBRUVICA 560 MG	30 film-coated tablets	726957	8.777,50	c)
JANSSEN CILAG SA	IMBRUVICA 140 MG	30 film-coated tablets	726954	2.194,38	c)
JANSSEN CILAG SA	IMBRUVICA 280 MG	30 film-coated tablets	726955	4.388,75	c)

Active substance: L01XE27- Ibrutinib

Therapeutic indication:

IMBRUVICA as a single agent is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).

IMBRUVICA as a single agent or in combination with rituximab or obinutuzumab is indicated for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL).

IMBRUVICA as a single agent or in combination with bendamustine and rituximab (BR) is indicated for the treatment of adult patients with CLL who have received at least one prior therapy.

IMBRUVICA as a single agent is indicated for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy.

IMBRUVICA in combination with rituximab is indicated for the treatment of adult patients with WM.

Prescription and dispensation conditions: Medical prescription. Hospital diagnosis.

Regarding this medicinal product, the Committee **agrees** to:

- **Propose financing** the following indications:

IMBRUVICA as a single agent is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL).

IMBRUVICA as a single agent is indicated for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL).

IMBRUVICA as a single agent or in combination with bendamustine and rituximab (BR) is indicated for the treatment of adult patients with CLL who have received at least one prior therapy.

IMBRUVICA as a single agent is indicated for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy.

- **Propose non-financing** the following indications:

IMBRUVICA in combination with obinutuzumab is indicated for the treatment of adult patients with previously untreated CLL.

IMBRUVICA in combination with rituximab is indicated for the treatment of adult patients with MW.

Additionally, the Committee **agrees** to:

- **Set the price** of the cited medicine, which is listed in the table above.
- Establishment for this medicine of **special dispensation conditions** within the scope of the National Health System, consistent with limiting its dispensation, without the need for a visa, to patients not hospitalised in the Pharmacy Services of Hospitals.
- **Annual revision of sales** and prices now set, to ensure that they are within the legally established parameters, and if not, proceed to their adaptation through the corresponding reduction
- The monitoring and control of the expense generated will be carried out through the **SEGUIMED computer process** and / or any other available. The laboratory will be obliged to register in the aforementioned application and to communicate on a monthly basis to the NHS the appropriate information regarding the sales of the medicine.

○ DUPIXENT®

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
SANOFI AVENTIS SA	DUPIXENT 300 MG SOLUTION FOR INJECTION	2 pre-filled pens of 2ml each	727471	1.211,54	c)

Active substance: D11AH05- Dupilumab

Therapeutic indication:

Atopic Dermatitis

Dupixent is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy.

Asthma

Dupixent is indicated in adults and adolescents 12 years and older as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment.

Chronic rhinosinusitis with nasal polyposis (CRSwNP)

Dupixent is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control.

Prescription and dispensation conditions: Medical prescription. Hospital diagnosis.

Regarding this medicinal product, the Committee **agrees** to:

- **Set the price** of the cited medicine, which is listed in the table above.
- Establishment for this medicine of **special dispensation conditions** within the scope of the National Health System, consistent with limiting its dispensation, without the need for a visa, to patients not hospitalised in the Hospitals Pharmacy Service.
- Propose **non-financing** the following indications:
- Atopic Dermatitis: Dupixent is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy.
- Asthma: Dupixent is indicated in adults and adolescents 12 years and older as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment.
- Chronic rhinosinusitis with nasal polyposis (CRSwNP): Dupixent is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control.
- **Propose financing** the prescription of this medicine in the **restricted** indication for the treatment of severe atopic dermatitis in adult patients who are candidates for systemic treatment, through a payment-for-results agreement whose conditions are as follows:
    1. **Clinical criteria** that patients must meet for its use
        - ✓ Eczema Area and Severity Index (EASI) ≥21
        - ✓ Physician global assessment (PGA) ≥3
        - ✓ Minimal impact on body surface area (BSA) ≥ 10%
        - ✓ Refractory to topical medication who also have previous experience of the use of cyclosporine with an unsatisfactory response or in which the use of cyclosporine is contraindicated.
    2. The payment by results agreement will be reviewable after one year from the date of inclusion in the financing of the first presentations.
- The determination of individual compliance with the payment conditions will be made through a **Monitoring Committee in each Autonomous Community** that will be established between the health administrations and the offering / supplier laboratory. This information will be transferred to the Directorate-General for Basic Portfolio of Services of the National Health System and Pharmacy in order to determine the need for a price review.
- The Directorate-General for Basic Portfolio of Services of the National Health System and Pharmacy will prepare a **pharmaco-clinical protocol** that must be completed throughout the NHS, through VALTERMED, which contains both the criteria for starting, monitoring and discontinuing treatment as

well as the variables to be recorded to determine the results of the use of this medicine in clinical practice.

- **Annual revision of sales** and prices now set, to ensure that they are within the legally established parameters, and if not, proceed to their adaptation through the corresponding reduction
- In addition, **the price may be revised** if sales exceed by more than 10 percent the sales figure declared by the laboratory and this has an upward impact on the pharmaceutical spending of the NHS.
- The monitoring and control of the expense generated will be carried out through the **SEGUIMED computer process** and / or any other available. The laboratory will be obliged to register in the aforementioned application and to communicate on a monthly basis to the NHS the appropriate information regarding the sales of the medicine.

