



Ministry of Health and Medical Educations
Islamic Republic of Iran

14-May-2026

Subject: Notification regarding a public posting on the French Health Authority (ANSM) website with the Jan 2026 Permanent Scientific Committee meeting minutes

Dear Sir/Madam:

The purpose of this communication is to alert you of the France Health Authority (ANSM) publication of the minutes of the January 2026 French Permanent Scientific Committee meeting to discuss notable adverse events regarding different medicines. The public posting regarding pembrolizumab can be found under “Questions diverses.”

The public posting occurred on 14-Apr-2026 on the France ANSM website and can be accessed at the following link: [Event - Standing Scientific Committee on Pharmaco-surveillance and proper use - Signal restricted training - ANSM](#)

Company position:

Based on a comprehensive review, as well as ongoing robust pharmacovigilance activities, the medical concept of myocarditis-myositis-myasthenia gravis overlap syndrome was added to the Warnings and Precautions section of the Company Core Data Sheet (CCDS) for pembrolizumab in October 2025. This label update was communicated globally and there are currently ongoing procedures to update local labels to include myocarditis-myositis-myasthenia gravis overlap syndrome.

The Company closely monitors adverse events associated with pembrolizumab through a robust routine pharmacovigilance program that includes regular ongoing internal signal detection activities. Based on ongoing pharmacovigilance activities, there has been insufficient evidence to support a causal relationship between the topics of keratitis or tuberculosis with pembrolizumab administration. Any new information regarding events of keratitis or tuberculosis with pembrolizumab will be assessed through routine pharmacovigilance activities and communicated as appropriate.

Vasculitis is currently included in pembrolizumab product labeling as an adverse drug reaction (ADR). While the concept of acral vasculitis is not presented as a standalone ADR, the event of vasculitis is well described in the product labeling, as well as dose modifications for immune related adverse events. Ongoing pharmacovigilance has not revealed any new safety concerns beyond what is currently labeled for vasculitis. The Company will continue to monitor vasculitis via routine pharmacovigilance activities, and no further action is required at this time.



Kindly note that the labeling reference market for Keytruda IV for Iran is USA.

Please refer to page 8 in the below English translation of the France ANSM posting.

Best Regards

Emad Samir Naguib Electronically signed by:
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Report

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Signal management Person in charge:
Evelyne PIERRON

STANDING SCIENTIFIC COMMITTEE Pharmaco-Surveillance and Proper Use SIGNAL restricted training

Agenda of the sitting of 20/01/2026

No.	Agenda items	For opinion, hearing, information, adoption or discussion
1.	Introduction	
1.1	Update on public declarations of interest and conflict of interest situations	For information
1.2	Adoption of the sitting of 18 November 2025 and 09/12/2025	For adoption
2.	Thematic files	
2.1	Review of Landmark Cases and Medication Errors	For discussion
2.2	Other business	For information

Members and other participants

Names of participants	Full Member	On-site	Present video	Absent/ excused
AUFFRET Marine	Full Member	o	[X]	o
BELLET Florelle	Full Member	o	o	[X]
CHENAF Chouki	Substitute Member	o	[X]	o
DRICI Snowy	Full Member	o	o	[X]
DUBOURDIEU Jean-Louis	Full Member	o	[X]	o
FEDRIZZI Sophie	Substitute Member	o	[X]	o
GRAS-CHAMPEL Valérie	Full Member	o	[X]	o
JANTZEM Hélène	Substitute Member	o	[X]	o
JONVILLE-BERA Annie-Pierre	Full Member	o	o	[X]
LACON François	Full Member	o	[X]	o
LAGARCE Laurence	Full Member	o	o	[X]
LAROCHE Marie-Laure	Substitute Member	o	o	[X]
LEBRUN-VIGNES Bénédicte	Substitute Member	o	o	[X]
LEPELLEY Marion	Substitute Member	o	o	[X]
PINEL Sylvine	Full Member	o	[X]	o
TEINTURIER Nathalie	Full Member	o	[X]	o
THOMAS Laure	Full Member	o	o	[X]
YELEHE-OKOUMA Mélissa	Substitute Member	o	[X]	o

Participants ANSM

LAST NAME First name	Management	Present On-site	Present Visio	Absent/ excused
BENKEBIL Mehdi	Director SURV	0	0	[X]
LAFOREST-BRUNEAUX Agnès	Assistant Director SURV	[X]	0	0
POROKHOV Beatrice	Executive Advisor SURV	0	[X]	0
FAIDI Souad	SURV Project Manager	0	0	[X]
PIERRON Evelyne	Head of division SURV / SIGNAL	[X]	0	0
BACHA Sabrina	Evaluator SURV / SIGNAL	[X]	0	0
BIDAULT Irène	Evaluator SURV / SIGNAL	[X]	0	0
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EMERY-MOREL Frédérique	Project Manager RS SURV / SIGNAL	[X]	0	0
PAGE Annabelle	SURV/ Referent SECURITY	0	[X]	0
MONZON Emilie	Misuse Prevention Referent SURV/ SECURITY	0	0	[X]
TONNAY Véronique	SURV/ Referent SECURITY	0	[X]	0
VITTAZ Emilie	Evaluator SURV / RGA	[X]	0	0
BONAMANT Marine	Internal SURV/ SECURITY	[X]	0	0
ADELAIDE Marie-Camille	SURV Apprentice / SIGNAL	[X]	0	0

