INESSS
LE SAVOIR PREND FORME

MAI 2022

ÉTAT DES CONNAISSANCES

Pertinence de l'exigence d'un essai préalable avec un immunosuppresseur dans les indications de paiement des médicaments biologiques – gastroentérologie et dermatologie

Annexes complémentaires

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Direction de l'évaluation des médicaments et des technologies à des fins de remboursement

Québec

Le présent document contient les annexes complémentaires à l'état des connaissances *Pertinence de l'exigence d'un essai préalable avec un immunosuppresseur dans les indications de paiement des médicaments biologiques.*

Le contenu de cette publication a été rédigé et édité par l'INESSS.

Ces annexes et le rapport final sont accessibles en ligne dans la section *Publications* de notre site *Web*.

Renseignements
Institut national d'excellence en santé et en services sociaux (INESSS)

2535, boulevard Laurier, 5e étage
Québec (Québec) G1V 4M3
Téléphone : 418 643-1339
Télécopieur : 418 646-8349

2021, avenue Union, bureau 1200
Montréal (Québec) H3A 2S9
Téléphone : 514 873-2563
Télécopieur : 514 873-1369

inesss@inesss.qc.ca
www.inesss.qc.ca

Responsabilité

L'Institut rend accessibles les principales informations qui ont servi à la préparation du rapport *Pertinence de l'exigence d'un essai préalable avec un immunosuppresseur dans les indications de paiement des médicaments biologiques* aux lecteurs qui désirent plus de détails sur sa démarche scientifique.

Ce document n'a pas fait l'objet d'une révision linguistique. Il ne reflète pas forcément les opinions des autres personnes consultées aux fins du présent dossier.

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Stratégies de repérage de l'information scientifique

Bases de données bibliographiques

MEDLINE (Ovid) **Date du repérage : 28 octobre 2021** **Limites : 2000- (ligne 27 : 2016-) ; anglais, français**	
1	exp *Inflammatory Bowel Diseases/dt
2	(colitis gravis OR crohn disease OR crohns disease OR crohn's disease OR crohn's enteritis OR enteritis regionalis OR granulomatous colitis OR granulomatous enteritis OR ibd OR idiopathic proctocolitis OR ileocolitis OR inflammatory bowel disease* OR morbus crohn OR regional enteritis OR regional enterocolitis OR regional ileitis OR terminal ileitis OR ulcerative colitis).ti,ab
3	1 OR 2
4	*Psoriasis/dt
5	(psorias* OR psoriatic epidermis OR psoriatic skin).ti,ab
6	4 OR 5
7	3 OR 6
8	exp *Biological Products/
9	(anti-tnf* OR (tnf* ADJ3 (antagonist* OR block* OR inhibitor*)) OR (anti ADJ (il-17 OR interleukin-17 OR il-17a OR interleukin-17a OR il-12 OR interleukin-12 OR il-23 OR interleukin-23)) OR (anti ADJ (itga4 AND itgb7)) OR ((il-17 OR interleukin-17 OR il-17a OR interleukin-17a OR il-12 OR interleukin-12 OR il-23 OR interleukin-23 OR itga4 OR itgb7 OR cd20) ADJ3 (antagonist* OR block* OR inhibitor*))).ti,ab
10	(biologic agent* OR biologic drug* OR biologic medicine* OR biologic pharmaceutic* OR biologic product* OR biologic therap* OR biologic treatment* OR biological drug* OR biological medicine* OR biological product* OR biological therap* OR biological treatment* OR biologicals OR biologics OR biomedicament* OR biomedicine* OR bio-medicine* OR biopharmaceutic* OR bio-pharmaceutic* OR biosimilar* OR bio-similar* OR biotherap* OR bio-therap* OR originator* OR reference biologic* OR reference product*).ti,ab
11	(adalimumab OR amjevita OR avsola OR brenzys OR brodalumab OR certolizumab OR cimzia OR cosentyx OR cyltezo OR enbrel OR entyvio OR erelzi OR etanercept OR guselkumab OR hadlima OR hulio OR humira OR hyrimoz OR idacio OR inflectra OR infliximab OR ixekizumab OR monoclonal antibod* OR remicade OR renflexis OR risankizumab OR secukinumab OR siliq OR skyrizi OR stelara OR taltz OR tremfya OR ustekinumab OR vedolizumab).ti,ab
12	8 OR 9 OR 10 OR 11
13	*Immunosuppressive Agents/
14	(((immune OR immuno) ADJ (depressant* OR modula* OR suppressant* OR suppressive* OR suppressor* OR therap*)) OR immunodepressant* OR immunomodula* OR immunosuppressant* OR immunosuppressive* OR immunosuppressor* OR immunotherap*).ti,ab
15	13 OR 14
16	((conventional OR systemic) ADJ2 (agent* OR systemic OR therap* OR treat*)).ti,ab
17	(acitretin* OR amethopterin OR azathioprine OR calcineurin antagonist* OR calcineurin blocker* OR calcineurin inhibitor* OR ciclosporin* OR cyclosporin* OR etretin OR immuran OR imuran OR imurel OR isoacitretin OR isoetretin OR leupurin OR mercaptopurine OR methotrexate OR mexate OR mtx OR neoral OR neotigason OR purimethol OR purinethol OR puri-nethol OR sandimmun* OR soriatane OR thiopurine).ti,ab
18	15 OR 16 OR 17
19	((early ADJ3 (therap* OR treat*)) OR top down OR "treat to target").ti,ab
20	(algorithm* ADJ3 (therap* OR treat*)).ti,ab
21	first line.ti,ab
22	(7 AND 12 AND 18) OR (7 AND 12 AND 19) OR (7 AND 20) OR (7 AND (12 OR 18) AND 21)
23	exp Algorithms/ OR exp Clinical Protocols/ OR exp Consensus/ OR exp Consensus Development Conference/ OR exp Consensus Development Conferences as Topic/ OR exp Critical Pathways/ OR exp Guideline/ OR exp Guidelines as Topic/ OR Health Planning Guidelines/ OR Clinical Conference.pt OR

	(guideline* OR guide line* OR CPG OR CPGs OR guidance OR practical guide* OR (best ADJ3 practice*) OR (evidence ADJ2 (base* OR report* OR synthes* OR research OR practice* OR best)) OR consensus OR algorithm* OR (clinical ADJ2 (path OR paths OR pathway* OR protocol*)) OR ((critical OR clinical) ADJ2 (path OR paths OR pathway*)) OR recommendation* OR committee opinion* OR policy statement* OR position statement* OR practice parameter* OR practice pathway* OR practice protocol* OR ((standard OR standards) ADJ2 (care* OR practice*)) OR (gold ADJ2 standard*) OR rapid response*).ti,ab,kw
24	Meta-Analysis.pt OR exp Meta-Analysis as Topic/ OR Systematic Review/ OR exp Technology Assessment, Biomedical/ OR (meta-analy* OR metaanaly* OR met analy* OR metanaly* OR meta-review* OR metareview* OR meta regression* OR metaregression* OR meta synthesis OR metasynthesis OR overview of review* OR overviews of reviews OR (systematic* ADJ3 (review* OR overview* OR literature OR search* OR research*)) OR ((quantitative OR methodologic* OR integrativ*) ADJ (review* OR overview* OR synthes*)) OR umbrella review* OR hta or htas OR technology assessment* OR technology overview* OR technology appraisal* OR technology reassessment*).ti,ab,kw OR (review.mp AND ((medline OR pubmed) AND (cochrane OR embase)).ti,ab,kw)
25	23 OR 24
26	22 AND 25
27	limit 26 to yr="2016 - 2021"
28	Cohort Studies/ OR Double-Blind Method/ OR Observational Study/ OR exp Randomized Controlled Trial/ OR (cohort OR comparison group* OR comparison stud* OR control group* OR (doubl* ADJ (blind* OR mask*)) OR followup stud* OR follow-up stud* OR longitudinal OR observational OR prospective OR random* OR rct OR rcts OR "rct's" OR retrospective).ti,ab
29	(practical clinical trial* OR pragmatic clinical trial* OR pragmatic randomized controlled trial* OR pragmatic trial* OR real-world clinical trial* OR real-world context OR real-world data OR real-world efficacy OR real-world evidence OR real-world stud* OR real-world treatment* OR real-world trial*).ti,ab
30	28 OR 29
31	22 AND 30
32	limit 31 to yr="2000 - 2021"
33	27 OR 32
34	Case Reports/ OR Comment/ OR Editorial/ OR Letter/ OR (case report* OR case stud* OR case series OR comment* OR editorial* OR letter* OR reply OR replies).ti
35	33 NOT 34
36	Animals/ NOT (Humans/ AND Animals/)
37	35 NOT 36

Embase (Ovid) **Date du repérage : 28 octobre 2021** **Limites : 2000- (ligne 27 : 2016-) ; anglais, français**	
1	exp *Inflammatory Bowel Disease/dt
2	(colitis gravis OR crohn disease OR crohns disease OR crohn's disease OR crohn's enteritis OR enteritis regionalis OR granulomatous colitis OR granulomatous enteritis OR ibd OR idiopathic proctocolitis OR ileocolitis OR inflammatory bowel disease* OR morbus crohn OR regional enteritis OR regional enterocolitis OR regional ileitis OR terminal ileitis OR ulcerative colitis).ti,ab
3	1 OR 2
4	*Psoriasis/dt
5	(psorias* OR psoriatic epidermis OR psoriatic skin).ti,ab
6	4 OR 5
7	3 OR 6
8	exp *Biological Product/
9	(anti-tnf* OR (tnf* ADJ3 (antagonist* OR block* OR inhibitor*)) OR (anti ADJ (il-17 OR interleukin-17 OR il-17a OR interleukin-17a OR il-12 OR interleukin-12 OR il-23 OR interleukin-23)) OR (anti ADJ (itga4 AND itgb7)) OR ((il-17 OR interleukin-17 OR il-17a OR interleukin-17a OR il-12 OR interleukin-12 OR il-23 OR interleukin-23 OR itga4 OR itgb7 OR cd20) ADJ3 (antagonist* OR block* OR inhibitor*))).ti,ab

10	(biologic agent* OR biologic drug* OR biologic medicine* OR biologic pharmaceutic* OR biologic product* OR biologic therap* OR biologic treatment* OR biological drug* OR biological medicine* OR biological product* OR biological therap* OR biological treatment* OR biologicals OR biologics OR biomedicament* OR biomedicine* OR bio-medicine* OR biopharmaceutic* OR bio-pharmaceutic* OR biosimilar* OR bio-similar* OR biotherap* OR bio-therap* OR originator* OR reference biologic* OR reference product*).ti,ab
11	(adalimumab OR amjevita OR avsola OR brenzys OR brodalumab OR certolizumab OR cimzia OR cosentyx OR cyltezo OR enbrel OR entyvio OR erelzi OR etanercept OR guselkumab OR hadlima OR hulio OR humira OR hyrimoz OR idacio OR inflectra OR infliximab OR ixekizumab OR monoclonal antibod* OR remicade OR renflexis OR risankizumab OR secukinumab OR siliq OR skyrizi OR stelara OR taltz OR tremfya OR ustekinumab OR vedolizumab).ti,ab
12	8 OR 9 OR 10 OR 11
13	*Immunosuppressive Agent/
14	(((immune OR immuno) ADJ (depressant* OR modula* OR suppressant* OR suppressive* OR suppressor* OR therap*)) OR immunodepressant* OR immunomodula* OR immunosuppressant* OR immunosuppressive* OR immunosuppressor* OR immunotherap*).ti,ab
15	13 OR 14
16	((conventional OR systemic) ADJ2 (agent* OR systemic OR therap* OR treat*)).ti,ab
17	(acitretin* OR amethopterin OR azathioprine OR calcineurin antagonist* OR calcineurin blocker* OR calcineurin inhibitor* OR ciclosporin* OR cyclosporin* OR etretin OR immuran OR imuran OR imurel OR isoacitretin OR isoetretin OR leupurin OR mercaptopurine OR methotrexate OR mexate OR mtx OR neoral OR neotigason OR purimethol OR purinethol OR puri-nethol OR sandimmun* OR soriatane OR thiopurine).ti,ab
18	15 OR 16 OR 17
19	((early ADJ3 (therap* OR treat*)) OR top down OR "treat to target").ti,ab
20	(algorithm* ADJ3 (therap* OR treat*)).ti,ab
21	first line.ti,ab
22	(7 AND 12 AND 18) OR (7 AND 12 AND 19) OR (7 AND 20) OR (7 AND (12 OR 18) AND 21)
23	*Algorithm/ OR *Clinical Pathway/ OR *Clinical Protocol/ OR *Consensus/ OR *Consensus Development/ OR *Health Care Planning/ OR exp *Practice Guideline/ OR (algorithm* OR best evidence OR (best ADJ3 practice*) OR clinical path OR clinical paths OR (clinical ADJ3 pathway*) OR clinical protocol* OR committee opinion* OR CPG OR CPGs OR consensus OR (critical ADJ3 pathway*) OR gold standard* OR guidance* OR guideline* OR guide line* OR policy statement* OR position statement* OR practical guide* OR practice parameter* OR practice pathway* OR practice protocol* OR practice standard* OR recommendation* OR standard care* OR standard of care OR standards of care).ti,ab,kw
24	*Biomedical Technology Assessment/ OR *Meta Analysis/ OR *"Meta Analysis (topic)"/ OR *Systematic Review/ OR *"Systematic Review (topic)"/ OR (hta or htas OR evidence base* OR evidence report* OR evidence synthesis OR evidence syntheses OR meta-analy* OR metaanaly* OR met analy* OR metanaly* OR meta regression* OR metaregression* OR meta review* OR metareview* OR meta synthesis OR metasynthesis OR overview of review* OR (systematic* ADJ3 (review* OR overview* OR search* OR research*)) OR research evidence* OR technology appraisal* OR technology assessment* OR technology overview* OR technology reassessment* OR umbrella review*).ti,ab,kw. OR (review.tw. AND ((medline OR pubmed) AND (cochrane OR embase)).ti,ab,kw)
25	23 OR 24
26	22 AND 25
27	limit 26 to yr="2016 - 2021"
28	*Cohort Analysis/ OR *Double Blind Procedure/ OR *Observational Study/ OR exp *Randomized Controlled Trial/ OR (cohort OR comparison group* OR comparison stud* OR control group* OR (doubl* ADJ (blind* OR mask*)) OR followup stud* OR follow-up stud* OR longitudinal OR observational OR prospective OR random* OR rct OR rcts OR "rct's" OR retrospective).ti,ab
29	(practical clinical trial* OR pragmatic clinical trial* OR pragmatic randomized controlled trial* OR pragmatic trial* OR real-world clinical trial* OR real-world context OR real-world data OR real-world efficacy OR real-world evidence OR real-world stud* OR real-world treatment* OR real-world trial*).ti,ab
30	28 OR 29
31	22 AND 30
32	limit 31 to yr="2000 - 2021"
33	27 OR 32

34	Case Report/ OR Editorial/ OR Letter/ OR (case report* OR case stud* OR case series OR comment* OR editorial* OR letter* OR reply OR replies).ti
35	33 NOT 34
36	Nonhuman/ NOT (Human/ AND Nonhuman/)
37	35 NOT 36
38	Conference Abstract.pt
39	37 NOT 38

