

Référentiel Observatoire dédié au Cancer B PL

Rituximab Mabthéra®

Création le 22 novembre 2005

Modifications le 6 avril 2006, le 11 mai 2006, le 12 octobre 2006.

Déclinaison des PTT Afssaps en avril 2008

Déclinaison du référentiel **hématologique INCa** en décembre 2008, avril 2010, juillet 2011, mars 2012 réglementaire

Déclinaison du référentiel **Tumeurs cérébrales malignes de l'adulte INCa** en décembre 2011, mars 2012 réglementaire

Extension AMM en novembre 2010

Reévaluation du PTT « Prolifération EBV post-greffe » en cours à l'INCa-(info INCa du 28 octobre 2011).

Références biblio décembre 2011, avril 2012

Réunion inter régionale Obs Cancer B PL 11 1 2012

Avant traitement, vous pouvez consulter les essais en cours sur COTREC <http://www.cotrec.org/>

Présentations : mabthéra® 100 mg et 500 mg, solutions à diluer pour perfusion en flacons de 10 et 50 mL respectivement

Prix unitaires HT fixés par le CEPS (JO 28/05/2009) : 263.670 € et 1318.350 €

AMM

➤ Lymphome non hodgkinien (LNH)

- En association à une chimiothérapie pour le traitement des patients présentant un **lymphome folliculaire** de stade III-IV n'ayant jamais été précédemment traités
- Mabthéra® en traitement d'entretien est indiqué chez les patients présentant un lymphome folliculaire répondant à un traitement d'induction (Salles [Lancet](#) 11)
- En monothérapie pour le traitement des patients atteints de lymphomes folliculaires de stade III-IV en cas de chimiorésistance ou à partir de la deuxième rechute après chimiothérapie.
- En association à une chimiothérapie CHOP (Cyclophosphamide, Doxorubicine, Vincristine, Prednisone) pour le traitement des patients présentant un **lymphome non-hodgkinien** agressif diffus à grandes cellules B, CD20+.

Posologie à 375 mg/m² hebdomadaire ou toutes les 3 semaines avec des ajustements thérapeutiques.

- Mabthéra®, en association à une chimiothérapie, est indiqué pour le traitement des patients atteints de **LLC** (leucémie lymphoïde chronique), non précédemment traités et en rechute ou réfractaire (AMM 2009). Les données disponibles sur l'efficacité et la tolérance sont limitées chez les patients précédemment traités par des anticorps monoclonaux dont Mabthéra®, ou chez les patients réfractaires à un traitement antérieur par MabThera en association à une chimiothérapie.

Posologie J0 cycle 1 : 375 mg/m² J1 cycles 2 à 6 : 500 mg/m²

Situations temporairement acceptables PTT (hématologique, Afssaps)

- **Prolifération EBV post-greffe (cellules souches et organes solides)** (Choquet, Blood 06 ; Milpied, Ann Oncol 00) **Pour autant cette situation ne figure pas dans les insuffisances de données mais est en cours de réévaluation par l'INCa** (Info INCa du 28 octobre 2011).
- **Lymphome non hodgkinien diffus à grandes cellules B CD20+ en 2ème ligne en association à une chimiothérapie de type R-ICE ou R-DHAP** (Gisselbrecht ASCO 09 A8509, Vellenga Blood 08)

- **Traitement de dernière ligne de l'anémie hémolytique auto-immune (AHAI) cortico-résistante et en rechute après splénectomie** (Narat S. Haematologica. 2005. Shanafelt TD Mayo Clin Proc. 2003. Zecca M Blood. 2003. Gupta N Leukemia. 2002. Quartier P Lancet. 2001. Berentsen S Schollkopf C Leuk Lymphoma. 2006)
- **Maladie du greffon contre l'hôte (GVHD) chronique en échec d'une bithérapie immunosuppressive bien menée** (Zaja F Bone Marrow Transplant 2007. Cutler C. Blood 2006. Ratanatharathorn V Blood Marrow Transplant. 2003. Canninga-van Djik M. Blood 2004. Bornhaeuser M Blood 2004)
- **Purpura thrombopénique idiopathique sévère PTAI (plaquettes < 30 000/ mm3) en cas de : contre-indication ou échec ou rechute aux corticoïdes et/ ou aux immunoglobulines IV et contre-indication ou échec à la splénectomie** (Braendstrup P. Am J Hematol. 2005. Cooper N Br J Haematol. 2004. Wang J J Pediatr. 2005. Zaja F Haematologica. 2003. Giagounidis AA Haematol. 2002. Stasi R. Blood. 2001. Saleh MN. Semin Oncol. 2000. Vesely SK. Ann Intern Med. 2004. Bennett CM. Blood. 2006. Garcia-Chavez J Ann Hematol. 2007. Arnold DM. Ann Intern Med. 2007).

Situations Non Acceptables SNA (hématologique)

- **Sans objet**

Situations médicales HORS GROUPE

JF¹ Justifications Forums biblio

La plupart des situations médicales sont fondées sur la liste d'indications validées par la COMEDIMS et la collégiale des hématologues de l'AP-HP.