○ TIRODRIL®

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
LABORATORIOS ESTEDI S.L.	TIRODRIL 10 MG	40 tablets	728122	8,93	c)

Active substance: H02BB02- Tiamazol

Therapeutic indication:

Tirodril is indicated for the treatment of the following pathologies in adults and children of 3 years or more:

- Treatment of hyperthyroidism
- Treatment of thyrotoxic crises (thyroid storm).
- Preparation for thyroidectomy in patients with hyperthyroidism.
- Preparation before and after the application of radioactive iodine for the treatment of hyperthyroidism.
- Prophylactic treatment in patients with subclinical hyperthyroidism, autonomic adenomas or a history of hyperthyroidism, in whom exposure to iodine is essential (e.g. exploration with contrast media containing iodine).

Prescription and dispensation conditions: Medical prescription.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Set the price** of the cited medicine, which is listed in the table above.

○ DROPERIDOL EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
HIKMA FARMACEUTICA (PORTUGAL) SA	DROPERIDOL HIKMA 2,5 MG/ML EFG	10 vials of 1ml solution for injection	721204	24,84	d)

Active substance: N05AD08- Droperidol

Therapeutic indication:

Prevention and treatment of post-operative nausea and vomiting in adults and, as second line, in children (2 to 11 years) and adolescents (12 to 18 years).

Prevention of nausea and vomiting induced by morphine derivates during post-operative patient-controlled analgesia (PCA) in adults.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Set the price** of the cited medicine, which is listed in the table above.

○ SODIUM VALPROATE AUROVITAS 200MG/ML ORAL SOLUTION EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	MSL (MHS) €	CRITERIA FOR REIMBURSEMENT
AUROVITAS SPAIN SA	SODIUM VALPROATE AUROVITAS	40ml bottle + graduated syringe 2ml	728593	2,23	d)

Active substance: N03AG01-Sodium valproate

Therapeutic indication:

Treatment of partial or generalised epilepsy: - Primary generalised epilepsy: convulsive (clonic, tonic, tonic-clonic, myoclonic) and non-convulsive or absence seizures. - Partial epilepsy: simple or complex seizures. - Secondary generalised seizures. Treatment of idiopathic generalised and mixed seizures and / or symptomatic generalised epilepsy (West and Lennox-Gastaut). Treatment of manic episodes in bipolar disorder in adults, when lithium is contraindicated or not tolerated. Continuation of treatment after the manic episode in patients who have responded to valproate for acute mania should be considered.

Prescription and dispensation conditions: Medical prescription. Long-term treatment.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Set the price** of the cited medicine, which is listed in the table above.

○ IBUPROFEN B.BRAUN IV PAEDIATRIC

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
BBRAUN MEDICAL SA	IBUPROFEN B.BRAUN PAEDIATRIC 200MG	10 bottles of 50ml solution for intravenous infusion	728767	10,20	b) and c)
BBRAUN MEDICAL SA	IBUPROFEN B.BRAUN PAEDIATRIC 200MG	20 bottles of 50ml solution for intravenous infusion	607361	0,00	e)

Active substance: M01AE01 - Ibuprofen

Therapeutic indication:

This medicine is indicated in adolescents and children weighing 20 kg and over 6 years of age for the short-term symptomatic treatment of moderate acute pain and the short-term symptomatic treatment of fever, when intravenous administration is clinically justified and other routes of administration are not possible.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Set the price** of the cited medicine, which is listed in the table above with national code 728767.

It proposes the non-inclusion of the drug with the national code 607361 in the NHS pharmaceutical service and therefore not setting the price, considering that the company has not requested financing for this presentation.

○ LENALIDOMIDE CIPLA HARD CAPSULES EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATION. CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
CIPLA EUROPE NV branch in Spain	LENALIDOMIDE CIPLA 5MG EFG	21 capsules	728184	1.958,28	d)
CIPLA EUROPE NV branch in Spain	LENALIDOMIDE CIPLA 10MG EFG	21 capsules	728180	2053,22	d)
CIPLA EUROPE NV branch in Spain	LENALIDOMIDE CIPLA 15MG EFG	21 capsules	728181	2232,72	d)
CIPLA EUROPE NV branch in Spain	LENALIDOMIDE CIPLA 20MG EFG	21 capsules	728182	2344,36	d)
CIPLA EUROPE NV branch in Spain	LENALIDOMIDE CIPLA 25MG EFG	21 capsules	728183	2455,99	d)

Active substance: L04AX04- Lenalidomide

Therapeutic indication:

Multiple myeloma

Lenalidomide Cipla as monotherapy is indicated for the maintenance treatment of adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation.

Lenalidomide Cipla as combination therapy is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant.

Lenalidomide Cipla in combination with dexamethasone is indicated for the treatment of multiple myeloma in adult patients who have received at least one prior therapy.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Set the price** of the cited medicine, which is listed in the table above.

○ SORAFENIB SANDOZ 200MG FILM COATED TABLET EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
SANDOZ FARMACEUTICA SA	SORAFENIB SANDOZ 200MG EFG	112 film-coated tablets	728935	1.937,27	d)

Active substance: L01XE05-Sorafenib

Therapeutic indication:

Hepatocellular carcinoma

Sorafenib is indicated for the treatment of hepatocellular carcinoma.