EBM Reviews (Ovid) : Cochrane Database of Systematic Reviews; Health Technology Assessment; NHS Economic Evaluation Database **Date du repérage : 28 octobre 2021** **Limites : 2016- (2000- NHS Economic Evaluation Database) ; anglais, français**	
1	(colitis gravis OR crohn disease OR crohns disease OR crohn's disease OR crohn's enteritis OR enteritis regionalis OR granulomatous colitis OR granulomatous enteritis OR ibd OR idiopathic proctocolitis OR ileocolitis OR inflammatory bowel disease* OR morbus crohn OR regional enteritis OR regional enterocolitis OR regional ileitis OR terminal ileitis OR ulcerative colitis).ti,ab
2	(psorias* OR psoriatic epidermis OR psoriatic skin).ti,ab
3	1 OR 2
4	(anti-tnf* OR (tnf* ADJ3 (antagonist* OR block* OR inhibitor*)) OR (anti ADJ (il-17 OR interleukin-17 OR il-17a OR interleukin-17a OR il-12 OR interleukin-12 OR il-23 OR interleukin-23)) OR (anti ADJ (itga4 AND itgb7)) OR ((il-17 OR interleukin-17 OR il-17a OR interleukin-17a OR il-12 OR interleukin-12 OR il-23 OR interleukin-23 OR itga4 OR itgb7 OR cd20) ADJ3 (antagonist* OR block* OR inhibitor*))).ti,ab
5	(biologic agent* OR biologic drug* OR biologic medicine* OR biologic pharmaceutic* OR biologic product* OR biologic therap* OR biologic treatment* OR biological drug* OR biological medicine* OR biological product* OR biological therap* OR biological treatment* OR biologicals OR biologics OR biomedicament* OR biomedicine* OR bio-medicine* OR biopharmaceutic* OR bio-pharmaceutic* OR biosimilar* OR bio-similar* OR biotherap* OR bio-therap* OR originator* OR reference biologic* OR reference product*).ti,ab
6	(adalimumab OR amjevita OR avsola OR brenzys OR brodalumab OR certolizumab OR cimzia OR cosentyx OR cyltezo OR enbrel OR entyvio OR erelzi OR etanercept OR guselkumab OR hadlima OR hulio OR humira OR hyrimoz OR idacio OR inflectra OR infliximab OR ixekizumab OR monoclonal antibod* OR remicade OR renflexis OR risankizumab OR secukinumab OR siliq OR skyrizi OR stelara OR taltz OR tremfya OR ustekinumab OR vedolizumab).ti,ab
7	4 OR 5 OR 6
8	(((immune OR immuno) ADJ (depressant* OR modula* OR suppressant* OR suppressive* OR suppressor* OR therap*)) OR immunodepressant* OR immunomodula* OR immunosuppressant* OR immunosuppressive* OR immunosuppressor* OR immunotherap*).ti,ab
9	((conventional OR systemic) ADJ2 (agent* OR systemic OR therap* OR treat*)).ti,ab
10	(acitretin* OR amethopterin OR azathioprine OR calcineurin antagonist* OR calcineurin blocker* OR calcineurin inhibitor* OR ciclosporin* OR cyclosporin* OR etretin OR immuran OR imuran OR imurel OR isoacitretin OR isoetretin OR leupurin OR mercaptopurine OR methotrexate OR mexate OR mtx OR neoral OR neotigason OR purimethol OR purinethol OR puri-nethol OR sandimmun* OR soriatane OR thiopurine).ti,ab
11	8 OR 9 OR 10
12	((early ADJ3 (therap* OR treat*)) OR top down OR "treat to target").ti,ab
13	(algorithm* ADJ3 (therap* OR treat*)).ti,ab
14	first line.ti,ab
15	(3 AND 7 AND 11) OR (3 AND 7 AND 12) OR (3 AND 13) OR (3 AND (7 OR 11) AND 14)

Sites Web, registres d'essais cliniques et autres sources

Recherche effectuée en juin 2021 avec les mots clés « guideline » ou « biologic agent », en utilisant le moteur de recherche Google et en visitant les sites suivants :

Agency for Healthcare Research and Quality (AHRQ) https://www.ahrq.gov/research/findings/evidence-based-reports/search.html

Agence canadienne des médicaments et des technologies de la santé/Canadian Agency for Drugs and Technologies in Health (ACMTS/CADTH) https://www.cadth.ca/fr

Australian Clinical Practice Guidelines (NHMRC) https://www.clinicalguidelines.gov.au/

BCGuidelines.ca http://www.bcguidelines.ca/

Centre fédéral d'expertise des soins de santé (KCE) https://kce.fgov.be/fr

ECRI Guidelines Trust https://guidelines.ecri.org/

Guidelines International Network (G-I-N) https://g-i-n.net/

Haute Autorité de Santé (HAS) https://www.has-sante.fr/jcms/c_6056/fr/recherche-avancee

Health Quality Ontario (HQO) https://hqontario.ca/Evidence-to-Improve-Care/Quality-Standards

Infobanque AMC (Association médicale canadienne – Canadian Medical Association) https://www.cma.ca/fr

Institute for Clinical Evaluative Sciences https://www.ices.on.ca/

Institute of Health Economics (IHE) https://www.ihe.ca/

International Network of Agencies for Health Technology Assessment (INAHTA) https://www.inahta.org/

NHS National Institute for Health and Care Excellence (NICE) https://www.nice.org.uk/guidance

Scottish Intercollegiate Guidelines Network (SIGN) https://www.guidelinesinpractice.co.uk/home

Campbell Collaboration Library of Systematic Reviews https://www.campbellcollaboration.org/

Accelerating Change Transformation Team (ACTT) - Toward Optimized Practice (TOP) https://actt.albertadoctors.org/pages/default.aspx

World Health Organization (WHO) https://www.who.int/

Santé Canada https://www.canada.ca/fr/sante-canada/services/medicaments-produits-sante/medicaments/base-donnees-produits-pharmaceutiques.html

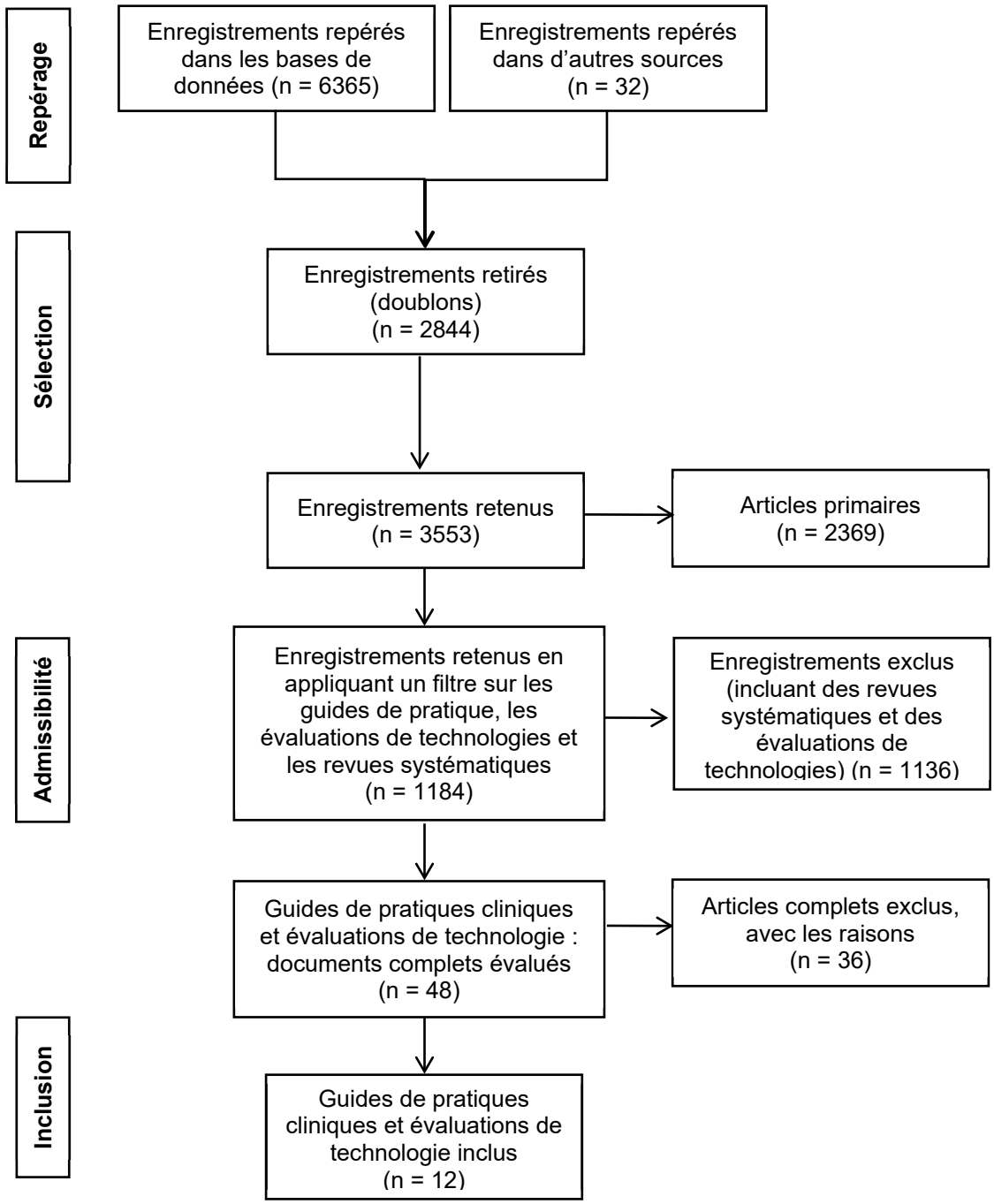
Sites Web des agences ou organismes liées au remboursement des médicaments dans les provinces canadiennes

Provinces	Agence ou organisme	Site
Alberta	Alberta Health Care Insurance (AHCI)	https://www.ab.bluecross.ca/dbl/idbl_main1.html
Colombie-Britannique	British Columbia PharmaCare Special Authority	https://pharmacareformularysearch.gov.bc.ca/
Île-du-Prince-Édouard	Health Prince Edward Island	https://www.princeedwardisland.ca/en/information/health-pei/pei-pharmacare-formulary
Manitoba	Manitoba Pharmacare Program	https://web22.gov.mb.ca/eFormulary/
Ontario	Ontario Ministry of Health and Long-Term Care	http://www.health.gov.on.ca/en/pro/programs/drugs/odbf_eformulary.aspx
Québec	Régie de l'assurance maladie du Québec	http://www.ramq.gouv.qc.ca/fr/citoyens/assurance-medicaments/Pages/medicaments-couverts.aspx
Nouveau-Brunswick	New Brunswick Health	http://www2.gnb.ca/content/gnb/en/departments/health/MedicarePrescriptionDrugPlan/NBDrugPlan/ForHealthCareProfessionals/NewBrunswickDrugPlansFormulary.html
Nouvelle-Écosse	Nova Scotia Pharmacare	https://novascotia.ca/dhw/pharmacare/formulary.asp
Saskatchewan	Saskatchewan Drug Plan	http://formulary.drugplan.ehealthsask.ca/SearchFormulary
Terre-Neuve et Labrador	Newfoundland Labrador Health and Community Services	http://www.health.gov.nl.ca/health/prescription/newformulary.asp

ANNEXE B

Sélection des documents

Figure B-1 Diagramme de flux



ANNEXE C

Liste des documents retenus

Tableau C-1 Liste des documents contenant des recommandations qui ont été retenus par champ thérapeutique et population visés par les travaux

Titres et références (par ordre alphabétique du nom du 1er auteur)	Type de document	Identification
Maladie de Crohn chez l'adulte		
Feuerstein JD, Ho EY, Shmidt E, Singh H, Falck-Ytter Y, Sultan S, Terdiman JP. AGA clinical practice guidelines on the medical management of moderate to severe luminal and perianal fistulizing Crohn's disease. Gastroenterology 2021;160(7):2496-508. [Feuerstein *et al.*, 2021]	Guide de pratique clinique	AGA 2021
Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut 2019;68(Suppl 3):s1-s106. [Lamb *et al.*, 2019]	Guide de pratique clinique	BSG 2019
National Institute for Health and Care Excellence (NICE). Crohn's disease: Management. NICE guideline [NG129]. Londres, Angleterre : NICE; 2019b. [NICE, 2019b]	Guide de pratique clinique	NICE 2019 NG129
Panaccione R, Steinhart AH, Bressler B, Khanna R, Marshall JK, Targownik L, et al. Canadian Association of Gastroenterology clinical practice guideline for the management of luminal Crohn's disease. J Can Assoc Gastroenterol 2019;2(3):e1-e34. [Panaccione *et al.*, 2019]	Guide de pratique clinique	CAG 2019
Torres J, Bonovas S, Doherty G, Kucharzik T, Gisbert JP, Raine T, et al. ECCO guidelines on therapeutics in Crohn's disease: Medical treatment. J Crohns Colitis 2020;14(1):4-22. [Torres *et al.*, 2020]	Guide de pratique clinique	ECCO 2020
Maladie de Crohn pédiatrique		
Mack DR, Benchimol EI, Critch J, deBruyn J, Tse F, Moayyedi P, et al. Canadian Association of Gastroenterology clinical practice guideline for the medical management of pediatric luminal Crohn's disease. Gastroenterology 2019;157(2):320-48. [Mack *et al.*, 2019]	Guide de pratique clinique	CAG 2019
National Institute for Health and Care Excellence (NICE). Crohn's disease: Management. NICE guideline [NG129]. Londres, Angleterre : NICE; 2019b. [NICE, 2019b]	Guide de pratique clinique	NICE 2019 NG129
Colite ulcéreuse chez l'adulte		
Feuerstein JD, Isaacs KL, Schneider Y, Siddique SM, Falck-Ytter Y, Singh S. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. Gastroenterology 2020;158(5):1450-61. [Feuerstein *et al.*, 2020]	Guide de pratique clinique	AGA 2020
Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut 2019;68(Suppl 3):s1-s106. [Lamb *et al.*, 2019]	Guide de pratique clinique	BSG 2019
National Institute for Health and Care Excellence (NICE). Ulcerative colitis: Management. NICE guideline [NG130]. Londres, Angleterre : NICE; 2019a. [NICE, 2019a]	Guide de pratique clinique	NICE 2019 NG130

Titres et références (par ordre alphabétique du nom du 1er auteur)	Type de document	Identification
Psoriasis en plaques chez l'adulte		
Nast A, Smith C, Spuls PI, Avila Valle G, Bata-Csorgo Z, Boonen H, et al. EuroGuiDerm Guideline on the systemic treatment of Psoriasis vulgaris – Part 1: Treatment and monitoring recommendations. J Eur Acad Dermatol Venereol 2020;34(11):2461-98. Nast A, Smith C, Spuls PI, Avila Valle G, Bata-Csorgo Z, Boonen H, et al. EuroGuiDerm Guideline on the systemic treatment of Psoriasis vulgaris – Part 2: Specific clinical and comorbid situations. J Eur Acad Dermatol Venereol 2021;35(2):281-317. [Nast *et al.*, 2021; Nast *et al.*, 2020]	Guide de pratique clinique	EuroGuiDerm 2020/2021
National Institute for Health and Care Excellence (NICE). Psoriasis: Assessment and management. Clinical guideline [CG153]. Londres, Angleterre : NICE; 2017. [NICE, 2017]	Guide de pratique clinique	NICE 2017 CG153
Smith CH, Yiu ZZ, Bale T, Burden AD, Coates LC, Edwards W, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: A rapid update. Br J Dermatol 2020;183(4):628-37. [Smith *et al.*, 2020]	Guide de pratique clinique	BAD 2020

ANNEXE D

Liste des documents exclus et raison de l'exclusion

Tableau D-1 Documents contenant des recommandations qui ont été exclus et raisons de l'exclusion

Titres et références (par ordre alphabétique du nom du 1er auteur)	Raison de l'exclusion
Gastroentérologie (maladie de Crohn chez l'adulte et chez l'enfant et colite ulcéreuse)	
Abdulrazeg *et al.*, 2019	Méthodologie employée jugée inadéquate pour les travaux
Amiot *et al.*, 2021	Méthodologie employée jugée inadéquate pour les travaux
Bermejo *et al.*, 2018	Méthodologie employée jugée inadéquate pour les travaux
Biancone *et al.*, 2017	Méthodologie employée jugée inadéquate pour les travaux
Choi *et al.*, 2017	Méthodologie employée jugée inadéquate pour les travaux
Feld *et al.*, 2019	Recommandations sur la prise en charge post-chirurgicale
Feuerstein *et al.*, 2017	Version plus récente accessible
Gionchetti *et al.*, 2017	Méthodologie employée jugée inadéquate pour les travaux
Glick *et al.*, 2020	Recommandations sur la colite légère à modérée
Gomollon *et al.*, 2017	Version plus récente accessible
Harbord *et al.*, 2017; Magro *et al.*, 2017	Méthodologie employée jugée inadéquate pour les travaux
Ko *et al.*, 2019	Recommandations sur la colite légère à modérée
Kucharzik *et al.*, 2020	Absence de recommandations
Lichtenstein *et al.*, 2018	Méthodologie employée jugée inadéquate pour les travaux
Martins *et al.*, 2019	Méthodologie employée jugée inadéquate pour les travaux
Ooi *et al.*, 2019	Méthodologie employée jugée inadéquate pour les travaux
Park *et al.*, 2017	Méthodologie employée jugée inadéquate pour les travaux
Peyrin-Biroulet *et al.*, 2016	Méthodologie employée jugée inadéquate pour les travaux
Sicilia *et al.*, 2020	Langue autre que français ou anglais
Van Rheenen *et al.*, 2021	Méthodologie employée jugée inadéquate pour les travaux
Dermatologie (psoriasis en plaques chez l'adulte)	
Amatore *et al.*, 2019	Méthodologie employée jugée inadéquate pour les travaux
Amin *et al.*, 2018	Méthodologie employée jugée inadéquate pour les travaux
Anonymous, 2017	Langue autre que français ou anglais
Canadian Psoriasis Guidelines Addendum Committee, 2016	Absence de recommandations sur la séquence de traitement
Dauden *et al.*, 2016	Méthodologie employée jugée inadéquate pour les travaux
Eisert *et al.*, 2019a; Eisert *et al.*, 2019b	Population pédiatrique
Elmets *et al.*, 2019	Absence de recommandations sur la séquence de traitement
Fortina *et al.*, 2017	Population pédiatrique