MENARD Honorine	SURV Intern / SIGNAL	[X]	<input type="radio"/>	<input type="radio"/>
LAST NAME First name	Management	Present On-site	Present Visio	Absent/ excused
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SAINTE-MARIE Isabelle	Assistant Director DMM1	<input type="radio"/>	<input type="radio"/>	[X]
DELVILLE Marianne	Head of division DMM1 / BioHER	<input type="radio"/>	[X]	<input type="radio"/>
HARE Valerie	Evaluator DMM1 / BioHER	<input type="radio"/>	[X]	<input type="radio"/>
LAST NAME First name	Management	Present On-site	Present Visio	Absent/ excused
VELLA Philippe	Director DMM2	<input type="radio"/>	<input type="radio"/>	[X]
DHANANI Alban	Deputy Director DMM2	<input type="radio"/>	<input type="radio"/>	[X]
DUMARCET Nathalie	Head of division DMM2 / DREAM	<input type="radio"/>	[X]	<input type="radio"/>
HUEBER Stephanie	Evaluator DMM2 / DREAM	<input type="radio"/>	[X]	<input type="radio"/>

Introduction

Update on IPRs and conflict of interest situations

The moderator, after checking that members have no new links to declare and that the IPRs are up to date, specifies that no conflict of interest situation has been identified or reported with regard to the agenda files.

The adoption of the minutes of the CSP of 18 November and 9 December 2025 will be done by email.

IMUREL (azathioprine)

Myelosuppression

Number/Type	12225/SRI
Laboratory(s)	H.A.C. PHARMA - CAEN
Product management concerned	DMM 2-POLE 3-GASTRO
Expert(s)	Mrs. Valérie GRAS-CHAMPEL Mrs. Marie-Laure LAROCHE

Presentation of the application

This case reports pancytopenia due to myelosuppression on Azathioprine in a patient in his thirties, who had been treated for 3 months for uveitis. A mutation in the TPMT gene was discovered during the patient's hospitalization. No search for a TPMT deficiency was carried out before the initiation of treatment, contrary to the information present in the SmPC of the Imurel specialty on the dosage adjustments to be expected in patients with a partial genetic deficiency in TPMT, or even the preferential use of another treatment in the event of a complete deficiency.

The SmPC of the Imurel specialty mentions the risk of myelosuppression linked to a mutation in the TPMT gene and thus informs healthcare professionals of the interest of screening for TPMT, which remains at the discretion of the prescriber. Systematic screening seems difficult to envisage, in particular because of the time taken to obtain results, which would not allow optimal patient care.

Monitoring should be performed weekly with a Complete Blood Count (CBC), which is the most important criterion for patient follow-up and early detection of a haematological disorder.

An expert gastroenterologist, hepatologist and pharmacoepidemiologist was consulted and confirmed that the time it took to obtain the results of the screening in the city was not compatible with the time needed to start treatment. In addition, it is well established that the assay or genotyping of TPMT does not prevent all neutropenia.

The proposal for the pharmacist to monitor the performance of an CBC was not retained because the pharmacist cannot check the CBC every week during the first 8 weeks of treatment as planned.

Conclusions of the CSP

Continue to focus on monitoring the risk of myelosuppression with azathioprine by performing regular CBC scans without waiting for the result of screening. The opinion was adopted unanimously.

CARIBAN 10 mg/10 mg, modified-release capsule (doxylamine succinate/pyridoxine hydrochloride)

Newborn apnea - Neonatal oxygen desaturation - Extrasystoles - Maternal exposure throughout pregnancy

Number/Type	12489/SRI
Laboratory(s)	EFFIK
Product management concerned	GROSS
Expert(s)	Mrs. Sylvine PINEL Mrs. Bénédicte LEBRUN-VIGNES

Presentation of the application

This landmark case reports the occurrence of apnea with desaturation from the second day of life and several extrasystoles on ECG recording on the fifth day of life (D5) in a full-term newborn (40 weeks + 2 days). No etiology other than drug has been identified.

The mother, due to persistent nausea, had received Cariban (doxylamine, pyridoxine hydrochloride) at a dose of 4 tablets per day (i.e. 40 mg/day of doxylamine) during the first four months of pregnancy, and then 1 tablet per day until delivery.

Doxylamine, a first-generation antihistamine, has anticholinergic and sedative activity. A precaution for use related to this effect is mentioned in section 4.6 of the SmPC for Cariban: " Due to the anticholinergic and sedative properties of doxylamine succinate (see section 5.1), if the mother is treated until delivery, precautions should be taken with the newborn". This information is harmonized with that of other doxylamine products, such as Donormyl.