Renal cell carcinoma

Sorafenib is indicated for the treatment of patients with advanced renal cell carcinoma who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy.

Prescription and dispensation conditions: Medical prescription. Hospital diagnosis.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Set the price** of the cited medicine, which is listed in the table above.
- Establishment for this medicine of **special dispensation conditions** within the scope of the National Health System, consistent with limiting its dispensation, without the need for a visa, to patients not hospitalised in the Hospitals Pharmacy Service.

B. NEW INDICATIONS

○ MOZOBIL®

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
SANOFI AVENTIS SA	MOZOBIL 20 MG/ML	1 vial of 1,2ml solution for injection	663769	5.482,31	b) and c)

Active substance: L03AX16- Plerixafor

Therapeutic indication:

Adult patients

Mozobil is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in adult patients with lymphoma or multiple myeloma whose cells mobilise poorly.

Paediatric patients (1 to less than 18 years)

Mozobil is indicated in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in children with lymphoma or solid malignant tumours, either:

- pre-emptively, when circulating stem cell count on the predicted day of collection after adequate mobilization with G-CSF (with or without chemotherapy) is expected to be insufficient with regards to desired hematopoietic stem cells yield, or
- who previously failed to collect sufficient haematopoietic stem cells.

Financed therapeutic indication:

Adult patients

Mozobil is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in adult patients with lymphoma or multiple myeloma whose cells mobilise poorly.

Indication of the reason for the file:
Paediatric patients (1 to less than 18 years)

Mozobil is indicated in combination with G-CSF to enhance mobilisation of haematopoietic stem cells to the peripheral blood for collection and subsequent autologous transplantation in children with lymphoma or solid malignant tumours, either:

- pre-emptively, when circulating stem cell count on the predicted day of collection after adequate mobilization with G-CSF (with or without chemotherapy) is expected to be insufficient with regards to desired hematopoietic stem cells yield, or
- who previously failed to collect sufficient haematopoietic stem cells.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Maintain the maximum industrial price** of the mentioned drug, which is listed in the table above.

○ YERVOY®

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	PRICE (€)	CRITERIA FOR REIMBURSEMENT
BRISTOL-MYERS SQUIBB SA.	YERVOY 5 MG/ML	1 vial for 10ml concentrate solution for infusion	682152	4.250	a) and c)
BRISTOL-MYERS SQUIBB SA.	YERVOY 5 MG/ML	1 vial for 40ml concentrate solution for infusion	682084	17.000	a) and c)

Active substance: L01XC11- Ipilimumab

Financed therapeutic indication:

Melanoma

YERVOY as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults, and adolescents 12 years of age and older.

YERVOY in combination with nivolumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults. Relative to nivolumab monotherapy, an increase in progression-free survival (PFS) and overall survival (OS) for the combination of nivolumab with ipilimumab is established only in patients with low tumour PD-L1 expression.

Renal Cell Carcinoma (RCC)

YERVOY in combination with nivolumab is indicated for the first-line treatment of adult patients with intermediate/poor-risk advanced renal cell carcinoma.

Indication of the reason for the file:
YERVOY in combination with nivolumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults. Relative to nivolumab monotherapy, an increase in progression-free survival (PFS) and overall survival (OS) for the combination of nivolumab with ipilimumab is established only in patients with low tumour PD-L1 expression.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding this medicinal product, the Committee **agrees** to its financing under the following conditions:

- **Restrict its funding** in combination with nivolumab for the treatment of advanced (unresectable or metastatic) melanoma in adults to:
    - Patients with PD-L1 expression ≤1% once the risks have been individually balanced against the possible benefit.
    - Patients with non-active brain metastases or uveal melanoma, once the risks have been individually balanced against the possible benefit. In such cases, treatment can be maintained until clinical, radiological progression, or unacceptable toxicity, whichever comes first.

- **Annual revision of sales** and prices now set, to ensure that they are within the legally established parameters, and if not, proceed to their adaptation through the corresponding reduction
- The monitoring and control of the expense generated will be carried out through the **SEGUIMED computer process** and / or any other available. The laboratory will be obliged to register in the aforementioned application and to communicate on a monthly basis to the NHS the appropriate information regarding the sales of the medicine.

D. ALLEGATIONS

○ BILINA®

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CURRENT PRICE (€)	NEW PRICE (€)	CRITERIA FOR REVIEW
ESTEVE PHARMACEUTICALS, S.A.	BILINA 0,5 mg/ml	1 bottle of 4 ml eye drops, suspension	682120	4,36	4,95	Article 96.2

Active substance: S01GX02- Levocabastina

Financed therapeutic indication:

Symptomatic treatment of allergic conjunctivitis in adults and in children and adolescents from 4 to 18 years of age.

Prescription and dispensation conditions: Medical prescription.

Regarding this medicinal product, the Committee **agrees** to partially accept the allegations and:

- **Modify the price** of the cited medicine, which is listed in the table above.