Titres et références (par ordre alphabétique du nom du 1er auteur)	Raison de l'exclusion
Gisondi *et al.*, 2017	Absence de recommandations sur la séquence de traitement
Kogan *et al.*, 2019	Méthodologie employée jugée inadéquate pour les travaux
Lambert *et al.*, 2020	Populations particulières exclues des travaux
Menter *et al.*, 2019	Absence de recommandations sur la séquence de traitement
Reich *et al.*, 2018	Méthodologie employée jugée inadéquate pour les travaux
Romiti *et al.*, 2021	Méthodologie employée jugée inadéquate pour les travaux

ANNEXE E

Évaluation de la qualité méthodologique des documents retenus

Tableau E-1a Évaluation des guides de pratique clinique – Grille AGREE II détaillée

Guides	AGA 2021 (MC)	ECCO 2020 (MC)	BSG 2019 (MICI)	CAG 2019 (MC)	NICE 2019 NG129 (MC)	CAG 2019 (MC pédiatrique)
Domaines de la grille AGREE II						
Domaine 1. Champ et objectifs						
1. Le ou les objectifs de la RPC sont décrits explicitement.	6	6	7	7	7	7
2. La ou les questions de santé couvertes par la RPC sont décrites explicitement.	7	6	4	2	6	5
3. La population à laquelle la RPC doit s'appliquer est décrite explicitement.	6	5	6	5	7	6
Domaine 2. Participation des groupes concernés						
4. Le groupe de travail ayant élaboré la RPC inclut des représentants de tous les groupes professionnels concernés.	7	6	7	7	6	7
5. Les opinions et les préférences de la population cible ont été identifiées.	5	1	6	4	4	3
6. Les utilisateurs cibles de la RPC sont clairement définis.	4	5	6	7	7	6
Domaine 3. Rigueur d'élaboration de la RPC						
7. Des méthodes systématiques ont été utilisées pour rechercher les preuves scientifiques.	3	7	7	7	7	7
8. Les critères de sélection des preuves sont clairement décrits.	1	7	6	5	7	7
9. Les forces et les limites des preuves scientifiques sont clairement définies.	7	5	7	6	6	7
10. Les méthodes utilisées pour formuler les recommandations sont clairement décrites.	2	7	7	7	3	7
11. Les bénéfices, les effets secondaires et les risques en termes de santé ont été pris en considération dans la formulation des recommandations.	6	7	6	7	6	7
12. Il y a un lien explicite entre les recommandations et les preuves scientifiques sur lesquelles elles reposent.	7	7	5	7	6	7
13. La RPC a été revue par des experts externes avant sa publication.	3	4	2	3	7	4
14. Une procédure d'actualisation de la RPC est décrite.	6	3	7	1	3	1

Guides	AGA 2021 (MC)	ECCO 2020 (MC)	BSG 2019 (MICI)	CAG 2019 (MC)	NICE 2019 NG129 (MC)	CAG 2019 (MC pédiatrique)
Domaine 4. Clarté et présentation						
15. Les recommandations sont précises et sans ambiguïté.	6	6	7	7	6	7
16. Les différentes options de prise en charge de l'état ou du problème de santé sont clairement présentées.	6	6	6	7	5	6
17. Les recommandations clés sont facilement identifiables.	7	7	7	7	7	7
Domaine 5. Applicabilité						
18. La RPC décrit les éléments facilitant son application et les obstacles.	2	4	1	3	4	1
19. La RPC offre des conseils et/ou des outils sur les façons de mettre les recommandations en pratique.	2	7	1	1	6	3
20. Les répercussions potentielles sur les ressources de l'application des recommandations ont été examinées.	3	1	3	3	7	1
21. La RPC propose des critères de suivi et de vérification.	1	1	1	1	5	1
Domaine 6. Indépendance éditoriale						
22. Le point de vue des organismes de financement n'a pas influencé le contenu de la RPC.	7	4	6	6	4	7
23. Les intérêts divergents des membres du groupe ayant élaboré la RPC ont été pris en charge et documentés.	6	4	7	5	7	6
Qualité générale du guide (1 à 7)	5	5	6	5	6	6
Recommandation de l'utilisation du guide	Oui	Oui	Oui	Oui	Oui	Oui

MICI : maladies inflammatoires chroniques de l'intestin; MC : maladie de Crohn.

Tableau E-1b Évaluation des guides de pratique clinique – Grille AGREE II détaillée

Guides	AGA 2020 (CU)	NICE 2019 NG130 (CU)	BAD 2020 (psoriasis)	EuroGuiDerm 2020/2021 (psoriasis)	NICE 2017 CG153 (psoriasis)
Domaines de la grille AGREE II					
Domaine 1. Champ et objectifs					
1. Le ou les objectifs de la RPC sont décrits explicitement.	7	7	6	7	7
2. La ou les questions de santé couvertes par la RPC sont décrites explicitement.	7	7	7	7	7
3. La population à laquelle la RPC doit s'appliquer est décrite explicitement.	7	7	7	6	7
Domaine 2. Participation des groupes concernés					
4. Le groupe de travail ayant élaboré la RPC inclut des représentants de tous les groupes professionnels concernés.	5	7	7	7	6
5. Les opinions et les préférences de la population cible ont été identifiées.	6	4	4	4	3
6. Les utilisateurs cibles de la RPC sont clairement définis.	5	7	5	7	6
Domaine 3. Rigueur d'élaboration de la RPC					
7. Des méthodes systématiques ont été utilisées pour rechercher les preuves scientifiques.	7	7	7	7	7
8. Les critères de sélection des preuves sont clairement décrits.	7	7	7	7	6
9. Les forces et les limites des preuves scientifiques sont clairement définies.	6	6	6	6	6
10. Les méthodes utilisées pour formuler les recommandations sont clairement décrites.	3	3	6	7	3
11. Les bénéfices, les effets secondaires et les risques en termes de santé ont été pris en considération dans la formulation des recommandations.	6	6	7	7	6
12. Il y a un lien explicite entre les recommandations et les preuves scientifiques sur lesquelles elles reposent.	7	7	6	5	6
13. La RPC a été revue par des experts externes avant sa publication.	4	7	4	6	7
14. Une procédure d'actualisation de la RPC est décrite.	6	3	6	7	3

Guides	AGA 2020 (CU)	NICE 2019 NG130 (CU)	BAD 2020 (psoriasis)	EuroGuiDerm 2020/2021 (psoriasis)	NICE 2017 CG153 (psoriasis)
Domaine 4. Clarté et présentation					
15. Les recommandations sont précises et sans ambiguïté.	6	6	7	7	6
16. Les différentes options de prise en charge de l'état ou du problème de santé sont clairement présentées.	6	7	7	7	7
17. Les recommandations clés sont facilement identifiables.	7	7	6	7	7
Domaine 5. Applicabilité					
18. La RPC décrit les éléments facilitant son application et les obstacles.	1	4	1	4	4
19. La RPC offre des conseils et/ou des outils sur les façons de mettre les recommandations en pratique.	1	6	7	7	6
20. Les répercussions potentielles sur les ressources de l'application des recommandations ont été examinées.	2	7	4	3	7
21. La RPC propose des critères de suivi et de vérification.	1	5	5	7	5
Domaine 6. Indépendance éditoriale					
22. Le point de vue des organismes de financement n'a pas influencé le contenu de la RPC.	7	4	7	7	4
23. Les intérêts divergents des membres du groupe ayant élaboré la RPC ont été pris en charge et documentés.	6	7	7	7	7
Qualité générale du guide (1 à 7)	6	6	6	7	6
Recommandation de l'utilisation du guide	Oui	Oui	Oui	Oui	Oui

CU : colite ulcéreuse.

ANNEXE F

Tableaux exhaustifs des résultats

Tableau F-1a Indications reconnue par Santé Canada et indications de paiement au Québec des médicaments biologiques utilisés pour le traitement de la maladie de Crohn chez l'adulte

Biologique	Indication reconnue par Santé Canada (monographie)	Indication de paiement (RAMQ)
Adalimumab [Amgen Canada, 2021; Corporation AbbVie, 2021; Pfizer Canada, 2021; Sandoz Canada, 2021a; BGP Pharma, 2020; Fresenius Kabi Canada, 2020; Merck Canada, 2020a]	• Indiqué pour atténuer les signes et les symptômes et induire et maintenir une rémission clinique chez les adultes atteints de la maladie de Crohn modérément à fortement évolutive qui n'ont pas répondu de façon satisfaisante à un traitement classique, y compris un traitement par des corticostéroïdes et (ou) des immunosuppresseurs. L'adalimumab est également indiqué pour atténuer les signes et les symptômes et induire une rémission clinique chez ces patients s'ils ne répondent plus ou sont intolérants au traitement par l'infliximab.	♦ pour le traitement des adultes atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes. L'essai d'un immunosuppresseur doit avoir été d'au moins 8 semaines. ♦ pour le traitement des adultes atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes, lorsque les immunosuppresseurs sont contre-indiqués, non tolérés ou qu'ils ont été inefficaces dans le passé lors d'un épisode similaire après un traitement combiné avec des corticostéroïdes.
Infliximab [Janssen Inc., 2021a; Amgen Canada, 2020; Merck Canada, 2020b; Pfizer Canada, 2020]	• Indiqué pour la réduction des signes et des symptômes, l'induction et le maintien de la rémission clinique et de la cicatrisation de la muqueuse, et la réduction du recours à un traitement par corticostéroïdes chez les adultes atteints de maladie de Crohn modérément à sévèrement active qui ont présenté une réponse insuffisante à un traitement par corticostéroïdes et/ou aminosalicylés. L'infliximab peut être administré seul ou en association avec un traitement standard; • Indiqué pour le traitement de la maladie de Crohn avec fistulisation, chez les adultes qui n'ont pas répondu à un traitement standard complet et approprié;	♦ pour le traitement des adultes atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes. L'essai d'un immunosuppresseur doit avoir été d'au moins 8 semaines. ♦ pour le traitement des adultes atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes, lorsque les immunosuppresseurs sont contre-indiqués, non tolérés ou qu'ils ont été inefficaces dans le passé lors d'un épisode similaire après un traitement combiné avec des corticostéroïdes.

Biologique	Indication reconnue par Santé Canada (monographie)	Indication de paiement (RAMQ)
Vedolizumab [Takeda Canada, 2020]	• Indiqué pour le traitement des patients adultes atteints de maladie de Crohn active modérée à grave qui ont présenté une réponse inadéquate, une perte de réponse ou une intolérance aux immunomodulateurs ou à un inhibiteur du facteur de nécrose tumorale alpha (TNFα); ou qui ont présenté une réponse inadéquate, une intolérance ou une dépendance aux corticostéroïdes.	♦ pour le traitement des adultes atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes. L'essai d'un immunosuppresseur doit avoir été d'au moins 8 semaines. ♦ pour le traitement des adultes atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes, lorsque les immunosuppresseurs sont contre-indiqués, non tolérés ou qu'ils ont été inefficaces dans le passé lors d'un épisode similaire après un traitement combiné avec des corticostéroïdes.
Ustekinumab [Janssen Inc., 2021b]	• Indiqué dans le traitement de la maladie de Crohn modérément à sévèrement active chez les patients adultes qui ont présenté une réponse insatisfaisante, une perte de réponse ou une intolérance aux immunomodulateurs ou à au moins un inhibiteur du facteur de nécrose tumorale alpha (TNFα), ou qui ont présenté une réponse insatisfaisante, une intolérance ou une dépendance aux corticostéroïdes.	Non inscrit (décision du ministre à venir) Recommandation d'inscription émise par l'INESSS [2017]:

Tableau F-1b Indications reconnue par Santé Canada et indications de paiement au Québec des médicaments biologiques utilisés pour le traitement de la maladie de Crohn chez l'enfant

Biologique	Indication reconnue par Santé Canada (monographie)	Indication de paiement (RAMQ)
Adalimumab [Amgen Canada, 2021; Corporation AbbVie, 2021; Pfizer Canada, 2021; Sandoz Canada, 2021a; BGP Pharma, 2020; Fresenius Kabi Canada, 2020; Merck Canada, 2020a]	• Indiqué pour atténuer les signes et les symptômes et induire et maintenir une rémission clinique chez les enfants âgés de 13 à 17 ans pesant 40 kg ou plus atteints de la maladie de Crohn fortement évolutive et (ou) qui n'ont pas répondu de façon satisfaisante ou qui présentent une intolérance à un traitement classique (traitement par des corticostéroïdes et [ou] des aminosalicylates et [ou] des immunosuppresseurs) et (ou) à un inhibiteur du facteur de nécrose tumorale (TNF) alpha.	Non inscrit
Infliximab [Janssen Inc., 2021a; Amgen Canada, 2020; Merck Canada, 2020b; Pfizer Canada, 2020]	• Indiqué pour la réduction des signes et des symptômes, ainsi que pour l'induction et le maintien de la rémission clinique chez les patients pédiatriques atteints de maladie de Crohn modérément à sévèrement active qui ont présenté une réponse insuffisante à un traitement standard (c.-à-d. corticostéroïdes et/ou aminosalicylés et/ou immunosuppresseurs). L'innocuité et l'efficacité de l'infliximab n'ont pas été établies chez les patients de moins de 9 ans;	♦ pour le traitement des enfants atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes. L'essai d'un immunosuppresseur doit avoir été d'au moins 8 semaines. ♦ pour le traitement des enfants atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes, lorsque les immunosuppresseurs sont contre-indiqués, non tolérés ou qu'ils ont été inefficaces dans le passé lors d'un épisode similaire après un traitement combiné avec des corticostéroïdes.

Tableau F-1c Indications reconnue par Santé Canada et indications de paiement au Québec des médicaments biologiques utilisés pour le traitement de la maladie de colite ulcéreuse chez l'adulte

Biologique	Indication reconnue par Santé Canada (monographie)	Indication de paiement (RAMQ)
Adalimumab [Amgen Canada, 2021; Corporation AbbVie, 2021; Pfizer Canada, 2021; Sandoz Canada, 2021a; BGP Pharma, 2020; Fresenius Kabi Canada, 2020; Merck Canada, 2020a]	• Indiqué pour traiter la colite ulcéreuse modérément à fortement évolutive chez les adultes qui n'ont pas répondu de façon satisfaisante ou qui présentent une intolérance à un traitement classique, y compris un traitement par des corticostéroïdes et (ou) l'azathioprine ou la 6- mercaptopurine (6-MP). L'efficacité de l'adalimumab chez les patients qui ne répondaient plus ou étaient intolérants au traitement par des inhibiteurs du facteur de nécrose tumorale (TNF) n'a pas été établie.	♦ pour le traitement des adultes atteints de colite ulcéreuse modérée à grave toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs à moins d'intolérance sérieuse ou de contreindication.
Infliximab [Janssen Inc., 2021a; Amgen Canada, 2020; Merck Canada, 2020b; Pfizer Canada, 2020]	• Indiqué pour la réduction des signes et des symptômes, l'induction et le maintien de la rémission clinique et de la cicatrisation de la muqueuse, et la réduction ou l'abandon du recours à un traitement par corticostéroïdes chez les adultes atteints de colite ulcéreuse modérément à sévèrement active qui ont présenté une réponse insuffisante à un traitement standard (c.-à-d. aminosalicylés et/ou corticostéroïdes et/ou immunosuppresseurs).	♦ pour le traitement des adultes atteints de colite ulcéreuse modérée à grave toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs à moins d'intolérance sérieuse ou de contreindication.
Vedolizumab [Takeda Canada, 2020]	• Indiqué pour le traitement des patients adultes atteints de colite ulcéreuse active modérée à grave qui ont présenté une réponse inadéquate, une perte de réponse ou une intolérance au traitement standard ou à l'infliximab (un inhibiteur du facteur de nécrose tumorale alpha [TNFα]).	♦ pour le traitement des adultes atteints de colite ulcéreuse modérée à grave toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs à moins d'intolérance sérieuse ou de contreindication.
Ustekinumab [Janssen Inc., 2021b]	• Indiqué dans le traitement de la colite ulcéreuse modérément à sévèrement active chez les patients adultes qui ont présenté une réponse insatisfaisante, une perte de réponse ou une intolérance au traitement classique ou à un traitement par un médicament biologique ou qui ont présenté des contre-indications médicales à de tels traitements.	Non inscrit (décision du ministre à venir) Recommandation d'inscription émise par l'INESSS [2020a].