A request has been made to specify, in the SmPC, the clinical signs expected in newborns in the event of in utero exposure to this medicinal product corresponding to these sedative and atropinic properties. It was recalled that the modification of the SmPC can be complex with regard to European procedures and that there is no major data that could justify it at this stage. The next PSUSA is scheduled for 2033.

An update of the web page entitled: "Treatment of nausea during pregnancy" on the ANSM website is planned, with a new presentation and the integration of information on Cariban, which was not on the market at the time when it was first published

Conclusions of the CSP

Update the ANSM web page dedicated to the "Treatment of nausea during pregnancy" with information on the Cariban specialty and thus specify the risks at birth related to the sedative and anticholinergic properties of doxylamine used at the end of pregnancy.

The opinion was adopted unanimously.

Other business

Several prominent cases involving pembrolizumab have been reported recently. Their evaluation was initially planned in the framework of a PSUSA whose periodicity has been revised, leading to a postponement of it to 2028. As a result, a meeting was organised at the beginning of January with the rapporteur of the survey in order to adjust the timetable for the submission of the report, initially set for January, to 5 March 2026, thus making it possible to integrate these new significant cases received after the date of data freeze.

These significant cases concern the following adverse effects:

- 3M Syndrome (Myasthenia gravis, Myocarditis, Myositis), for which a variation has been filed by the laboratory for inclusion in the SmPC.
- A prominent case of corneal ulcer, for which it was specified that the risk of keratitis/keratoconjunctivitis was a potential signal already identified as part of the investigation. These ocular disorders will be discussed in the next report, including the recent landmark case.
- In addition, the risk of tuberculosis, which is an already known signal, linked to the immunosuppressive nature of pembrolizumab was again addressed but from another aspect because the last CM received raised the question of the occurrence of tuberculosis on pembrolizumab in a patient previously treated for his bladder cancer by BCG therapy. A focus is therefore planned on this risk in the next report.
- Finally, a prominent case of acral vasculitis with digital necrosis also attracted our attention because of its severity. This type of involvement with "cutaneous necrosis" in the context of cutaneous vasculitis is listed in the SmPC as a footnote to severe skin reactions. However, the special case of necrosis of the extremities and/or vasoconstriction of the small vessels are not present in the SmPC. A focus is therefore planned on this risk in the next report.

Abbreviations

ANSM:	National Agency for the Safety of Medicines and Products health
ASMR:	Improvement of the medical service provided, evaluated by the High Court Health Authority
NPVP:	National pharmacovigilance database
B/R:	Benefit-risk ratio of a drug (efficacy ratio versus drug safety)
CM:	Notable case
CMDh:	Coordination Group for Mutual Recognition and Decentralised Procedures – Human (at the EMA).
NOC:	National Council of the Order of Pharmacists
CRPV:	Regional Pharmacovigilance Centre
DMI:	Request to change information relating to Pharmacological and clinical data of the MA
DP:	ANSM Product Directorate
EI:	Adverse reaction
EM:	Medication error
EMA:	European medicines agency
EMM:	Significant medication error
EVDAS:	Automated signal detection in the EudraVigilance database (EVDAS)
FDA:	Food and Drug Administration
GIS EPI-PHAR:	Scientific Interest Group Public Expertise in Epidemiology of health products
HAS	Haute Autorité de Santé
HLGT:	High Level Group Term level of MedDRA
HLT:	High Level Term level of MedDRA
MEdDRA :	Medical Dictionary for Regulatory Activities or dictionary regulatory affairs.
WHO:	World Health Organization
NFS:	Blood Count
PE:	Precautions for use

PRAC:	Pharmacovigilance risk assessment committee (at the EMA)
PSUR:	Periodic safety update report
PSUSA:	Periodic safety update report single assessment
PV:	Pharmacovigilance
PT:	Preferred term of MedDRA
SmPC:	Summary of product characteristics
QMS:	Standardized MedDRA Queries
SMR:	Medical service rendered, evaluated by the French National Authority for Health
SOC:	System Organ Class
SRF:	Low risk signal
SRM:	Medium Risk Signal
SRI:	Important risk signal








Notification regarding a public posting on the ANSM website Pembrolizumab_NSS_449

Final Audit Report

2026-05-14

Created:	2026-05-14
By:	Seba Elbarkouky (seba.elbarkouky@msd.com)
Status:	Signed
Transaction ID:	CBJCHBCAABAAzOvr939Sb5pwW3VY__RRMqC6KMf8uaye

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2026-05-14 - 12:20:43 PM GMT- IP address: 147.161.132.189
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2026-05-14 - 12:21:31 PM GMT
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2026-05-14 - 12:27:26 PM GMT
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Signing reason: Approved
Signature Date: 2026-05-14 - 12:27:28 PM GMT - Time Source: server- IP address: 165.225.240.160 - Signature Appearance Selected: TYPE
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2026-05-14 - 12:27:28 PM GMT