2. P&R REJECTIONS

A. NEW MEDICINAL PRODUCTS

A.1. NEW MEDICINAL PRODUCTS

The **non-inclusion** in the pharmaceutical provision of the NHS of the medicinal products is agreed:

○ LAMZEDE

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
CHIESI ESPAÑA SA	LAMZEDE 10 MG	5 vials with powder for solution for infusion	722449	d)

Active substance: A16AB – Velmanasa alfa

Therapeutic indication:

Enzyme replacement therapy for the treatment of non-neurological manifestations in patients with mild to moderate alpha-mannosidosis.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding to this medicinal product, the Committee **agrees** to propose to the General Directorate of Pharmacy the non-inclusion of the medicine in the pharmaceutical benefit of the NHS, taking into account the proposal presented by the company, the uncertainty in relation to the clinical and functional benefit of velmanasa alfa with respect to the results from the placebo comparator arm and criteria for rationalising public spending and budgetary impact on the NHS.

These are some of the legally established criteria for the selective and non-indiscriminate financing of medicinal products necessary to continue ensuring a sustainable pharmaceutical provision of the NHS, given the continued growth of needs in terms of pharmaceutical provision.

A.2. OTHER MEDICINAL PRODUCTS

○ RIVAROXABAN 2,5MG EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
REDDY PHARMA IBERIA SA	RIVAROXABAN DR REDDYS 2,5 MG EFG	56 film-coated tablets	726271	e)
REDDY PHARMA IBERIA SA	RIVAROXABAN DR REDDYS 2,5 MG EFG	100 film-coated tablets	727253	e)

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
KRKA FARMACEUTICA SL	RIVAROXABAN TAD 2,5 MG EFG	56 film-coated tablets	728410	e)

Active substance: B01AF01-Rivaroxaban

Therapeutic indication:

Rivaroxaban, co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine, is indicated for the prevention of atherothrombotic events in adult patients after an acute coronary syndrome (ACS) with elevated cardiac biomarkers.

Rivaroxaban, co-administered with acetylsalicylic acid (ASA), is indicated for the prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk of ischaemic events.

Prescription and dispensation conditions: Medical prescription.

Regarding to this medicinal product, the Committee **agrees to propose to the General Directorate of Pharmacy the non-inclusion** of the medicine in the pharmaceutical provision of the NHS considering the existence of medicinal products or therapeutic alternatives for the same diseases at a lower cost of treatment.

○ RIVAROXABAN 10MG EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
KRKA FARMACEUTICA SL	RIVAROXABAN TAD 10 MG EFG	10 film-coated tablets	728411	e)

Active substance: B01AF01-Rivaroxaban

Therapeutic indication:

Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery.

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Prescription and dispensation conditions: Medical prescription. Differentiated seal coupon (CPD) per indication.

Regarding to this medicinal product, the Committee **agrees to propose to the General Directorate of Pharmacy the non-inclusion** of the medicine in the pharmaceutical provision of the NHS, since the laboratory has requested not to include it and there are drugs or other therapeutic alternatives for the same conditions.

○ RIVAROXABAN 15MG EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
KRKA FARMACEUTICA SL	RIVAROXABAN TAD 15 MG EFG	14 film-coated tablets	728413	e)
KRKA FARMACEUTICA SL	RIVAROXABAN TAD 15 MG EFG	42 film-coated tablets	728415	e)

Active substance: B01AF01-Rivaroxaban

Therapeutic indication:

Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack.

Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

Prescription and dispensation conditions: Medical prescription. Differentiated seal coupon (CPD) per indication.

Regarding to this medicinal product, the Committee **agrees to propose to the General Directorate of Pharmacy the non-inclusion** of the medicine in the pharmaceutical provision of the NHS, since the laboratory has requested not to include it and there are drugs or other therapeutic alternatives for the same conditions.

○ STRIASCAN EFG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
CURIUM PHARMA SPAIN, SA.	STRIASCAN 74 MBQ/ML EFG	1 vial of 2,5ml solution for injection	726401	d)
CURIUM PHARMA SPAIN, SA.	STRIASCAN 74 MBQ/ML EFG	1 vial of 5ml solution for injection	726402	d)

Active substance: V09AB03-Iodo (123I) ioflupano

Therapeutic indication:

This medicinal product is for diagnostic use only. Striascan is indicated for detecting loss of functional dopaminergic neuron terminals in the striatum:

- In adult patients with clinically uncertain parkinsonian syndromes, for example those with early symptoms, in order to help differentiate essential tremor from parkinsonian syndromes related to idiopathic Parkinson's disease, multiple system atrophy and progressive supranuclear palsy. Striascan

is unable to discriminate between Parkinson's disease, multiple system atrophy and progressive supranuclear palsy.

- In adult patients, to help differentiate probable dementia with Lewy bodies from Alzheimer's disease. Striascan is unable to discriminate between dementia with Lewy bodies and Parkinson's disease dementia.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding to this medicinal product, the Committee **agrees** to propose to the General Directorate of Pharmacy the non-inclusion of the medicine in the pharmaceutical provision of the NHS, since it does not meet the criteria agreed by CIPM for the reimbursement of generic medicines.