Tableau F-1d Indications reconnue par Santé Canada et indications de paiement au Québec des médicaments biologiques utilisés pour le traitement du psoriasis en plaques chez l'adulte

Biologique	Indication reconnue par Santé Canada (monographie)	Indication de paiement (RAMQ)
Adalimumab [Amgen Canada, 2021; Corporation AbbVie, 2021; Pfizer Canada, 2021; Sandoz Canada, 2021a; BGP Pharma, 2020; Fresenius Kabi Canada, 2020; Merck Canada, 2020a]	• Indiqué pour traiter le psoriasis en plaques chronique modéré à grave chez les adultes qui sont candidats à un traitement à action générale. Chez les patients atteints de psoriasis en plaques chronique modéré, l'adalimumab ne devrait être administré que lorsque la photothérapie s'est révélée inefficace ou inappropriée.	Indication de paiement commune pour tous les agents biologiques : ♦ pour le traitement des personnes atteintes d'une forme grave de psoriasis en plaques chronique : • lorsqu'un traitement de photothérapie de 30 séances ou plus pendant 3 mois n'a pas permis un contrôle optimal de la maladie, à moins que ce traitement soit contre-indiqué, ne soit pas toléré, ne soit pas accessible ou qu'un traitement de 12 séances ou plus pendant 1 mois n'ait pas procuré d'amélioration significative des lésions; et • lorsqu'un traitement avec 2 agents de rémission, utilisés en concomitance ou non, pendant au moins 3 mois chacun n'a pas permis un contrôle optimal de la maladie. À moins d'intolérance ou de contreindication sérieuses, ces 2 agents doivent être : - le méthotrexate à la dose de 15 mg ou plus par semaine; ou - la cyclosporine à la dose de 3 mg/kg ou plus par jour; ou - l'acitrétine à la dose de 25 mg ou plus par jour.
Étanercept [Samsung Bioepis, 2022; Immunex Corporation, 2021; Sandoz Canada, 2021b]	• Indiqué pour traiter les adultes atteints d'une forme chronique, modérée ou grave, de psoriasis en plaques dont le cas relève d'un traitement général ou de la photothérapie.	
Infliximab [Janssen Inc., 2021b; Amgen Canada, 2020; Merck Canada, 2020b; Pfizer Canada, 2020]	• Indiqué pour le traitement des adultes qui sont atteints de psoriasis en plaques chronique de sévérité modérée à élevée et candidats à un traitement systémique. Chez les patients atteints de psoriasis en plaques chronique de sévérité modérée, l'infliximab ne doit être administré que lorsque la photothérapie s'est révélée inefficace ou inappropriée.	
Brodalumab [Bausch Health, 2019]	• Indiqué pour le traitement du psoriasis en plaques modéré à sévère chez les patients adultes qui sont candidats à un traitement systémique ou à une photothérapie.	
Ixékizumab [Eli Lilly Canada, 2021]	• Indiqué pour le traitement du psoriasis en plaques modéré ou grave chez les adultes qui sont candidats au traitement à action générale ou à la photothérapie.	
Risankizumab [Corporation AbbVie, 2022]	• Indiqué pour le traitement du psoriasis en plaques modéré à grave chez les patients adultes qui sont candidats à un traitement à action générale ou à une photothérapie.	
Sécukinumab [Novartis Pharma Canada, 2022]	• Indiqué pour le traitement du psoriasis en plaques modéré à grave chez les patients adultes qui sont candidats à un traitement à action générale ou à une photothérapie.	

Biologique	Indication reconnue par Santé Canada (monographie)	Indication de paiement (RAMQ)
Ustekinumab [Janssen Inc., 2021b]	• Indiqué dans le traitement du psoriasis en plaques chronique de sévérité modérée à élevée chez les patients adultes qui sont candidats à une photothérapie ou à un traitement systémique.	
Certolizumab [UCB Canada, 2019]	• Indiqué pour le traitement des patients adultes atteints de psoriasis en plaques modéré à sévère qui sont candidats à une thérapie systémique	Non inscrit (décision du ministre à venir) Advenant l'inscription, l'indication recommandée par l'INESSS est la même que celle des autres agents biologiques pour le traitement du psoriasis en plaques [INESSS, 2020b].
Guselkumab [Janssen Inc., 2022]	• Indiqué pour le traitement du psoriasis en plaques modéré à grave chez les adultes qui sont candidats à un traitement systémique ou à une photothérapie.	Non inscrit (décision du ministre à venir) Advenant l'inscription, l'indication recommandée par l'INESSS est la même que celle des autres agents biologiques pour le traitement du psoriasis en plaques [INESSS, 2018].

Tableau F-2a Indications de paiement des médicaments biologiques d'intérêt employés pour le traitement de la maladie de Crohn chez l'adulte

Province	Indication de paiement des médicaments biologiques
Colombie-Britannique	**Adalimumab, infliximab, vedolizumab** Pre-treatment clinical information for moderate to severe Crohn's • Current Harvey Bradshaw Index (Hbi ≥ 8) Prior therapies (initial coverage) • For patients with moderate to severe active crohns - details of glucocorticoid trial (required) o Patient has had a course of steroids equivalent to oral prednisone 40 mg or more daily for a minimum of 14 days. ▪ Patient is steroid resistant, displaying a lack of a symptomatic response to therapy. ▪ Patient is steroid dependent, unable to withdraw oral corticosteroid within 3 months of initiation without a recurrence of symptoms; a symptomatic relapse within 3 months of stopping; or the need for two or more courses of corticosteroids within one year OR o Patient is unable to complete a course of steroids equivalent to oral prednisone 40 mg or more daily for a minimum of 14 days. ▪ Corticosteroid use is contraindicated (specify): ▪ Intolerances/side effect(s) (specify)
Alberta	**Adalimumab, infliximab, vedolizumab** Prior to initiation of therapy, patients must have a HBI score ≥ 7, AND be refractory. Refractory is defined as one or more of the following: 1) Serious adverse effects or reactions to the treatments specified below; OR 2) Contraindications (as defined in product monographs) to the treatments specified below; OR 3) Previous documented lack of effect at doses and for duration of all treatments specified below: a. mesalamine minimum of 3 grams/day for a minimum of 6 weeks; AND refractory to, or dependant on, glucocorticoids AND b. immunosuppressive therapy as follows: - azathioprine: minimum of 2 mg/kg/day for a minimum of 3 months; OR - 6-mercaptopurine : minimum of 1 mg/kg/day for a minimum of 3 months; OR - methotrexate: minimum or 15 mg/week for a minimum of 3 months. OR - immunosuppressive therapy discontinued at less than 3 months due to serious adverse effects or reactions.

Province	Indication de paiement des médicaments biologiques
Saskatchewan	**Adalimumab, infliximab** For the treatment of moderate to severely active Crohn's disease in patients refractory to or with contraindications to an adequate course of corticosteroids and other immunosuppressive therapy. **Vedolizumab** For the treatment of moderate to severely active Crohn's Disease (CD) patients who demonstrate continuing symptoms despite the use of optimal conventional therapies, such as glucocorticoids and immunosuppressive therapy, or are intolerant to glucocorticoids and immunosuppressive therapy **Ustekinumab** For treatment of adult patients with moderate to severely active Crohn's disease (CD) who have had an inadequate response to, loss of response to, or were intolerant to either immunomodulators or one or more tumor necrosis factor-alpha antagonists, or have had an inadequate response to, intolerance to or demonstrated dependence on corticosteroids.
Manitoba	**Adalimumab, infliximab, vedolizumab** For treatment of moderate to severely active Crohn's Disease in patients with inadequate response, intolerance or contraindications to an adequate course of corticosteroids AND an immunosuppressive agent.
Ontario	**Adalimumab, infliximab** For the treatment of moderate to severe (luminal) Crohn's Disease in patients who meet the following criteria: A. Harvey Bradshaw Index (HBI) score greater than or equal to 7; AND B. Failed to respond to conventional treatment with a corticosteroid equivalent to a daily dose of prednisone 40mg daily for at least 2 weeks OR the patient is stabilized on corticosteroid but cannot be tapered to a corticosteroid dose below prednisone 20mg daily or equivalent; AND C. Failed to respond to an immunosuppressive agent (azathioprine, 6-mercaptopurine, methotrexate, or cyclosporine) tried for at least 3 months (or where the use of immunosuppressants is contraindicated). **Védolizumab** For the treatment of moderate to severe (luminal) Crohn's Disease in patients who have: • HBI (Harvey Bradshaw Index) score ≥7*; AND • Failed to respond to conventional treatment with glucocorticoids (prednisone 40mg/day or equivalent for at least 2 weeks or dose cannot be tapered to below prednisone 20 mg/day or equivalent); AND • Failed to respond to an immunosuppressive agent (azathioprine, 6-mercaptopurine, methotrexate, or cyclosporine) tried for at least 3 months.

Province	Indication de paiement des médicaments biologiques
Québec	**Adalimumab, infliximab, vedolizumab** Pour le traitement de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes. L'essai d'un immunosuppresseur doit avoir été d'au moins 8 semaines. Pour le traitement de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes, lorsque les immunosuppresseurs sont contre-indiqués, non tolérés ou qu'ils ont été inefficaces dans le passé lors d'un épisode similaire après un traitement combiné avec des corticostéroïdes.
Nouveau-Brunswick	**Adalimumab** For the treatment of patients with moderately to severely active Crohn's disease who are refractory, intolerant or have contraindications to conventional therapy. **Infliximab, vedolizumab** For the treatment of patients with moderately to severely active Crohn's disease who have contraindications, or are refractory, to therapy with corticosteroids and other immunosuppressants.
Nouvelle-Écosse	**Adalimumab, vedolizumab** For patients with moderate to severely active Crohn's disease and are: • Refractory or have contraindications to an adequate course of 5-aminosalicylic acid and corticosteroids and other immunosuppressive therapy. **Infliximab** For treatment of Crohn's disease in patients with moderate to severe active disease refractory to 5-ASA products AND glucocorticoids (e.g.,prednisone) AND immunosuppressive therapy (azathioprine or 6-mercaptopurine or methotrexate) *Patients who are very ill and not candidates for surgery may qualify for infliximab therapy without a trial of AZA, 6-MP or MTX, as they may require a more rapid onset of response

Province	Indication de paiement des médicaments biologiques
Île-du-Prince-Édouard	**Adalimumab, infliximab, vedolizumab** For the treatment of patients with moderate to severe Crohn's disease who have active disease and are refractory, intolerant or have contraindications to: • Prednisone 40mg (or equivalent) daily for ≥ 2 weeks, AND • Azathioprine ≥ 2 mg/kg/day for ≥ 3 months, OR • Mercaptopurine ≥ 1 mg/kg/day for ≥ 3 months, OR • Methotrexate (SC or IM) ≥ 15 mg/week for ≥ 3 months *Consideration will be given for the approval of a biologic DMARD (disease modifying antirheumatic drug) without a trial of a traditional DMARD for patients who have an aggressive/severe disease course (e.g. extensive disease, a modified Harvey Bradshaw Index score > 16) and are refractory, intolerant or have contraindications to systemic corticosteroids.
Terre-Neuve et Labrador	**Adalimumab, infliximab** For the treatment of patients with moderately to severely active Crohn's disease who have contraindications, or are refractory, to therapy with corticosteroids and other immunosuppressants. **Vedolizumab** For the treatment of adult patients with moderately to severely active Crohn's disease (CD) with contraindications to or not achieving remission with glucocorticosteroids AND immunosuppressive therapy.

Tableau F-2b Indications de paiement des médicaments biologiques d'intérêt employés pour le traitement de la maladie de Crohn chez l'enfant

Province	Indication de paiement des agents biologiques
Colombie-Britannique	**Infliximab** Pre-treatment clinical information for moderate to severe Crohn's • Current Harvey Bradshaw Index (Hbi ≥ 8) Prior therapies (initial coverage) • For patients with moderate to severe active crohns - details of glucocorticoid trial (required) o Patient has had a course of steroids equivalent to oral prednisone 40 mg or more daily for a minimum of 14 days. ▪ Patient is steroid resistant, displaying a lack of a symptomatic response to therapy. ▪ Patient is steroid dependent, unable to withdraw oral corticosteroid within 3 months of initiation without a recurrence of symptoms; a symptomatic relapse within 3 months of stopping; or the need for two or more courses of corticosteroids within one year OR o Patient is unable to complete a course of steroids equivalent to oral prednisone 40 mg or more daily for a minimum of 14 days. ▪ Corticosteroid use is contraindicated (specify): ▪ Intolerances/side effect(s) (specify)
Alberta	**Infliximab** Non inscrit (les patients couverts doivent être âgés de 18 ans ou plus).
Saskatchewan	**Infliximab** For the treatment of moderate to severely active Crohn's disease in patients refractory to or with contraindications to an adequate course of corticosteroids and other immunosuppressive therapy.
Manitoba	**Infliximab** For treatment of moderate to severely active Crohn's Disease in patients with inadequate response, intolerance or contraindications to an adequate course of corticosteroids AND an immunosuppressive agent.

Province	Indication de paiement des agents biologiques
Ontario	**Infliximab** For the treatment of moderate to severe (luminal) Crohn's Disease in patients who meet the following criteria A. Harvey Bradshaw Index (HBI) score greater than or equal to 7; AND B. Failed to respond to conventional treatment with a corticosteroid equivalent to a daily dose of prednisone 40mg daily for at least 2 weeks OR the patient is stabilized on corticosteroid but cannot be tapered to a corticosteroid dose below prednisone 20mg daily or equivalent; AND C. Failed to respond to an immunosuppressive agent (azathioprine, 6-mercaptopurine, methotrexate, or cyclosporine) tried for at least 3 months (or where the use of immunosuppressants is contraindicated).
Québec	**Infliximab** Pour le traitement des enfants atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes. L'essai d'un immunosuppresseur doit avoir été d'au moins 8 semaines. Pour le traitement des enfants atteints de la maladie de Crohn intestinale modérée ou grave, toujours active malgré un traitement par les corticostéroïdes, à moins d'intolérance importante ou de contre-indication aux corticostéroïdes, lorsque les immunosuppresseurs sont contre-indiqués, non tolérés ou qu'ils ont été inefficaces dans le passé lors d'un épisode similaire après un traitement combiné avec des corticostéroïdes.
Nouveau-Brunswick	**Infliximab** For the treatment of patients with moderately to severely active Crohn's disease who have contraindications, or are refractory, to therapy with corticosteroids and other immunosuppressants.
Nouvelle-Écosse	**Infliximab** For treatment of Crohn's disease in patients with moderate to severe active disease refractory to 5-ASA products AND glucocorticoids (e.g.,prednisone) AND immunosuppressive therapy (azathioprine or 6-mercaptopurine or methotrexate) *Patients who are very ill and not candidates for surgery may qualify for infliximab therapy without a trial of AZA, 6-MP or MTX, as they may require a more rapid onset of response
Île-du-Prince-Édouard	**Infliximab** • For the treatment of patients with moderate to severe Crohn's disease who have active disease and are refractory, intolerant or have contraindications to: • Prednisone 40mg (or equivalent) daily for ≥ 2 weeks, AND • colitiAzathioprine ≥ 2 mg/kg/day for ≥ 3 months, OR • Mercaptopurine ≥ 1 mg/kg/day for ≥ 3 months, OR • Methotrexate (SC or IM) ≥ 15 mg/week for ≥ 3 months

Province	Indication de paiement des agents biologiques
	*Consideration will be given for the approval of a biologic DMARD (disease modifying antirheumatic drug) without a trial of a traditional DMARD for patients who have an aggressive/severe disease course (e.g. extensive disease, a modified Harvey Bradshaw Index score > 16) and are refractory, intolerant or have contraindications to systemic corticosteroids.
Terre-Neuve et Labrador	**Infliximab** For the treatment of pediatric* and adult patients with moderately to severely active Crohn's disease who have contraindications, or are refractory, to therapy with corticosteroids and other immunosuppressants. *Inflectra, Renflexis or Avsola are indicated for use in pediatric patients 9 years of age and older. The safety and efficacy is not established in patients less than 9 years of age.