- **LNH agressif DGC B, CD20+** en association avec une chimiothérapie autre que CHOP (A.Borgerding Ann Hematol 2009, A.Martin Haematologica 2008, Haematologica 2009, Rohit Sud Haematologica 2008, Min Kyoung Transfusion V 47, 2007 Rekha Hartind Lymphoma & Myéloma 2007, Tarella Leukemia 07, Vellega Blood 2008, Gisselbrecht Blood 07, El Gnaoui Ann Oncol 07, Witzig Leuk Lymphoma 08, Fenske Blood 07, Khouri JCO 05, Tarella JCO 08)
- **Maladies autoimmunes :**
 - Cryoglobulinémies (Basse Transplant Proc 06, Quartuccio Rheumatology 06, Sansonno Blood 03, Zaja Haematologica 99 Blood 03)
 - Cytopénies (Zaja 03)
 - Anémie Hémolytique Auto-immune (AHAI) (Bader Meunier Haematologica 07, Breentsen Haematologica 07, Cabrera ASH 04, D'Arena Am J Hematol 06, D'Arena Eur J Haematol 07, Gupta Eur J Haematol 07, Motto Isr Med Assoc 02, Narat Haematologica 05, Provan Haematologica 07, Quartier Lancet 01, Trape Haematologica 03, Zecca Blood 03) VOIR PTT AFSSAPS
 - Maladie des agglutinines froides (Berentsen et al Blood 04, Schollkopf et al Leuk Lymphoma 06)
- **Lymphomes type Burkitt B** (lymphome agressif CD20+) : en 1^{ère} ligne en association à une chimiothérapie (De vries Br J Haematologica 04, Dunleavy JCO 07, Gong Am J Surg Pathol 03, Thomas Cancer 06, Yokohama Ann Hematol 04, Cohen et al Haematologica 02)
- **Proliférations EBV hors-grefe** en 1^{ère} ligne en monothérapie ou en association avec une chimiothérapie (Thomas Cancer 06, Garnier 02 Consensus d'experts EBPG 02)

➤ **LNH du manteau**

Représentent 5 à 10% des LNH

- ***En rechute en association autre que FMC ou en monothérapie***

Nouvelles publications soumises aux Institutions depuis la version de juillet 2011

Baiocchi Cancer 2011
 Dreyling Leuk lymph 2011
 Robert Cancer 2011
 Friedberg Blood 2011
 Ansell Lancet Oncol 2011
 Dreyling Leuk Lymph 2010

¹ JF : Justifications Forum biblio : remplace l'ancienne appellation SMA Situation Médicale Acceptée

Ruan Cancer 2010
Zaja Blood 2010
Habermann Br J Haematol 2009
Viernik J Clin Oncol 2008
[Orciuolo E Br J Haematol](#), 2009
A.Borgerding Ann Haematol 2009
Kaufmann Blood 04
Rodriguez. Leuk Lymphoma 07
Robinson JCO 08

- **En rechute en entretien**

Forstpointner R.Blood. 2006

- **En 1ère ligne en association avec une chimiothérapie**

Pour le lymphome du manteau en 1^e ligne, le futur protocole européen proposera rituximab CHOP versus rituximab DHAP CHOP puis entretien par rituximab dans les 2 bras. Le rituximab est considéré comme thérapie de référence.

Nouvelles publications soumises aux Institutions depuis la version de juillet 2011

Houot Ann Oncol 2011
Griffiths Blood 2011
Dreyling Leuk Lymph 2011
Spurgeon Luek Lymph 2011
Kluin Nelemans Haematologica 2011
Dreyling Leuk Lymph 2010
Gressin Haematologica 2010
Romaguera Br J Haematology 2010
Lossos Leuk Lymph 2010
Thomas S. Lin, JCO 2009
Dreyling Hematology Am Soc Hematol Educ Program 2009
Martin JCO 2009
Ghielmini Blood 2009
Lloyd E JCO 2009
HE. EVE Leuk and Lym 2009
Wang Cancer 08
Herold ASH 04
Kahl An Oncol 06
Dreger Haematologica 07
Foran 2000
Forstpointner 04

Rappel : Lenz JCO 05 PHASE III

- **En 1ère ligne en entretien chez le sujet agé (>65 ans) après R-CHOP**

Kluin-Nelemans Haematologica 2011,
Vaishalee Leuk Lymph 2011

➤ **Lymphomes de Hodgkin CD20+ de type Poppema en 1^{ère} ligne ou en rechute, en monothérapie**

Représente moins de 5% des Lymphomes de Hodgkin (maladie rare)

Nouvelles publications soumises aux Institutions depuis la version de juillet 2011 :

Eichenauer DA Blood 2011
Jackson C Annals of Oncology, 2010
Galán L Clin Transl Oncol 2010
Maeda LS Current Opinion in Oncology 2009
Nogová L Current Hematologic Malignancy Reports 2006

➤ **Maladie de Waldenström**

Représente 2% des hémopathies (maladie rare)

Dans les essais cliniques, le rituximab est considéré comme bras de référence.