○ CHENODESOXICOLIC ACID LEADIANT

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
DECO PHARMA SERVICIOS LOGÍSTICOS S.L.	CHENODESOXICOLIC ACID LEADIANT 250 MG	100 hard capsules	725392	d)

Active substance: A05AA01 Chenodesoxicolic acid

Therapeutic indication:

Chenodeoxycholic acid is indicated for the treatment of inborn errors of primary bile acid synthesis due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis (CTX)) in infants, children and adolescents aged 1 month to 18 years and adults.

Prescription and dispensation conditions: Medical prescription. Hospital diagnosis.

Regarding to this medicinal product, the Committee **agrees** to propose to the General Directorate of Pharmacy the non-inclusion of the medicine in the pharmaceutical provision of the NHS, since it is a classic medicine for which the proposed price has not been justified and generates a high budgetary impact.

○ RIZMOIC

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
SHIONOGI SL.	RIZMOIC 200 MCG	28 film-coated tablets	726062	d) and e)

Active substance: 06AH05-Naldemedina

Therapeutic indication:

Rizmoic is indicated for the treatment of opioid-induced constipation (OIC) in adult patients who have previously been treated with a laxative.

Prescription and dispensation conditions: Medical prescription.

Regarding to this medicinal product, the Committee **agrees** to propose to the General Directorate of Pharmacy the non-inclusion of the medicine in the pharmaceutical provision of the NHS, based on criteria of rationalisation of public spending and budgetary impact on the NHS compared to the reimbursed therapeutic alternatives.

These are some of the legally established criteria for the selective and non-indiscriminate financing of medicinal products necessary to continue ensuring a sustainable pharmaceutical provision of the NHS, given the continued growth of needs in terms of pharmaceutical provision.

○ OBIZUR

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
TAKEDA FARMACEUTICA ESPAÑA SA	OBIZUR 500 U	10 vials with powder and solvent for solution for injection + 10 syringes	712234	d)
TAKEDA FARMACEUTICA ESPAÑA SA	OBIZUR 500 U	5 vials with powder and solvent for solution for injection + 5 syringes	712233	d)
TAKEDA FARMACEUTICA ESPAÑA SA	OBIZUR 500 U	1 vial with powder and solvent for solution for injection + 1 syringe	712231	d)

Active substance: B02BD14 -Susoctocog alfa

Therapeutic indication:

Treatment of bleeding episodes in patients with acquired haemophilia caused by antibodies to Factor VIII.

OBIZUR is indicated in adults.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding to this medicinal product, the Committee **agrees** to propose to the General Directorate of Pharmacy the non-inclusion of the medicine in the provision of the NHS, taking into account the uncertainties regarding the therapeutic value and rationalisation of public expenditure and budget impact.

These are some of the legally established criteria for the selective and non-indiscriminate financing of medicinal products necessary to continue ensuring a sustainable pharmaceutical provision of the NHS, given the continued growth of needs in terms of pharmaceutical provision.

○ PROKAM

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
THEA S.A.	PROKAM 50 MG	10 vials of 50 mg powder for solution for injection + 10 sterile filter needles	606818	e)

Active substance: S01AA27- Cefuroxima

Therapeutic indication:

Antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery.

Consideration should be given to official guidance on the appropriate use of antibacterial agents, including guidance on the antibiotic prophylaxis on eye surgery.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding to this medicinal product, the Committee **agrees** to propose to the General Directorate of Pharmacy the non-financing based on the price proposed by the laboratory, taking into account the lower cost of the therapeutic alternatives available.

B. NEW INDICATIONS

○ HIZENTRA

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
BEHRING, S.A.	HIZENTRA 200 MG/ML	20 vials of 20ml solution for subcutaneous injection	677742	d)
BEHRING, S.A.	HIZENTRA 200 MG/ML	100 vials of 50ml solution for subcutaneous injection	699282	d)
BEHRING, S.A.	HIZENTRA 200 MG/ML	10 vials of 10ml solution for subcutaneous injection	677734	d)
BEHRING, S.A.	HIZENTRA 200 MG/ML	10 vials of 50ml solution for subcutaneous injection	677730	d)

Active substance: J06BA01 - human plasma protein

Authorised therapeutic indications:

Replacement therapy in adults, children and adolescents (0-18 years) in:

- Primary immunodeficiency syndromes with impaired antibody production.

- Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia (CLL), in whom prophylactic antibiotics have failed or are contraindicated.
- Hypogammaglobulinaemia and recurrent infections in multiple myeloma (MM) patients.
- Hypogammaglobulinaemia in patients, pre- and post-allogeneic haematopoietic stem cell transplantation (HSCT).

Immunomodulatory therapy in adults, children and adolescents (0-18 years):

- Hizentra is indicated for the treatment of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy after stabilization with IVIg

Financed therapeutic indications:

Replacement therapy in adults, children and adolescents (0-18 years) in:

- Primary immunodeficiency syndromes with impaired antibody production.
- Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia (CLL), in whom prophylactic antibiotics have failed or are contraindicated.
- Hypogammaglobulinaemia and recurrent infections in multiple myeloma (MM) patients.
- Hypogammaglobulinaemia in patients, pre- and post-allogeneic haematopoietic stem cell transplantation (HSCT).

Therapeutic indications object for this report:

Immunomodulatory therapy in adults, children and adolescents (0-18 years):

- Hizentra is indicated for the treatment of patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy after stabilization with IVIg

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding to this medicinal product, the Committee agrees to propose to the General Directorate of Pharmacy the **non-financing** NHS taking into account criteria for the rationalisation of public spending and budgetary impact on the NHS.