Tableau F-2c Indications de paiement des médicaments biologiques d'intérêt employés pour le traitement de la colite ulcéreuse chez l'adulte

Biologique	Indication de paiement des agents biologiques

Colombie-Britannique	**Adalimumab, infliximab, vedolizumab**
	
	Prior to initiation of therapy, patients must have a score of ≥ 4, with rectal a bleeding subscore of ≥ 2
	
	Prior therapy (initial coverage)
	• Details of trial with 5-ASA products (for a minimum of 4 weeks)
	• Details of glucocorticoid trial (required)
	  ○ Patient has had a course of steroids equivalent to oral prednisone 40 mg or more daily for a minimum of 14 days.
	  ▪ Patient is steroid resistant, displaying a lack of symptomatic response to therapy.
	  ▪ Patient is steroid dependent: unable to withdraw oral corticosteroid within 3 months of initiation without a recurrence of symptoms; a symptomatic relapse
	  OR
	  ○ Patient is unable to complete a course of steroids equivalent to oral prednisone 40 mg or more daily for a minimum of 14 days
	  ▪ Corticosteroid use is contraindicated (specify)
	  ▪ Intolerances/side effect(s) (specify)

Alberta	**Adalimumab, infliximab, vedolizumab** Prior to initiation of therapy, patients must have an active disease (characterized by a partial Mayo score >4 prior to initiation of biologic therapy) and be refractory or intolerant to: • mesalamine; minimum of 4 grams/day for a minimum of 4 weeks AND • corticosteroids (failure to respond to prednisone 40 mg daily for 2 weeks, or; steroid dependent i.e. failure to taper off steroids without recurrence of disease or disease requiring a second dose of steroids within 12 months of previous dose) 'Refractory' is defined as lack of effect at the recommended doses and for duration of treatments specified above. 'Intolerant' is defined as demonstrating serious adverse effects or contraindications to treatments as defined in product monographs. Immunosuppressive therapy as follows may also be initiated if in the clinician's judgment a trial is warranted: • Azathioprine: minimum of 2 mg/kg/day for a minimum of 2 months; OR • 6-mercaptopurine: minimum of 1 mg/kg/day for a minimum of 2 months
Saskatchewan	**Adalimumab, infliximab, vedolizumab** For the treatment of ulcerative colitis in patients unresponsive to high dose steroids.

Biologique	Indication de paiement des agents biologiques
Manitoba	**Adalimumab, infliximab, vedolizumab** For the treatment of patients over 18 years of age with moderate to severely active ulcerative colitis who have had inadequate response, intolerance or contraindications to conventional therapy including 5-aminosalicylate compounds AND corticosteroids.
Ontario	**Adalimumab** For the treatment of ulcerative colitis disease in patients who meet the following criteria: 1. Moderate disease a. Mayo score between 6 and 10 (inclusive); AND b. Endoscopic* subscore of 2; AND c. Failed 2 weeks of oral prednisone at daily doses greater than or equal to 40mg (or a 1 week course of IV equivalent) and 3 months of azathioprine (AZA)/6-mercatopurine (6-MP) (or where the use of immunosuppressants is contraindicated); OR Stabilized with 2 weeks of oral prednisone at daily doses greater than or equal to 40mg (or 1 week of IV equivalent) but the corticosteroid dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated). 2. Severe disease a. Mayo score greater than 10; AND b. Endoscopy* subscore of greater than or equal to 2; AND c. Failed 2 weeks of oral prednisone at daily doses greater than or equal to 40mg (or 1 week IV equivalent) OR Stabilized with 2 weeks oral prednisone at daily doses greater than or equal to 40mg (or 1 week of IV equivalent) but demonstrated that the corticosteroid dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated). **Infliximab** For the treatment of ulcerative colitis disease in patients who meet the following criteria: 1. Moderate disease a. Mayo score between 6 and 10 (inclusive) AND b. Endoscopic* subscore of 2 AND c. Failed 2 weeks of oral prednisone at daily doses greater than or equal to 40mg (or a 1 week course of IV equivalent) OR Stabilized with 2 weeks oral prednisone at daily doses greater than or equal to 40mg (or 1 week of IV equivalent) but demonstrated that the corticosteroid dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)

Biologique	Indication de paiement des agents biologiques
	2. Severe disease a. Mayo score greater than 10 AND b. Endoscopy* subscore of greater than or equal to 2 AND c. Failed 2 weeks of oral prednisone at daily doses greater than or equal to 40mg (or 1 week IV equivalent) OR Stabilized with 2 weeks oral prednisone at daily doses greater than or equal to 40mg (or 1 week of IV equivalent) but demonstrated that the corticosteroid dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated) **Vedolizumab** Mild disease a. Mayo score <6 AND b. Patients with mild disease will be considered on a case-by-case basis BUT submission must include the rationale for coverage Moderate disease a. Mayo score between 6 and 10 (inclusive) AND b. Endoscopic* subscore of 2 AND c. Failed 2 weeks of oral prednisone at daily doses ≥40mg (or a 1 week course of IV equivalent) and 3 months of azathioprine (AZA)/ 6-mercaptopurine (6MP) (or where the use of immunosuppressants is contraindicated) OR Stabilized with 2 weeks of oral prednisone at daily dose ≥ 40mg (or a 1 week course of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/ 6MP (or where the use of immunosuppressants is contraindicated) Severe disease a. Mayo score >10 AND b. Endoscopic* subscore of ≥2 AND c. Failed 2 weeks of oral prednisone at daily dose ≥ 40mg (or 1 week IV equivalent) OR Stabilized with 2 weeks oral prednisone ≥ 40mg (or 1 week of IV equivalent) but the prednisone dose cannot be tapered despite 3 months of AZA/6MP (or where the use of immunosuppressants is contraindicated)

Biologique	Indication de paiement des agents biologiques
Québec	**Adalimumab, infliximab, vedolizumab** Pour le traitement des adultes atteints de colite ulcéreuse modérée à grave toujours active malgré un traitement par les corticostéroïdes et les immunosuppresseurs à moins d'intolérance sérieuse ou de contreindication.
Nouveau-Brunswick	**Adalimumab** For the treatment of patients with moderately to severely active ulcerative colitis who are refractory, intolerant or have contraindications to conventional therapy. **Infliximab, vedolizumab** For the treatment of patients with moderately to severely active ulcerative colitis who have a partial Mayo score greater than 4, and a rectal bleeding subscore greater than or equal to 2 and are: • refractory or intolerant to conventional therapy (i.e. aminosalicylates for a minimum of four weeks, and prednisone greater than or equal to 40mg daily for two weeks or IV equivalent for one week); or • corticosteroid dependent (i.e. cannot be tapered from corticosteroids without disease recurrence; or have relapsed within three months of stopping corticosteroids; or require two or more courses of corticosteroids within one year).
Nouvelle-Écosse	**Adalimumab, infliximab, vedolizumab** For the treatment of patients with moderately to severely active ulcerative colitis who have a partial Mayo score > 4, and a rectal bleeding subscore ≥ 2 and are: • Refractory or intolerant to conventional therapy (i.e. 5-ASA for a minimum of 4 weeks, and prednisone ≥ 40mg daily for two weeks or IV equivalent for one week); OR • Corticosteroid dependent (i.e. cannot be tapered from corticosteroids without disease recurrence; or have relapsed within three months of stopping corticosteroids; or require two or more courses of corticosteroids within one year.) *Patients with severe disease (partial Mayo > 6) do not require a trial of 5-ASA.
Île-du-Prince-Édouard	**Adalimumab, infliximab, vedolizumab** For the treatment of adult patients with moderately to severely active ulcerative colitis who have a partial Mayo score > 4, and a rectal bleeding subscore ≥ 2 and are: • Refractory or intolerant to conventional therapy (i.e. aminosalicylates for a minimum of four weeks AND prednisone ≥ 40mg daily for two weeks or IV equivalent for one week) OR • Corticosteroid dependent (i.e. cannot be tapered from corticosteroids without disease recurrence; or have relapsed within three months of stopping corticosteroids; or require two or more courses of corticosteroids within one year. *Patients with severe disease (partial Mayo > 6) do not require a trial of 5-ASA.

Biologique	Indication de paiement des agents biologiques
Terre-Neuve et Labrador	**Adalimumab, infliximab, vedolizumab** For the treatment of patients with moderately to severely active ulcerative colitis who have a partial Mayo score > 4, and a rectal bleeding subscore ≥ 2 and are: • refractory or intolerant to conventional therapy (i.e. 5-ASA for a minimum of 4 weeks, and prednisone ≥ 40mg daily for two weeks or IV equivalent for one week); or • corticosteroid dependent (i.e. cannot be tapered from corticosteroids without disease recurrence; or have relapsed within three months of stopping corticosteroids; or require two or more courses of corticosteroids within one year.) *Consideration will be given for patients who have not received a four week trial of aminosalicylates if disease is severe (partial Mayo score > 6)

Tableau F-2d Indications de paiement des médicaments biologiques employés pour le traitement du psoriasis en plaques chez l'adulte

Province	Indication de paiement des agents biologiques

Colombie-Britannique	**Adalimumab, etanercept, infliximab, ixékizumab, risankizumab, secukinumab, ustekinumab**
	
	THE FOLLOWING CRITERIA HAVE TO BE MET:
	
	• Patient failed to respond, is intolerant, or is unable to access UV phototherapy;
	
	• Patient has failed to respond, or experienced a specific intolerance, or has a specific contraindication to both of the following medications:
	  ○ methotrexate oral/parenteral 20 mg weekly (15 mg for ages > 65) for 3 months
	  ○ cyclosporine 4mg/Kg daily for 3 months

Alberta	**Adalimumab** For the reduction in signs and symptoms of severe, debilitating psoriasis in patients who are refractory or intolerant to: • Methotrexate at 20 mg (PO, SC or IM) or greater total weekly dosage (15 mg or greater if patient is 65 years of age or older) for more than 12 weeks. Patients who experience gastrointestinal intolerance to PO methotrexate must have a trial of parenteral methotrexate before being accepted as refractory; OR • Cyclosporine (6 weeks treatment); AND • Phototherapy (unless restricted by geographic location) 'Refractory' is defined as lack of effect at the recommended doses and for duration of treatments specified above. 'Intolerant' is defined as demonstrating serious adverse effects or contraindications to treatments as defined in product monographs. **Etanercept, infliximab, ixékizumab, risankizumab, secukinumab** For the reduction in signs and symptoms of severe, debilitating psoriasis in patients who are refractory or intolerant to: • Methotrexate at 20 mg (PO, SC or IM) or greater total weekly dosage (15 mg or greater if patient is 65 years of age or older) for more than 12 weeks. Patients who experience gastrointestinal intolerance to PO methotrexate must have a trial of parenteral methotrexate before being accepted as refractory; OR • Cyclosporine (6 weeks treatment); AND • Phototherapy (unless restricted by geographic location) 'Refractory' is defined as lack of effect at the recommended doses and for duration of treatments specified above. 'Intolerant' is defined as demonstrating serious adverse effects or contraindications to treatments as defined in product monographs.

Province	Indication de paiement des agents biologiques
	*Patients who have a contraindication to either cyclosporine or methotrexate will be required to complete an adequate trial of the other pre-requisite medication prior to potential coverage being considered. **Ustekinumab** For the reduction in signs and symptoms of severe, debilitating psoriasis in patients who are refractory or intolerant to at least three of the following • adalimumab • etanercept • infliximab • ixekizumab • risankizumab • secukinumab
Saskatchewan	**Adalimumab, etanercept, infliximab, ustekinumab, secukinumab, brodalumab, ixékizumab, risankizumab:** For the treatment of adult patients with severe debilitating plaque psoriasis who have failed, or are intolerant to methotrexate OR cyclosporine AND have failed, are intolerant to, or unable to access phototherapy.
Manitoba	**Adalimumab, etanercept, infliximab, ustekinumab, secukinumab, brodalumab, ixékizumab, risankizumab** For treatment of adult patients with severe plaque psoriasis presently with one or more of the following: • Psoriasis Area and the Severity Index (PASI) ≥ 10 • Body Surface Area (BSA) > 10% • Significant involvement of the face, hands feet or genital region • Dermatology Life Quality Index (DLQI) > 10 AND • Failure to respond to, contraindications to, intolerant of or unable to access methotrexate, cyclosporine and/or phototherapy.

Ontario	**Adalimumab, etanercept, infliximab, ustekinumab, secukinumab, brodalumab, ixékizumab, risankizumab**
	
	For the treatment of severe plaque psoriasis in patients 18 years of age or older who have experienced failure, intolerance, or have a contraindication to adequate trials of several standard therapies:
	
	• 6 month trial of at least 3 topical agents including vitamin D analogues and steroids
	• 12 week trial of phototherapy (unless not accessible)
	• 6 month trial of at least 2 systemic, oral agents used alone or in combination
	  ○ Methotrexate 15-30mg per week
	  ○ Acitretin (could have been used with phototherapy)
	  ○ Cyclosporine

Province	Indication de paiement des agents biologiques
Québec	**Adalimumab, etanercept, infliximab, ustekinumab, secukinumab, brodalumab, ixékizumab, risankizumab** Pour le traitement des personnes atteintes d'une forme grave de psoriasis en plaques chronique : • lorsqu'un traitement de photothérapie de 30 séances ou plus pendant 3 mois n'a pas permis un contrôle optimal de la maladie, à moins que ce traitement soit contre-indiqué, ne soit pas toléré, ne soit pas accessible ou qu'un traitement de 12 séances ou plus pendant 1 mois n'ait pas procuré d'amélioration significative des lésions; et • lorsqu'un traitement avec 2 agents de rémission, utilisés en concomitance ou non, pendant au moins 3 mois chacun n'a pas permis un contrôle optimal de la maladie. À moins d'intolérance ou de contreindication sérieuses, ces 2 agents doivent être : o le méthotrexate à la dose de 15 mg ou plus par semaine; ou o la cyclosporine à la dose de 3 mg/kg ou plus par jour; ou o l'acitrétine à la dose de 25 mg ou plus par jour.
Nouveau-Brunswick	**Adalimumab** For the treatment of patients with moderate to severe plaque psoriasis who are refractory, intolerant or have contraindications to conventional therapy. **Etanercept, infliximab, ustekinumab, secukinumab, brodalumab, ixékizumab, risankizumab** For the treatment of patients with chronic moderate to severe plaque psoriasis who meet all of the following criteria: • Refractory, intolerant or unable to access phototherapy • Refractory, intolerant or have contraindications to one of the following: o Methotrexate (oral or parenteral) at a dose of greater than or equal to 20 mg weekly (greater than or equal to 15 mg if patient is greater than or equal to 65 years of age) for a minimum of 12 weeks o Cyclosporine for a minimum of 6 weeks
Nouvelle-Écosse	**Adalimumab, etanercept, infliximab, ustekinumab, secukinumab, brodalumab, ixékizumab, risankizumab** For patients with severe, debilitating chronic plaque psoriasis who meet all of the following: • Failure to, contraindication to or intolerant of methotrexate and cyclosporine; • Failure to, intolerant of or unable to access phototherapy.