Nouvelles publications soumises aux Institutions depuis la version de juillet 2011 :

- **En 1^{ère} ligne en association**

Tedeschi Cancer 2012
Treon Br J Haematology 2011
Laszlo Clin Lymph
Myel Leuk 2011
Laszlo JCO 2010
Dimopoulos Clin Lymph Myel 2009
Treon Clin Cancer res 2009

- **En entretien**

Treon SP. British Journal of Haematology, 2011

➤ **Lymphome folliculaire en 1^e ligne en monothérapie dans les tumeurs de faible masse**

Représente 22% des Lymphomes Non Hodgkinien (LNH)

Nouvelles publications soumises aux Institutions depuis la version de juillet 2011 :

Kahl BS et al : 53rd ASH Annual Meeting and Exposition. 2011 : Abstract LBA-6.

Solal-Céligny P. Anti cancer drugs 2001

Ardeshtna KM et al . 52rd ASH Annual Meeting and Exposition. 2010 : oral communication.

➤ **Lymphome de la zone marginale B** (type MALT) tumeur CD20+: monothérapie ou en association en 1^{ère} ligne ou en rechute

Représentent 8% des LNH

Nouvelles publications soumises aux Institutions

Tsimberidou Cancer 06

Bennett Haematologica 05

Economopoulos Leuk Lymphoma 08

Martinelli JCO 05

Martinelli JCO 03

Raderer Oncology 03

Etude de phase III GLSG en cours

SMJ Situations Médicales à Justifier

Situations avec insuffisance de données INCa (hématologique, tumeur cérébrale)

➤ **Lymphome folliculaire en 1^e ligne et en monothérapie** (Hainsworth Blood 00; Colombat Blood 01; Ghielmini Ann Oncol 00)

➤ **Maladie de Waldenström en association en rechute** (Agathocleous A Br J Haematol 10, Ghobrial JCO 10, Treon Blood 09, Dimopoulos JCO 07)

➤ **Maladie de Waldenström en monothérapie en 1^e ligne ou en rechute** (Dimopoulos JCO 02, Gertz Leuk Lymphoma 04)

Les situations suivantes sont considérées comme « en insuffisance de données » dans les référentiels nationaux d'après l'analyse des données cliniques disponibles à la date du 03 février 2011. Aussi la communauté des hématologues des régions Bretagne et Pays de la Loire a proposé de nouvelles références bibliographiques aux Institutions en avril 2012. En attendant l'actualisation de ce référentiel, les situations suivantes peuvent être considérées comme des JF biblio.

➤ **Lymphome à cellules du manteau en rechute et en monothérapie**

Voir nouvelles publications soumises aux Institutions en avril 2012 dans JF biblio

➤ **Lymphome à cellules du manteau en 1^{ère} ligne en association avec une chimiothérapie de type hyper CVAD ou CHOP**

Voir Nouvelles publications soumises aux Institutions en avril 2012 dans JF biblio

➤ **Lymphome à cellules du manteau en 1^{ère} ligne**

Voir Nouvelles publications soumises aux Institutions en avril 2012 dans JF biblio

➤ **Maladie de Hodgkin CD20⁺ de type Poppema (LPHD) en monothérapie**

Voir Nouvelles publications soumises aux Institutions en avril 2012 dans JF biblio

➤ **Lymphome non hodgkinien de type MALT**

Voir Nouvelles publications soumises aux Institutions en avril 2012 dans JF biblio

➤ **Lymphome de la zone marginale en association**

*Voir Nouvelles publications soumises aux Institutions en avril 2012 dans JF biblio
Assimilé au lymphome non hodgkinien de type MALT*

- **Maladie de Waldenström en 1^{ère} ligne en association**
Voir Nouvelles publications soumises aux Institutions en avril 2012 dans JF biblio

- **Prévention d'un syndrome lymphoprolifératif lié à la prolifération d'EBV après transplantation d'organe solide ou de cellules souches hématopoïétiques chez l'adulte** (Blaes 10, Ahmad 09, Gruhn 03, Van Esser 02)

- **Lymphomes cérébraux primitifs en rechute, rituximab en association à une chimiothérapie.**
- **Chimiothérapie d'induction par rituximab, en association à une chimiothérapie dans les lymphomes cérébraux primitifs nouvellement diagnostiqués, avant radiothérapie** (Shah JCO 07, Enting Neurology. 04, Wong Cancer 04)

Autres situations

- **Les prescriptions en 3^{ème} et 4^{ème} rechute**
Progression sous rituximab ou rechutes \geq 3 mois après rituximab
- **Localisations et situations non citées dans AMM ou hors AMM décrites précédemment.**

Références bibliographiques

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Dreyling Blood 05

Dunleavy JCO 07

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Fenske Blood 07

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Gisselbrecht Blood 07

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