○ TECENTRIQ

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
ROCHE FARMA SA	TECENTRIQ 1200 MG	1 vial concentrate for solution for infusion	719470	c) and d)

Active substance: L01XC32 - Atezolizumab

Authorised therapeutic indications:

Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC):

- after prior platinum-containing chemotherapy, or

- who are considered cisplatin ineligible, and whose tumours have a PD-L1 expression ≥ 5%.

Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic NSCLC after prior chemotherapy. Patients with EGFR mutant or ALK-positive NSCLC should also have received targeted therapies before receiving Tecentriq.

Tecentriq in combination with bevacizumab, paclitaxel and carboplatin, is licensed for the first-line treatment of metastatic non-squamous NSCLC in adult patients. In patients with positive EGFR or ALK mutations, atezolizumab in combination with bevacizumab, paclitaxel, and carboplatin is indicated only after failure of targeted therapies.

Tecentriq in combination with nab-paclitaxel and carboplatin is indicated as the first line for the treatment of adult patients with metastatic non-squamous NSCLC who do not have EGFR or ALK positive mutations.

Tecentriq is also licensed in combination with carboplatin and etoposide for the first-line treatment of adult patients with advanced stage small cell lung cancer.

Tecentriq in combination with nab-paclitaxel is indicated for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumours have PD-L1 expression ≥ 1% and who have not received prior chemotherapy for metastatic disease.

Financed therapeutic indications:

Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic NSCLC after prior chemotherapy. Patients with EGFR mutant or ALK-positive NSCLC should also have received targeted therapies before receiving Tecentriq.

Tecentriq monotherapy funding is restricted for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) who have previously been treated with platinum-containing chemotherapy.

Tecentriq in combination with bevacizumab, paclitaxel and carboplatin, for the first-line treatment of metastatic non-squamous NSCLC in adult patients who meet the following requirements:

- Patients with PD-L1 expression <50%, negative or not possible to perform, in that the current therapy is chemotherapy.
- Patients whose tumours do not have positive EGFR or ALK tumour mutations given the existence of other more cost-effective targeted therapy alternatives.

Non-financed indications:

Tecentriq as monotherapy for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC):

- In those who are not considered suitable for treatment with cisplatin and whose tumors have a PDL1 expression> 5%

Tecentriq in combination with bevacizumab, paclitaxel and carboplatin for the treatment of patients with positive EGFR or ALK mutations after failure of targeted therapies.

Therapeutic indications object for this report:

Tecentriq in combination with carboplatin and etoposide for the first-line treatment of adult patients with advanced stage small cell lung cancer.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding to the new indication for Tecentriq, the Committee **agrees** to propose to the General Directorate of Pharmacy the non-funding of the new indication for Tecentriq in combination with carboplatin and etoposide for the first-line treatment of adult patients with advanced stage small cell lung cancer, taking into account the proposal presented by the company for this indication, the modest clinical benefit demonstrated compared to the comparator in the clinical trial and attending to criteria of rationalisation of public spending and budgetary impact on the NHS.

○ TECENTRIQ

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR THE REVISION
ROCHE FARMA SA	TECENTRIQ 840 MG	1 vial of 14ml concentrate for solution for infusion	726499	c) and d)

Active substance: L01XC32 - Atezolizumab

Authorised therapeutic indications:

Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC):

- after prior platinum-containing chemotherapy, or
- who are considered cisplatin ineligible, and whose tumours have a PD-L1 expression ≥ 5%.

Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic NSCLC after prior chemotherapy. Patients with EGFR mutant or ALK-positive NSCLC should also have received targeted therapies before receiving Tecentriq.

Tecentriq in combination with bevacizumab, paclitaxel and carboplatin, is licensed for the first-line treatment of metastatic non-squamous NSCLC in adult patients. In patients with positive EGFR or ALK mutations, atezolizumab in combination with bevacizumab, paclitaxel, and carboplatin is indicated only after failure of targeted therapies.

Tecentriq in combination with nab-paclitaxel and carboplatin is indicated as the first line for the treatment of adult patients with metastatic non-squamous NSCLC who do not have EGFR or ALK positive mutations.

Tecentriq is also licensed in combination with carboplatin and etoposide for the first-line treatment of adult patients with advanced stage small cell lung cancer.

Tecentriq in combination with nab-paclitaxel is indicated for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumours have PD-L1 expression ≥ 1% and who have not received prior chemotherapy for metastatic disease.

Financed therapeutic indications:

Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic NSCLC after prior chemotherapy. Patients with EGFR mutant or ALK-positive NSCLC should also have received targeted therapies before receiving Tecentriq.

Tecentriq monotherapy funding is restricted for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC) who have previously been treated with platinum-containing chemotherapy.

Tecentriq in combination with bevacizumab, paclitaxel and carboplatin, for the first-line treatment of metastatic non-squamous NSCLC in adult patients who meet the following requirements:

- Patients with PD-L1 expression <50%, negative or not possible to perform, in that the current therapy is chemotherapy.
- Patients whose tumours do not have positive EGFR or ALK tumour mutations given the existence of other more cost-effective targeted therapy alternatives.