Province	Indication de paiement des agents biologiques
Île-du-Prince-Édouard	**Adalimumab, etanercept, infliximab, ustekinumab, secukinumab, brodalumab, ixékizumab, risankizumab** For the treatment of patients with chronic moderate to severe plaque psoriasis who meet all of the following criteria: • Refractory, intolerant or have contraindications to: o Phototherapy (unless restricted by geographic location); and o Methotrexate (oral or parenteral) at a dose of ≥ 20mg weekly (≥15mg if patient is ≥65 years of age) for a minimum of 12 weeks or cyclosporine for a minimum of 6 weeks *For patients who do not demonstrate a clinical response to oral methotrexate, or who experience gastrointestinal intolerance, a trial of parenteral methotrexate must be considered
Terre-Neuve et Labrador	**Adalimumab, etanercept, infliximab, ustekinumab, secukinumab, brodalumab, ixékizumab, risankizumab** For patients with severe, debilitating psoriasis who meet all of the following criteria: • Failure to respond to, contraindications to, or intolerant of methotrexate and cyclosporine; • Failure to respond to, intolerant to, or unable to access phototherapy

Tableau F-3a Recommandations issues des guides de pratique clinique pour maladie de Crohn chez l'adulte

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
Recommandations en lien avec l'usage des agents biologiques en première intention pour le traitement de la maladie de Crohn chez l'adulte				
7. In adult outpatients with moderate to severe CD, the AGA suggests early introduction with a biologic with or without an immunomodulator rather than delaying their use until after failure of 5-aminosalicylates and/or corticosteroids. Conditional Low 10B. In adult outpatients with CD and active perianal fistula, the AGA suggests the use of adalimumab, ustekinumab, or vedolizumab over no treatment for the induction or maintenance of fistula remission. Comment: Evidence suggests certolizumab pegol may not be effective for induction of fistula remission. Conditional Low 11. In adult outpatients with CD and active perianal fistula without perianal abscess, the AGA recommends the use of biologic agents in combination with an antibiotic over a biologic drug alone for the induction of fistula remission. Strong Moderate	Aucune recommandation sur l'usage des agents biologiques en première intention de traitement.	20. In patients with moderate to severe luminal Crohn's disease with risk factors of poor prognosis, we recommend anti-TNF therapy (infliximab, adalimumab) as first-line therapy to induce complete remission. GRADE: Strong recommendation, moderate-quality evidence	Statement 37. We recommend that moderate to severely active uncomplicated luminal Crohn's disease should be treated initially with systemic corticosteroids (GRADE: strong recommendation, high-quality evidence), but we suggest that those with extensive disease or other poor prognostic features should be considered for early introduction of biological therapy (GRADE: weak recommendation, moderate-quality evidence. Agreement: 86.7%)	Aucune recommandation sur l'usage des agents biologiques en première intention de traitement.

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
Recommandations en lien avec la place des agents biologiques par rapport aux immunosuppresseurs pour le traitement de la maladie de Crohn chez l'adulte				
4. In adult outpatients with moderate to severe CD, the AGA recommends the use of biologic drug monotherapy over thiopurine monotherapy for the induction of remission. Strong Moderate 5A. In adult outpatients with moderate to severe CD who are naïve to biologics and immunomodulators, the AGA suggests the use of infliximab in combination with thiopurines for the induction and maintenance of remission over infliximab monotherapy. Comment: Based on indirect evidence, combination infliximab with methotrexate may be more effective over infliximab monotherapy. Conditional Moderate 5B. In adult outpatients with moderate to severe CD who are naïve to biologics and immunomodulators, the AGA suggests the use of adalimumab in combination with thiopurines for the induction and maintenance of remission over adalimumab monotherapy. Comment: Based on indirect evidence, combination adalimumab with methotrexate may be more effective over adalimumab	**1. Induction of remission** Recommendation 1.5. ECCO CD Treatment GL [2019] We recommend the use of TNF inhibitors [infliximab, adalimumab, and certolizumab pegol] to induce remission in patients with moderate-to-severe Crohn's disease who have not responded to conventional therapy [strong recommendation, moderate-quality evidence] Recommendation 1.6. ECCO CD Treatment GL [2019] We suggest against the combination of adalimumab and thiopurines over adalimumab alone to achieve clinical remission and response [weak recommendation, moderate quality evidence]. Recommendation 1.7. ECCO CD Treatment GL [2019] We recommend combination therapy with a thiopurine when starting infliximab to induce remission in patients with moderate-to-severe Crohn's disease, who have had an inadequate response to conventional therapy [strong	21. In patients with moderate to severe Crohn's disease who fail to achieve complete remission with any of corticosteroids, thiopurines, or methotrexate, we recommend anti-TNF therapy (infliximab, adalimumab) to induce complete remission. GRADE: Strong recommendation, high-quality evidence 22. In patients with active Crohn's disease, when starting anti-TNF therapy, we suggest it be combined with a thiopurine over monotherapy to induce complete remission. GRADE: Conditional recommendation, low-quality evidence 23. In patients with active Crohn's disease, when starting anti-TNF therapy, we suggest it be combined with a thiopurine or methotrexate over monotherapy to improve pharmacokinetic parameters. GRADE: Conditional recommendation, very low-quality evidence for infliximab, very low-quality evidence for adalimumab 25. In patients with Crohn's disease who have achieved	Statement 43. We recommend that patients refractory to immunomodulator therapy despite dose optimisation should be considered for biological therapy. Choice between anti-TNF therapy, ustekinumab and vedolizumab should be made on an individual basis, considering patient preference, cost, likely adherence, safety data and speed of response to the drug (GRADE: strong recommendation, very low-quality evidence. Agreement: 95.7%). Statement 44. We recommend that combination therapy of infliximab with a thiopurine should be used as it is more effective than monotherapy infliximab in induction and maintenance of remission in active Crohn's disease (GRADE: strong recommendation, high-quality evidence. Agreement: 97.7%). Statement 45. We suggest that combination therapy of infliximab with methotrexate therapy may be used in Crohn's disease to reduce immunogenicity (GRADE: weak recommendation,	**1.2 Inducing remission in Crohn's disease** <u>Infliximab and adalimumab</u> The recommendations in the following section (except for the recommendation on discussing the options of monotherapy or combined therapy) are from the NICE technology appraisal guidance on infliximab and adalimumab for the treatment of Crohn's disease [TA187]. 1.2.12 Infliximab and adalimumab, within their licensed indications, are recommended as treatment options for adults with severe active Crohn's disease (see recommendation 1.2.18) whose disease has not responded to conventional therapy (including immunosuppressive and/or corticosteroid treatments), or who are intolerant of or have contraindications to conventional therapy. Infliximab or adalimumab should be given as a planned course of treatment until treatment failure (including the need for surgery), or until 12 months after the start of

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
monotherapy. Conditional Very low 5C. In adult outpatients with moderate to severe CD, the AGA makes no recommendation regarding the use of, ustekinumab or vedolizumab in combination with thiopurines or methotrexate over biologic drug monotherapy for the induction and maintenance of remission. No recommendation Knowledge gap	recommendation, moderate-quality evidence] Recommendation 1.8. ECCO CD Treatment GL [2019] We recommend ustekinumab for induction of remission in patients with moderate-to-severe Crohn's disease with inadequate response to conventional therapy and/or to anti-TNF therapy [strong recommendation, high-quality evidence]. Recommendation 1.9. ECCO CD Treatment GL [2019] We recommend vedolizumab for induction of response and remission in patients with moderate-to-severe Crohn's disease with inadequate response to conventional therapy and/or to anti-TNF therapy [strong recommendation, moderate-quality evidence] Recommendation 1.10. ECCO CD Treatment GL [2019] We equally suggest the use of either ustekinumab or vedolizumab for the treatment of moderate-to-severe active luminal Crohn's disease in patients who have previously failed anti-TNF therapy [weak recommendation, very low-quality evidence]. 2. Maintenance of Remission	symptomatic response with anti-TNF induction therapy, we recommend continued anti-TNF therapy to achieve and maintain complete remission. GRADE: Strong recommendation, high-quality evidence 30. In patients with moderate to severe Crohn's disease who fail to achieve complete remission with any of corticosteroids, thiopurines, methotrexate, or anti-TNF therapy, we recommend vedolizumab to induce complete remission. GRADE: Strong recommendation, moderate-quality evidence 31. In patients with Crohn's disease who fail to achieve or maintain corticosteroid-free symptomatic remission with anti-TNF therapy, we suggest vedolizumab to induce complete remission. GRADE: Conditional recommendation, low-quality evidence 33. In patients with Crohn's disease who have achieved symptomatic response with vedolizumab induction therapy, we recommend continued vedolizumab therapy to achieve and maintain complete remission. GRADE: Strong recommendation, moderate-quality evidence	moderate-quality evidence. Agreement: 90.5%). Statement 46. We recommend that in Crohn's disease, vedolizumab can be used in both anti-TNF naïve patients and in those where anti-TNF treatment fails. Choice of treatment in biologics-naïve patients should be individualised (GRADE for induction therapy: strong recommendation, moderate quality evidence; GRADE for maintenance therapy: strong recommendation, high-quality evidence. Agreement: 95.5%). Statement 47. We recommend that ustekinumab can be used in the induction and maintenance of remission of Crohn's disease, both in anti-TNF naïve patients and in those where anti-TNF treatment fails. No direct comparison data are available with other biological therapies (GRADE: strong recommendation, high-quality evidence. Agreement: 97.7%). Statement 48. We suggest that, where a switch from anti-TNF therapy to a different drug class is required in Crohn's disease, the choice to use vedolizumab or ustekinumab may be made on an individual basis. Factors to be included in	treatment, whichever is shorter. People should then have their disease reassessed (see recommendation 1.2.16) to determine whether ongoing treatment is still clinically appropriate. [2010] 1.2.13 Treatment as described in recommendation 1.2.12 should normally be started with the less expensive drug (taking into account drug administration costs, required dose and product price per dose). This may need to be varied for individuals because of differences in the method of administration and treatment schedules. [2010] 1.2.14 When a person with Crohn's disease is starting infliximab or adalimumab (in line with recommendations 1.2.12, 1.2.15, 1.2.17 and 1.2.20), discuss options of: • monotherapy with one of these drugs or • combined therapy (either infliximab or adalimumab, combined with an immunosuppressant). Tell the person there is uncertainty about the comparative effectiveness and long-term adverse effects of monotherapy and combined therapy. [2016]

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
	Recommendation 2.5. ECCO CD Treatment GL [2019] In patients with Crohn's disease who achieved remission with anti-TNF agents, maintenance treatment using the same treatment is recommended [strong recommendation, moderate-quality evidence]. Recommendation 2.6. ECCO CD Treatment GL [2019] We recommend vedolizumab for maintaining clinical remission in patients with moderate-to-severe Crohn's disease who achieved remission with vedolizumab [strong recommendation, moderate-quality evidence]. Recommendation 2.7. ECCO CD Treatment GL [2019] We recommend the use of ustekinumab to maintain clinical remission in patients with Crohn's disease who achieved remission with ustekinumab [strong recommendation, moderate-quality evidence]. Recommendation 2.11. ECCO CD Treatment GL [2019] In patients with Crohn's disease who have achieved long-term remission with the combination of infliximab and immunosuppressants, we suggest monotherapy with	34. In patients with moderate to severe Crohn's disease who fail to achieve complete remission with any of corticosteroids, thiopurines, methotrexate, or anti-TNF therapy, we recommend ustekinumab to induce complete remission. GRADE: Strong recommendation, moderate-quality evidence 36. In patients with Crohn's disease who have achieved symptomatic response with ustekinumab induction therapy, we recommend continued ustekinumab therapy to achieve and maintain complete remission. GRADE: Strong recommendation, moderate-quality evidence	the decision-making process should include patient preference, cost, likely adherence, safety data and speed of response to the drug. The potential for surgery as an alternative to further drug therapy should also be considered (GRADE: weak recommendation, very low-quality evidence. Agreement: 97.8%). Statement 51. Patients with jejunal or extensive small bowel disease have a worse prognosis. We suggest that they may be considered for early use of biological therapy, and should have nutritional assessment and support (GRADE: weak recommendation, very low-quality evidence. Agreement: 100%).	1.2.15 Infliximab, within its licensed indication, is recommended as a treatment option for people with active fistulising Crohn's disease whose disease has not responded to conventional therapy (including antibiotics, drainage and immunosuppressive treatments), or who are intolerant of or have contraindications to conventional therapy. Infliximab should be given as a planned course of treatment until treatment failure (including the need for surgery) or until 12 months after the start of treatment, whichever is shorter. People should then have their disease reassessed (see recommendation 1.2.16) to determine whether ongoing treatment is still clinically appropriate. [2010] 1.2.16 Treatment with infliximab or adalimumab (see recommendations 1.2.12 and 1.2.15) should only be continued if there is clear evidence of ongoing active disease as determined by clinical symptoms, biological markers and investigation, including endoscopy if necessary. Specialists should discuss the risks and benefits of continued treatment with

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
	infliximab [weak recommendation, very low-quality evidence]. Recommendation 2.12. ECCO CD Treatment GL [2019] In patients with Crohn's disease who have achieved long-term remission with the combination of adalimumab and immunosuppressants, we suggest monotherapy with adalimumab [weak recommendation, low-quality evidence]. Recommendation 3.1. ECCO CD Treatment GL [2019] We recommend infliximab for the induction and maintenance of remission in complex perianal fistulae in Crohn's disease [strong recommendation; low quality of evidence]. Recommendation 3.2. ECCO CD Treatment GL [2019] We suggest adalimumab may be used for induction and maintenance of remission in complex perianal fistulae in Crohn's disease [weak recommendation, very low-quality evidence]. Recommendation 3.3. ECCO CD Treatment GL [2019] In patients with Crohn's disease and complex perianal fistula there is insufficient evidence regarding the effect of adding			patients and consider a trial withdrawal from treatment for all patients who are in stable clinical remission. People who continue treatment with infliximab or adalimumab should have their disease reassessed at least every 12 months to determine whether ongoing treatment is still clinically appropriate. People whose disease relapses after treatment is stopped should have the option to start treatment again. [2010] 1.2.21 For guidance on using ustekinumab, see the *NICE technology appraisal guidance on ustekinumab for moderately to severely active Crohn's disease after previous treatment [TA456]*. [2019] 1.2.22 For guidance on using vedolizumab, see the *NICE technology appraisal guidance on vedolizumab for treating moderately to severely active Crohn's disease after prior therapy [TA352]. [2019]* <u>Ustekinumab for moderately to severely active Crohn's disease after previous treatment [TA456]</u> 1.1 Ustekinumab is recommended, within its marketing authorisation, as an option for treating moderately

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
	immunomodulators to anti-TNF on fistula healing [weak recommendation, very low-quality evidence]. Recommendation 3.4. ECCO CD Treatment GL [2019] In patients with Crohn's disease and complex perianal fistula there is insufficient evidence to recommend the use of ustekinumab for fistula healing [weak recommendation, moderate-quality evidence]. Recommendation 3.5. ECCO CD Treatment GL [2019] In patients with Crohn's disease and complex perianal fistula there is insufficient evidence to recommend the use of vedolizumab for fistula healing [weak recommendation, low-quality evidence]			to severely active Crohn's disease, that is, for adults who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF-alpha inhibitor or have medical contraindications to such therapies. 1.2 The choice of treatment between ustekinumab or another biological therapy should be made on an individual basis after discussion between the patient and their clinician about the advantages and disadvantages of the treatments available. If more than 1 treatment is suitable, the least expensive should be chosen (taking into account administration costs, dosage and price per dose). 1.3 Ustekinumab should be given until treatment failure (including the need for surgery) or until 12 months after the start of treatment, whichever is shorter. People should then have their disease reassessed in accordance with NICE's recommendations for infliximab and adalimumab for the treatment of Crohn's disease to see whether treatment should continue. <u>Vedolizumab for treating moderately to severely active</u>

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
				Crohn's disease after prior therapy [TA352] 1.1 Vedolizumab is recommended as an option for treating moderately to severely active Crohn's disease only if: • a tumour necrosis factor-alpha inhibitor has failed (that is, the disease has responded inadequately or has lost response to treatment) or • a tumour necrosis factor-alpha inhibitor cannot be tolerated or is contraindicated. Vedolizumab is recommended only if the company provides it with the discount agreed in the patient access scheme. 1.2 Vedolizumab should be given as a planned course of treatment until it stops working or surgery is needed, or until 12 months after the start of treatment, whichever is shorter. At 12 months, people should be reassessed to determine whether treatment should continue. Treatment should only continue if there is clear evidence of ongoing clinical benefit. For people in complete remission at 12 months, consider stopping vedolizumab, resuming treatment if there is a relapse.