Non-financed indications:

Tecentriq as monotherapy for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC):

- In those who are not considered suitable for treatment with cisplatin and whose tumors have a PDL1 expression> 5%

Tecentriq in combination with bevacizumab, paclitaxel and carboplatin for the treatment of patients with positive EGFR or ALK mutations after failure of targeted therapies.

Therapeutic indications object for this report:

Tecentriq in combination with nab-paclitaxel is indicated for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumours have PD-L1 expression ≥ 1% and who have not received prior chemotherapy for metastatic disease.

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding to the new indication for Tecentriq, the Committee **agrees** to propose to the General Directorate of Pharmacy the non-funding of the new indication, taking into account the proposal presented by the company for this indication and the uncertainty in its therapeutic value. In addition, the cost-effectiveness ratio has been considered compared to the comparator in the clinical trial and according to criteria of rationalisation of public spending and budgetary impact on the NHS.

D) ALLEGATIONS

○ MEKINIST

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR REIMBURSEMENT
NOVARTIS FARMACEUTICA S.A.	MEKINIST 0,5 MG	30 film-coated tablets	707728	d)
NOVARTIS FARMACEUTICA S.A.	MEKINIST 2 MG	30 film-coated tablets	707730	d)

Active substance: L01XE25 - Trametinib

Authorised therapeutic indications:

Melanoma

Trametinib as monotherapy or in combination with dabrafenib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

Trametinib monotherapy has not demonstrated clinical activity in patients who have progressed on a prior BRAF inhibitor therapy.

Adjuvant treatment of melanoma

Trametinib in combination with dabrafenib is indicated for the adjuvant treatment of adult patients with Stage III melanoma with a BRAF V600 mutation, following complete resection.

Non-small cell lung cancer (NSCLC)

Trametinib in combination with dabrafenib is indicated for the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600 mutation.

Financed therapeutic indications:

Trametinib as monotherapy or in combination with dabrafenib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

Therapeutic indications object for this report:

Trametinib in combination with dabrafenib is indicated for the adjuvant treatment of adult patients with Stage III melanoma with a BRAF V600 mutation, following complete resection.

Prescription and dispensation conditions: Hospital diagnosis.

Regarding to this medicinal product, the Committee **agrees** not to accept allegations and proposes to the General Directorate not to include this indication in pharmaceutical provision of the NHS, given the existence of drugs or other therapeutic alternatives for the same conditions at a lower price or lower cost of treatment, and according to criteria of rationalisation of public spending and budgetary impact on the NHS.

○ TAFINLAR

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR REIMBURSEMENT
NOVARTIS FARMACEUTICA S.A	TAFINLAR 50 MG CAPSULES	28 hard capsules	701613	d)
NOVARTIS FARMACEUTICA S.A	TAFINLAR 75 MG CAPSULES	28 hard capsules	699781	d)

Active substance: L01XE23 - Dabrafenib

Authorised therapeutic indications:

Dabrafenib as monotherapy or in combination with trametinib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

Dabrafenib in combination with trametinib is indicated for the adjuvant treatment of adult patients with Stage III melanoma with a BRAF V600 mutation, following complete resection.

Dabrafenib in combination with trametinib is indicated for the treatment of adult patients with advanced non-small cell lung cancer with a BRAF V600 mutation.

Financed therapeutic indications:

Dabrafenib as monotherapy or in combination with trametinib is indicated for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

Therapeutic indications object for this report:

Dabrafenib in combination with trametinib is indicated for the adjuvant treatment of adult patients with Stage III melanoma with a BRAF V600 mutation, following complete resection.

Prescription and dispensation conditions: Hospital diagnosis.

Regarding to this medicinal product, the Committee **agrees** not to accept allegations and proposes to the General Directorate not to include this indication in the pharmaceutical provision of the NHS, given the existence of drugs or other therapeutic alternatives for the same conditions at a lower price or lower cost of treatment, and according to criteria of rationalisation of public spending and budgetary impact on the NHS.

○ VYXEOS

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR REIMBURSEMENT
JAZZ PHARMACEUTICALS IBERIA SL	VYXEOS LIPOSOMAL 44 MG/100 MG	1 vial powder for concentrate for solution for infusion	723927	d) and e)

Active substance: L01XY01-Citarabina y Daunorubicina

Authorised therapeutic indications:

Vyxeos liposomal is indicated for the treatment of adults with newly diagnosed, therapy-related acute myeloid leukaemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC).

Prescription and dispensation conditions: Medical prescription. Hospital use.

Regarding to this medicinal product, the Committee **agrees** not to accept the allegations and proposes to the General Directorate the non-financing of this medicine under the terms requested by the company, considering that there are no changes that would modify the meaning of the previous agreement of this Commission.

The existence of other therapeutic alternatives for the same conditions at a lower cost of treatment, the rationalisation criterion of public spending for pharmaceutical services, as well as the budgetary impact on the NHS have been considered. These are some of the legally established criteria for the selective and non-indiscriminate financing of medicines necessary to continue ensuring a sustainable pharmaceutical provision of the NHS, given the continued growth of the pharmaceutical provision needs.

○ RXULTI

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR REIMBURSEMENT
OTSUKA PHARMACEUTICAL, S.A.	RXULTI 1 MG	10 film-coated tablets	724707	d) and e)
OTSUKA PHARMACEUTICAL, S.A.	RXULTI 2 MG	28 film-coated tablets	724739	d) and e)
OTSUKA PHARMACEUTICAL, S.A.	RXULTI 3 MG	28 film-coated tablets	724741	d) and e)
OTSUKA PHARMACEUTICAL, S.A.	RXULTI 4 MG	28 film-coated tablets	724742	d) and e)

Active substance: N05AX16 - Brexpiprazol

Authorised therapeutic indications:

RXULTI is indicated for the treatment of schizophrenia in adult patients.

Prescription and dispensation conditions: Medical prescription.

Regarding to this medicinal product, the Committee **agrees** not to accept allegations and proposes to the General Directorate the non-inclusion of this the medicine in the pharmaceutical provision of the NHS due to the existence of other medicinal products or other therapeutic alternatives for the same conditions, on which it does not provide an incremental clinical benefit, at a lower price or lower cost of treatment.

○ KYSPLYX

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR REIMBURSEMENT
EISAI FARMACEUTICA SA	KISPLYX 10 MG	30 hard capsules	713491	d) and e)
EISAI FARMACEUTICA SA	KISPLYX 4 MG	30 hard capsules	725066	d) and e)

Active substance: L01XE29- lenvatinib mesilato

Authorised therapeutic indications:

Kisplyx is indicated in combination with everolimus for the treatment of adult patients with advanced renal cell carcinoma (RCC) following one prior vascular endothelial growth factor (VEGF)-targeted therapy.

Prescription and dispensation conditions: Medical prescription. Hospital diagnosis.

Regarding to this medicinal product, the Committee **agrees** not to accept allegations and proposes to the General Directorate the non-inclusion of this the medicine in the pharmaceutical provision of the NHS, taking into account the uncertainty of its therapeutic value with respect to other therapeutic alternatives for the same condition and taking into account rationalisation of public spending and budgetary impact on the NHS.

○ HUMALOG

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR REIMBURSEMENT
LILLY, SA	HUMALOG 100U/ML	1 vial of 10ml solution for injection	677252	92.c

Active substance: A10AB04 - Insulina lispro

Authorised therapeutic indications:

For the treatment of adults and children with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis. Humalog is also indicated for the initial stabilisation of diabetes mellitus

Prescription and dispensation conditions: Medical prescription.

Regarding to this medicinal product, the Committee **agrees** not to accept allegations and proposes to the General Directorate the non-exclusion of this medicine from the pharmaceutical provision of the NHS, as it is a necessary medicine for certain groups.

○ EVOPAD

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR REIMBURSEMENT
THERAMEX IRELAND LIMITED	EVOPAD 25MCG/24 H	8 transdermal patches	668087	92.c
THERAMEX IRELAND LIMITED	EVOPAD 75MCG/24 H	8 transdermal patches	668079	92.c
THERAMEX IRELAND LIMITED	EVOPAD 50MCG/24 H	8 transdermal patches	692160	92.c
THERAMEX IRELAND LIMITED	EVOPAD 100MCG/24 H	8 transdermal patches	668061	92.c

Active substance: G03CA03 - Estradiol

Authorised therapeutic indications:

Estrogen replacement therapy to correct estrogen deficiency and associated symptoms due to menopause, natural or surgically induced, such as vasomotor disorders (hot flashes), urogenital disorder (vulvovaginal atrophy and atrophic urethritis).

Prevention of osteoporosis in postmenopausal women at high risk of future fractures, who do not tolerate or in whom other authorized therapeutic alternatives for the prevention of osteoporosis are contraindicated.

In women with an intact uterus, the administration of oestrogens should always be accompanied by the sequential administration of a progestogen.

Prescription and dispensation conditions: Medical prescription.

Regarding to this medicinal product, the Committee **agrees** not to accept allegations and proposes to the General Directorate the non-exclusion of this medicine from the pharmaceutical provision of the NHS, as it is a necessary medicine for certain groups.

○ METOPROLOL KRKA RETARD

MANUFACTURER	TRADENAME	PHARMACEUTICAL FORM	NATIONAL CODE	CRITERIA FOR REIMBURSEMENT
KRKA FARMACEUTICA SL	METOPROLOL KRKARETARD 95mg EFG	30 prolonged-release tablets	711485	92.c

Active substance: C07AB02-Metoprolol

Authorised therapeutic indications:

Adults:

- Hypertension.

- Angina pectoris.
- Cardiac arrhythmias, especially including supraventricular tachycardia, reduction of ventricular rhythm in atrial fibrillation and in ventricular extrasystoles.
- Functional heart problems with palpitations.
- Prevention of cardiac death and reinfarction after the acute phase of myocardial infarction.
- Migraine prophylaxis.
- Stable chronic symptomatic heart failure with impaired left ventricular systolic function.

Children and adolescents 6-18 years of age:

- Treatment of hypertension.

Prescription and dispensation conditions:

With regard to this medicine, the Commission proposes **not to accept** the allegations presented by the laboratory and proposes to the General Directorate the non-exclusion of the financing since it is the only presentation prolonged-release tablets and therefore, it is a necessary medicine for certain groups.