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
				People who continue vedolizumab should be reassessed at least every 12 months to decide whether continued treatment is justified. 1.3 People whose treatment with vedolizumab is not recommended in this NICE guidance, but was started within the NHS before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop. **1.3 Maintaining remission in Crohn's disease** <u>Maintenance treatment for people who choose this option</u> See recommendation 1.2.16 for when to continue infliximab or adalimumab during remission.
Recommandations en lien avec l'usage des thiopurines pour l'induction de la rémission				
Recommendation 3A. In adult outpatients with moderate to severe CD, the AGA suggests against the use of thiopurines monotherapy over no treatment for achieving remission. (Conditional recommendation, very low certainty evidence)	Recommendation 1.4. We suggest against the use of thiopurines as monotherapy for the induction of remission of moderate-to severe luminal Crohn's disease [weak recommendation, very low-quality evidence].	Statement 15. In patients with CD of any severity, we suggest against the use of thiopurine monotherapy to induce complete remission. GRADE: Conditional recommendation, low-quality evidence. Vote: strongly agree, 50%; agree, 45%; uncertain, 5%.	Aucune recommandation sur l'usage des thiopurines pour l'induction de la rémission. Toutefois, il est mentionné dans le corps du texte : Thiopurines should not be used for induction of remission in active Crohn's disease.	**1.2 Inducing remission in Crohn's disease** <u>Monotherapy</u> 1.2.6 Do not offer azathioprine, mercaptopurine or methotrexate as monotherapy to induce remission. **[2012]**

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
	Recommendation 3.7. ECCO CD Treatment GL [2019] We suggest against using thiopurine monotherapy [azathioprine, mercaptopurine] for fistula closure in patients with Crohn's disease and complex perianal fistulae [weak recommendation, very low-quality evidence].	Statement 19. We suggest that patients with CD receiving thiopurine or methotrexate who do not achieve corticosteroid-free remission within 12–16 weeks should have therapy modified. GRADE: Conditional recommendation, very low-quality evidence. Vote: strongly agree, 40%; agree, 55%; uncertain, 5%.		<u>Add-on treatment</u> 1.2.7 Consider adding azathioprine or mercaptopurine to a conventional glucocorticosteroid or budesonide to induce remission of Crohn's disease if: • there are 2 or more inflammatory exacerbations in a 12-month period or • the glucocorticosteroid dose cannot be tapered. [2012] In May 2019, the use of budesonide (in children and young people), mercaptopurine, and most preparations of azathioprine was off label. 1.2.8 Assess thiopurine methyltransferase (TPMT) activity before offering azathioprine or mercaptopurine. Do not offer azathioprine or mercaptopurine if TPMT activity is deficient (very low or absent). Consider azathioprine or mercaptopurine at a lower dose if TPMT activity is below normal but not deficient (according to local laboratory reference values). [2012] In May 2019, the use of mercaptopurine and most

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
				preparations of azathioprine was off label. 1.2.9 Consider adding methotrexate (follow British national formulary [BNF]/British national formulary for children [BNFC] cautions) to a conventional glucocorticosteroid or budesonide to induce remission in people who cannot tolerate azathioprine or mercaptopurine, or in whom TPMT activity is deficient, if: • there are 2 or more inflammatory exacerbations in a 12-month period or • the glucocorticosteroid dose cannot be tapered. [2012] In May 2019, the use of some formulations of methotrexate (in adults), all formulations of methotrexate (in children and young people), and budesonide (in children and young people) was off label. 1.2.10 Monitor the effects of azathioprine, mercaptopurine and methotrexate as advised in the BNF or BNFC. Consult the monographs of individual drugs for advice on monitoring immunosuppressives. Monitor for neutropenia in people taking azathioprine or mercaptopurine even if they

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
				have normal TPMT activity. [2012] In May 2019, the use of some formulations of methotrexate (in adults), all formulations of methotrexate (in children and young people), mercaptopurine, and most preparations of azathioprine was off label.
Recommandations en lien avec l'usage des thiopurines pour le maintien de la rémission				
Recommendation 3B. In adult outpatients with quiescent moderate to severe CD (or patients in corticosteroid-induced remission), the AGA suggests the use of thiopurines monotherapy over no treatment for the maintenance of remission. (Conditional recommendation, low certainty evidence)	Recommendation 2.2. ECCO CD Treatment GL [2019] Thiopurines are recommended for the maintenance of remission in patients with steroid-dependent Crohn's disease [strong recommendation, moderate-quality evidence]. Recommendation 2.3. ECCO CD Treatment GL [2019] We recommend against the early introduction of thiopurine therapy in patients with newly diagnosed Crohn's disease for maintaining remission [weak recommendation, low-quality evidence] Recommendation 2.10. ECCO CD Treatment GL [2019] We suggest continuation of thiopurines in Crohn's disease patients in long-term remission on thiopurine maintenance	Statement 16. In selected patients with CD who have achieved symptomatic remission on oral corticosteroids, we suggest thiopurine monotherapy to maintain complete remission. GRADE: Conditional recommendation, very low-quality evidence. Vote: strongly agree, 20%; agree, 60%; uncertain, 15%; disagree, 5%.	Statement 39. We recommend that for patients with moderate to severe Crohn's disease responding to prednisolone, early introduction of maintenance therapy with thiopurines (GRADE: strong recommendation, low-quality evidence) should be considered to minimise risk of flare as prednisolone is withdrawn (Agreement: 93.3%). Statement 40. We recommend that azathioprine or mercaptopurine can be used as monotherapy in the maintenance of remission in Crohn's disease (GRADE: strong recommendation, low-quality evidence. Agreement: 100%).	**1.3 Maintaining remission in Crohn's disease** <u>Maintenance treatment for people who choose this option</u> 1.3.4 Offer azathioprine or mercaptopurine as monotherapy to maintain remission when previously used with a conventional glucocorticosteroid or budesonide to induce remission. [2012] 1.3.5 Consider azathioprine or mercaptopurine to maintain remission in people who have not previously received these drugs (particularly people with adverse prognostic factors such as early age of onset, perianal disease, glucocorticosteroid use at presentation and severe presentations). [2012]

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
	therapy, as the risk of relapse is higher when the treatment is discontinued [weak recommendation, low-quality evidence].			See recommendations 1.2.10 and 1.2.11 for guidance on monitoring the effects of azathioprine, mercaptopurine and methotrexate.
Recommandations en lien avec l'usage le méthotrexate pour l'induction de la rémission				
Recommendation 3C. In adult outpatients with moderate to severe CD, the AGA suggests the use of subcutaneous or intramuscular methotrexate monotherapy over no treatment for the induction and maintenance of remission. (Conditional recommendation, moderate certainty evidence) Recommendation 3D. In adult outpatients with moderate to severe CD, the AGA suggests against the use of oral methotrexate monotherapy over no treatment for the induction and maintenance of remission. (Conditional recommendation, very low certainty evidence)	Aucun consensus et donc aucune recommandation sur l'usage du méthotrexate pour l'induction de la rémission.	Statement 17. In patients with moderate to severe corticosteroid-dependent/resistant CD, we suggest parenteral methotrexate to induce complete remission. GRADE: Conditional recommendation, very low-quality evidence. Vote: strongly agree, 10%; agree, 65%; uncertain, 10%; disagree, 15%. Statement 19. We suggest that patients with CD receiving thiopurine or methotrexate who do not achieve corticosteroid-free remission within 12–16 weeks should have therapy modified. GRADE: Conditional recommendation, very low-quality evidence. Vote: strongly agree, 40%; agree, 55%; uncertain, 5%.	Aucune recommandation sur l'usage du méthotrexate pour l'induction de la rémission. Toutefois, il est indiqué dans le corps du texte : Methotrexate should not be used as monotherapy for induction of remission, but may be used in Crohn's disease patients failing to respond to corticosteroids.	**1.2 Inducing remission in Crohn's disease** <u>Monotherapy</u> 1.2.6 Do not offer azathioprine, mercaptopurine or methotrexate as monotherapy to induce remission. **[2012]** <u>Add-on treatment</u> 1.2.9 **Consider** adding methotrexate (follow British national formulary [BNF]/British national formulary for children [BNFC] cautions) to a conventional glucocorticosteroid or budesonide to induce remission in people who cannot tolerate azathioprine or mercaptopurine, or in whom TPMT activity is deficient, if: • there are 2 or more inflammatory exacerbations in a 12-month period or • the glucocorticosteroid dose cannot be tapered. [2012]

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
				In May 2019, the use of some formulations of methotrexate (in adults), all formulations of methotrexate (in children and young people), and budesonide (in children and young people) was off label. 1.2.10 Monitor the effects of azathioprine, mercaptopurine and methotrexate as advised in the BNF or BNFC. Consult the monographs of individual drugs for advice on monitoring immunosuppressives. Monitor for neutropenia in people taking azathioprine or mercaptopurine even if they have normal TPMT activity. [2012] In May 2019, the use of some formulations of methotrexate (in adults), all formulations of methotrexate (in children and young people), mercaptopurine, and most preparations of azathioprine was off label.
Recommandations en lien avec l'usage le méthotrexate pour le maintien de la rémission				
Recommendation 3C. In adult outpatients with moderate to severe CD, the AGA suggests the use of subcutaneous or intramuscular methotrexate monotherapy over no treatment for the induction and maintenance of remission. (Conditional recommendation, moderate certainty evidence)	Recommendation 2.4. ECCO CD Treatment GL [2019] We recommend methotrexate administered parenterally for the maintenance of remission in patients with steroid-dependent Crohn's disease [weak recommendation, moderate-quality evidence].	Statement 18. In patients with CD who have achieved symptomatic remission on oral corticosteroids and parenteral methotrexate, we suggest parenteral methotrexate to maintain complete remission. GRADE: Conditional recommendation, very low-quality evidence. Vote:	Statement 39. We recommend that for patients with moderate to severe Crohn's disease responding to prednisolone, early introduction of maintenance therapy with methotrexate (GRADE: strong recommendation, moderate-quality evidence) should be considered to minimise risk of	**1.3 Maintaining remission in Crohn's disease** <u>Maintenance treatment for people who choose this option</u> 1.3.6 Consider methotrexate (follow BNF/BNFC cautions) to maintain remission only in people who:

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
Recommendation 3D. In adult outpatients with moderate to severe CD, the AGA suggests against the use of oral methotrexate monotherapy over no treatment for the induction and maintenance of remission. (Conditional recommendation, very low certainty evidence)		strongly agree, 10%; agree, 85%; uncertain, 5%.	flare as prednisolone is withdrawn (Agreement: 93.3%). Statement 41. We suggest that methotrexate may be used for the maintenance of remission of Crohn's disease, and the dose should be at least 15mg weekly. Subcutaneous administration has better bioavailability than oral, particularly at higher doses (GRADE: weak recommendation, moderate-quality evidence. Agreement: 88.4%).	• needed methotrexate to induce remission or • have tried but did not tolerate azathioprine or mercaptopurine for maintenance or • have contraindications to azathioprine or mercaptopurine (for example, deficient thiopurine methyltransferase [TPMT] activity or previous episodes of pancreatitis). [2012] See recommendations 1.2.10 and 1.2.11 for guidance on monitoring the effects of azathioprine, mercaptopurine and methotrexate.
Recommandations en lien avec l'usage des immunosuppresseurs pour le traitement de la maladie de Crohn autre que luminale chez l'adulte				
Aucune recommandation sur l'usage des immunosuppresseurs dans le traitement de la maladie de Crohn avec fistules.	Recommendation 3.7. ECCO CD Treatment GL [2019] We suggest against using thiopurine monotherapy [azathioprine, mercaptopurine] for fistula closure in patients with Crohn's disease and complex perianal fistulae [weak recommendation, very low-quality evidence].	Aucune recommandation. Le guide porte essentiellement sur la maladie de Crohn luminale.	Statement 52. We suggest that mild gastroduodenal Crohn's disease may be treated with proton pump inhibitors. We suggest that moderate or severe disease may also require treatment with corticosteroids, and other immunosuppressive or biological therapies as for Crohn's disease elsewhere in the gut (GRADE: weak recommendation, very low-quality evidence. Agreement: 92.7%).	Aucune recommandation sur l'usage des immunosuppresseurs dans le traitement de la maladie de Crohn avec fistules.

AGA 2021 [Feuerstein *et al.*, 2021]	ECCO 2020 [Torres *et al.*, 2020]	CAG 2019 [Panaccione *et al.*, 2019]	BSG 2019 [Lamb *et al.*, 2019]	NICE NG129 2019 [NICE, 2019b]
			Statement 59. We suggest that low volume enterocutaneous fistulae may be controlled with immunomodulator and biological therapy. High-volume fistulae usually require surgery to achieve symptom control (GRADE: weak recommendation, very low-quality evidence. Agreement: 100%).	

Tableau F-3b Recommandations issues des guides de pratique clinique pour la maladie de Crohn chez l'enfant

CAG 2019 [Mack *et al.*, 2019]	NICE 2019 NG129 [NICE, 2019b]
Recommandations en lien avec l'usage des agents biologiques en première intention pour le traitement de la maladie de Crohn chez l'enfant	
Recommendation 19: In patients with severe inflammatory CD judged at risk for progressive, disabling disease, we suggest anti-TNF therapy as first-line therapy to induce and maintain clinical remission. GRADE: Conditional recommendation, very-low-quality evidence. Vote: strongly agree, 47%; agree, 53%.	Aucune recommandation en lien avec l'usage des agents biologiques en première intention de traitement pour la maladie de Crohn pédiatrique.
Recommandations en lien avec la place des agents biologiques par rapport aux immunosuppresseurs pour l'induction et le maintien de la rémission chez les enfants atteints de la maladie de Crohn	
Recommendation 17: In patients with moderate to severe inflammatory CD who have failed to achieve clinical remission with corticosteroids, we recommend anti-TNF therapy (adalimumab, infliximab) to induce and maintain clinical remission. GRADE: Strong recommendation, high-quality evidence. Vote: strongly agree, 100%. Recommendation 18: In patients with moderate to severe inflammatory CD who fail to achieve or maintain clinical remission with a thiopurine or methotrexate, we recommend anti-TNF therapy to induce and maintain clinical remission. GRADE: Strong recommendation, high-quality evidence. Vote: strongly agree, 93%; agree, 7%. Recommendation 22: In male patients with CD receiving immunomodulator therapy in combination with an anti-TNF therapy, we suggest methotrexate in preference to thiopurines. GRADE: Conditional recommendation, very-low-quality evidence. Recommendation 24: In patients with moderate to severe CD who fail to achieve or maintain clinical remission with anti-TNF–based therapy, we suggest ustekinumab to induce and maintain clinical remission. GRADE: Conditional recommendation, moderate-quality evidence for induction, low-quality evidence for maintenance. Vote: strongly agree, 47%; agree, 53% No consensus I: In patients with moderate to severe inflammatory CD who have achieved clinical remission but not mucosal healing with a corticosteroid, thiopurine, or methotrexate, the consensus group does not make a recommendation (for or against) regarding anti-TNF therapy to induce and maintain mucosal healing.	**1.2 Inducing remission in Crohn's disease** <u>Infliximab and adalimumab</u> 1.2.17 Infliximab, within its licensed indication, is recommended for the treatment of people aged 6 to 17 years with severe active Crohn's disease whose disease has not responded to conventional therapy (including corticosteroids, immunomodulators and primary nutrition therapy), or who are intolerant of or have contraindications to conventional therapy. The need to continue treatment should be reviewed at least every 12 months. [2010]

CAG 2019 [Mack *et al.*, 2019]	NICE 2019 NG129 [NICE, 2019b]
No consensus M: In patients with moderate to severe CD who fail to achieve or maintain clinical remission with an anti-TNF–based therapy, the consensus group does not make a recommendation (for or against) regarding the use vedolizumab to induce and maintain clinical remission.	
Recommandations en lien avec l'usage des thiopurines pour l'induction de la rémission	
Recommendation 12: In patients with CD of any severity, we recommend against thiopurine monotherapy to induce clinical remission. GRADE: Strong recommendation, very-low-quality evidence. Vote: strongly agree, 87%; agree, 13%.	**1.2 Inducing remission in Crohn's disease** Monotherapy 1.2.6 Do not offer azathioprine, mercaptopurine or methotrexate as monotherapy to induce remission. **[2012]** Add-on treatment 1.2.7 **Consider** adding azathioprine or mercaptopurine to a conventional glucocorticosteroid or budesonide to induce remission of Crohn's disease if: • there are 2 or more inflammatory exacerbations in a 12-month period or • the glucocorticosteroid dose cannot be tapered. [2012] In May 2019, the use of budesonide (in children and young people), mercaptopurine, and most preparations of azathioprine was off label. 1.2.8 Assess thiopurine methyltransferase (TPMT) activity before offering azathioprine or mercaptopurine. Do not offer azathioprine or mercaptopurine if TPMT activity is deficient (very low or absent). Consider azathioprine or mercaptopurine at a lower dose if TPMT activity is below normal but not deficient (according to local laboratory reference values). [2012] In May 2019, the use of mercaptopurine and most preparations of azathioprine was off label. 1.2.10 Monitor the effects of azathioprine, mercaptopurine and methotrexate as advised in the BNF or BNFC. Consult the monographs of individual drugs for advice on monitoring immunosuppressives. Monitor for neutropenia in people taking azathioprine or mercaptopurine even if they have normal TPMT activity. [2012] In May 2019, the use of some formulations of methotrexate (in adults), all formulations of methotrexate (in children and young people), mercaptopurine, and most preparations of azathioprine was off label.

CAG 2019 [Mack *et al.*, 2019]	NICE 2019 NG129 [NICE, 2019b]
Recommandations en lien avec l'usage des thiopurines pour le maintien de la rémission	
Recommendation 13: In female patients with CD we suggest a thiopurine to maintain remission. GRADE: Conditional recommendation, low-quality evidence. Vote: strongly agree, 20%; agree, 73%; neutral, 7%. Recommendation 14: In patients with CD, we suggest that testing for TPMT by genotype or enzymatic activity be done prior to initiating thiopurine therapy to guide dosing. GRADE: Conditional recommendation, very-low-quality evidence. Vote: strongly agree, 27%; agree, 67%; neutral, 7%. No consensus F: In male patients with CD the consensus group does not make a recommendation (for or against) regarding a thiopurine to maintain remission.	**1.3 Maintaining remission in Crohn's disease** Maintenance treatment for people who choose this option 1.3.4 Offer azathioprine or mercaptopurine as monotherapy to maintain remission when previously used with a conventional glucocorticosteroid or budesonide to induce remission. [2012] 1.3.5 Consider azathioprine or mercaptopurine to maintain remission in people who have not previously received these drugs (particularly people with adverse prognostic factors such as early age of onset, perianal disease, glucocorticosteroid use at presentation and severe presentations). [2012] See recommendations 1.2.10 and 1.2.11 for guidance on monitoring the effects of azathioprine, mercaptopurine and methotrexate.
Recommandations en lien avec l'usage du méthotrexate pour l'induction de la rémission	
No consensus G: In patients with mild to moderate CD, the consensus group does not make a recommendation (for or against) regarding methotrexate monotherapy to induce clinical remission.	**1.2 Inducing remission in Crohn's disease** Monotherapy 1.2.6 Do not offer azathioprine, mercaptopurine or methotrexate as monotherapy to induce remission. **[2012]** Add-on treatment 1.2.9 **Consider** adding methotrexate (follow British national formulary [BNF]/British national formulary for children [BNFC] cautions) to a conventional glucocorticosteroid or budesonide to induce remission in people who cannot tolerate azathioprine or mercaptopurine, or in whom TPMT activity is deficient, if: • there are 2 or more inflammatory exacerbations in a 12-month period or • the glucocorticosteroid dose cannot be tapered. [2012] In May 2019, the use of some formulations of methotrexate (in adults), all formulations of methotrexate (in children and young people), and budesonide (in children and young people) was off label. 1.2.10 Monitor the effects of azathioprine, mercaptopurine and methotrexate as advised in the BNF or BNFC. Consult the monographs of individual drugs for

CAG 2019 [Mack *et al.*, 2019]	NICE 2019 NG129 [NICE, 2019b]
	advice on monitoring immunosuppressives. Monitor for neutropenia in people taking azathioprine or mercaptopurine even if they have normal TPMT activity. [2012] In May 2019, the use of some formulations of methotrexate (in adults), all formulations of methotrexate (in children and young people), mercaptopurine, and most preparations of azathioprine was off label.
Recommandations en lien avec l'usage du méthotrexate pour le maintien de la rémission	
Recommendation 15: In patients with CD we suggest parenteral methotrexate to maintain clinical remission. GRADE: Conditional recommendation, low-quality evidence. Vote: strongly agree, 40%; agree, 60%. No consensus H: In patients with CD, the consensus group does not make a recommendation (for or against) regarding oral methotrexate to maintain clinical remission.	**1.3 Maintaining remission in Crohn's disease** <u>Maintenance treatment for people who choose this option</u> 1.3.6 Consider methotrexate (follow BNF/BNFC cautions) to maintain remission only in people who: • needed methotrexate to induce remission or • have tried but did not tolerate azathioprine or mercaptopurine for maintenance or • have contraindications to azathioprine or mercaptopurine (for example, deficient thiopurine methyltransferase [TPMT] activity or previous episodes of pancreatitis). [2012] See recommendations 1.2.10 and 1.2.11 for guidance on monitoring the effects of azathioprine, mercaptopurine and methotrexate.

Tableau F-3c Recommandations issues des guides de pratique clinique pour la colite ulcéreuse chez l'adulte

AGA 2020 [Feuerstein *et al.*, 2020]	BSG 2019 [Lamb *et al.*, 2019]	NICE 2019 NG130 [NICE, 2019a]
Recommandations en lien avec l'usage des agents biologiques en première intention pour le traitement de la colite ulcéreuse chez l'adulte		
6. In adult outpatients with moderate to severe UC, the AGA suggests early use of biologic agents with or without immunomodulator therapy rather than gradual step up after failure of 5-ASA. Comment: Patients, particularly those with less severe disease, who place higher value on the safety of 5-ASA therapy and lower value on the efficacy of biologic agents or tofacitinib may reasonably chose gradual step therapy with 5-ASA therapy. Conditional Very low	Aucune recommandation sur l'usage des agents biologiques en première intention de traitement	Aucune recommandation sur l'usage des agents biologiques en première intention de traitement
Recommandations en lien avec la place des agents biologiques par rapport aux immunosuppresseurs pour l'induction et le maintien de la rémission chez les adultes atteints de colite ulcéreuse		
1. In adult outpatients with moderate to severe UC, the AGA recommends using infliximab, adalimumab, golimumab, vedolizumab, tofacitinib, or ustekinumab over no treatment. (Medications are ordered based on year of approval by the US FDA.) Strong Moderate 2a. In adult outpatients with moderate to severe UC who are naïve to biologic agents, the AGA suggests using infliximab or vedolizumab rather than adalimumab, for induction of remission. Comment: Patients, particularly those with less severe disease, who place higher value on the convenience of self-administered subcutaneous injection, and a lower value on the relative efficacy of medications, may reasonably chose adalimumab as an alternative. Conditional Moderate 2c. In adult outpatients with moderate to severe UC who have previously been exposed to infliximab, particularly those with primary nonresponse, the AGA suggests using ustekinumab or tofacitinib rather than vedolizumab or adalimumab for induction of remission. Conditional Low	Statement 9. We recommend that ulcerative colitis patients on maintenance therapy with high-dose mesalazine, who required two or more courses of corticosteroids in the past year, or who become corticosteroid-dependent or refractory, require treatment escalation with thiopurine (GRADE: strong recommendation, moderate-quality evidence), anti-TNF therapy (GRADE: strong recommendation, high-quality evidence), vedolizumab (GRADE: strong recommendation, high-quality evidence) or tofacitinib (GRADE: strong recommendation, high-quality evidence). The choice of drug should be determined by clinical factors, patient choice, cost, likely adherence and local infusion capacity (Agreement: 96.6%). Statement 10. We recommend that vedolizumab can be used in the induction and maintenance of remission of ulcerative colitis in patients where anti-TNF treatment has failed (GRADE: strong recommendation, high-quality evidence. Agreement: 97.7%).	**1.2 Inducing remission in people with ulcerative colitis** <u>Biologics inhibitors for moderately to severely active ulcerative colitis: all extents of disease</u> 1.2.14 For guidance on biologics inhibitors for treating moderately to severely active ulcerative colitis, see the: • NICE technology appraisal guidance on infliximab, adalimumab and golimumab for moderately to severely active ulcerative colitis (NICE TA329) • NICE technology appraisal guidance on vedolizumab for treating moderately to severely active ulcerative colitis (NICE TA342) • NICE technology appraisal guidance on Ustekinumab for treating moderately to severely active ulcerative colitis (NICE TA633)

AGA 2020 [Feuerstein *et al.*, 2020]	BSG 2019 [Lamb *et al.*, 2019]	NICE 2019 NG130 [NICE, 2019a]
4a. In adult outpatients with active moderate to severe UC, the AGA suggests using biologic monotherapy (TNF-a antagonists, vedolizumab, or ustekinumab) or tofacitinib rather than thiopurine monotherapy for induction of remission. Conditional Low 4b. In adult outpatients with moderate to severe UC in remission, the AGA makes no recommendation in favor of or against using biologic monotherapy or tofacitinib rather than thiopurine monotherapy for maintenance of remission. No recommendation Knowledge gap 5a. In adult outpatients with moderate to severe UC, the AGA suggests combining TNF-a antagonists, vedolizumab or ustekinumab with thiopurines or methotrexate rather than biologic monotherapy. Comment: Patients, particularly those with less severe disease, who place higher value on the safety of biologic monotherapy and lower value on the efficacy of combination therapy may reasonably chose biologic monotherapy. Conditional Low 5b. In adult outpatients with moderate to severe UC, the AGA suggests combining TNF-a antagonists, vedolizumab, or ustekinumab with thiopurines or methotrexate rather than thiopurine monotherapy. Conditional Low Recommendation 10. In hospitalized adult patients with ASUC refractory to intravenous corticosteroids, the AGA suggests using infliximab or cyclosporine. (conditional recommendation, low quality of evidence)	Statement 18. We recommend that patients with ASUC failing to respond by day 3, as judged by a suitable scoring system, should be treated with rescue therapy in the form of intravenous infliximab or ciclosporin for patients who have not previously failed thiopurine therapy (GRADE: strong recommendation, highquality evidence. Agreement: 97.8%).	<u>Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy [TA329]</u> *1. Guidance* 1.1 Infliximab, adalimumab and golimumab are recommended, within their marketing authorisations, as options for treating moderately to severely active ulcerative colitis in adults whose disease has responded inadequately to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who cannot tolerate, or have medical contraindications for, such therapies. Golimumab is recommended only if the company provides the 100 mg dose of golimumab at the same cost as the 50 mg dose, as agreed in the patient access scheme. 1.2 The choice of treatment between infliximab, adalimumab or golimumab should be made on an individual basis after discussion between the responsible clinician and the patient about the advantages and disadvantages of the treatments available. This should take into consideration therapeutic need and whether or not the patient is likely to adhere to treatment. If more than 1 treatment is suitable, the least expensive should be chosen (taking into account administration costs, dosage and price per dose). *3. The technologies* 3.1 Adalimumab (Humira, AbbVie), golimumab (Simponi, Merck Sharp & Dohme) and infliximab (Remicade, Merck Sharp & Dohme; Inflectra, Hospira; Remsima, Celltrion) are monoclonal antibodies that inhibit the pro-inflammatory cytokine, TNF-alpha. All 3 have the same marketing

AGA 2020 [Feuerstein *et al.*, 2020]	BSG 2019 [Lamb *et al.*, 2019]	NICE 2019 NG130 [NICE, 2019a]
		authorisation in the UK for the 'treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who are intolerant to or have medical contraindications for such therapies'. Infliximab is also indicated for the 'treatment of severely active ulcerative colitis, in children and adolescents aged 6 to 17 years, who have had an inadequate response to conventional therapy including corticosteroids and mercaptopurine or azathioprine, or who are intolerant to or have medical contraindications for such therapies'. <u>Vedolizumab for treating moderately to severely active ulcerative colitis, Technology appraisal guidance [TA342]</u> *1. Guidance* 1.1 Vedolizumab is recommended, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults only if the company provides vedolizumab with the discount agreed in the patient access scheme. *2. The technology* 2.1 Vedolizumab (Entyvio, Takeda) is a humanised monoclonal antibody. It targets α4β7 integrin, which is expressed in certain white blood cells that are found in the gut. α4β7 integrin is responsible for recruiting these cells to inflamed bowel tissue. Vedolizumab therefore specifically targets the gut. The marketing authorisation states that vedolizumab is indicated 'for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, or lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha antagonist'. The recommended dosage of vedolizumab is 300 mg

AGA 2020 [Feuerstein *et al.*, 2020]	BSG 2019 [Lamb *et al.*, 2019]	NICE 2019 NG130 [NICE, 2019a]
		given by intravenous infusion at 0, 2 and 6 weeks and then every 8 weeks thereafter. Continued therapy for people with ulcerative colitis should be carefully reconsidered if no evidence of therapeutic benefit is observed by week 10. <u>Ustekinumab for treating moderately to severely active ulcerative colitis [TA633]</u> *1. Recommendations* 1.1 Ustekinumab is recommended as an option for treating moderately to severely active ulcerative colitis in adults when conventional therapy or a biological agent cannot be tolerated, or the disease has responded inadequately or lost response to treatment, only if: • a tumour necrosis factor-alpha inhibitor has failed (that is the disease has responded inadequately or has lost response to treatment) or • a tumour necrosis factor-alpha inhibitor cannot be tolerated or is not suitable, and • the company provides ustekinumab at the same price or lower than that agreed with the Commercials Medicines Unit. *2. Information about ustekinumab* 2.1 Ustekinumab (Stelara, Janssen) has a marketing authorisation that includes the following indication: 'treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies'.

AGA 2020 [Feuerstein *et al.*, 2020]	BSG 2019 [Lamb *et al.*, 2019]	NICE 2019 NG130 [NICE, 2019a]
Recommandations en lien avec l'usage des thiopurines pour l'induction de la rémission		
3a. In adult outpatients with active moderate to severe ulcerative colitis, the AGA suggests against using thiopurine monotherapy for INDUCTION of remission. (Conditional recommendation, very low quality of evidence)	Aucune recommandation sur l'usage des thiopurines pour l'induction de la rémission. Toutefois, il est indiqué dans le corps du texte : While studies vary in quality, meta-analyses consistently report a benefit of thiopurines over placebo for the maintenance of steroid-induced remission in UC but not for induction of remission.	Aucune recommandation sur l'usage des thiopurines pour l'induction de la rémission.
Recommandations en lien avec l'usage des thiopurines pour le maintien de la rémission		
3b. In adult outpatients with moderate to severe ulcerative colitis in remission, the AGA suggests using thiopurine monotherapy, rather than no treatment, for MAINTENANCE of remission. (Conditional recommendation low quality of evidence)	Statement 9. We recommend that ulcerative colitis patients on maintenance therapy with high-dose mesalazine, who required two or more courses of corticosteroids in the past year, or who become corticosteroid-dependent or refractory, require treatment escalation with thiopurine (GRADE: strong recommendation, moderate-quality evidence), anti-TNF therapy (GRADE: strong recommendation, high-quality evidence), vedolizumab (GRADE: strong recommendation, high-quality evidence) or tofacitinib (GRADE: strong recommendation, high-quality evidence). The choice of drug should be determined by clinical factors, patient choice, cost, likely adherence and local infusion capacity (Agreement: 96.6%).	**1.4 Maintaining remission in people with ulcerative colitis** <u>All extents of disease</u> 1.4.4 **Consider** oral azathioprine or oral mercaptopurine to maintain remission: • after 2 or more inflammatory exacerbations in 12 months that require treatment with systemic corticosteroids or • if remission is not maintained by aminosalicylates. [2013] In May 2019, this was an off-label use of some brands of azathioprine and mercaptopurine. See NICE's information on prescribing medicines. 1.4.5 To maintain remission after a single episode of acute severe ulcerative colitis: • consider oral azathioprine or oral mercaptopurine • consider oral aminosalicylates if azathioprine and/or mercaptopurine are contraindicated or the person cannot tolerate them. [2013] In May 2019, this was an off-label use of some brands of azathioprine and mercaptopurine. See NICE's information on prescribing medicines.

AGA 2020 [Feuerstein *et al.*, 2020]	BSG 2019 [Lamb *et al.*, 2019]	NICE 2019 NG130 [NICE, 2019a]
Recommandations en lien avec l'usage du méthotrexate pour l'induction de la rémission		
3c. In adult outpatients with moderate to severe ulcerative colitis, the AGA suggests against using methotrexate monotherapy for induction or maintenance of remission. (Conditional recommendation, low quality evidence)	Aucune recommandation sur l'usage du méthotrexate pour l'induction de la rémission.	Aucune recommandation sur l'usage du méthotrexate pour l'induction de la rémission.
Recommandations en lien avec l'usage du méthotrexate pour le maintien de la rémission		
3c. In adult outpatients with moderate to severe ulcerative colitis, the AGA suggests against using methotrexate monotherapy for induction or maintenance of remission. (Conditional recommendation, low quality evidence)	Aucune recommandation sur l'usage du méthotrexate pour le maintien de la rémission. Toutefois, il est indiqué dans le corps du texte : Methotrexate has no role in the maintenance of remission in UC.	**1.4 Maintaining remission in people with ulcerative colitis** All extents of disease

Tableau F-3d Recommandations issues des guides de pratique clinique pour le psoriasis en plaques chez l'adulte

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
Recommandations en lien avec l'usage des agents biologiques en première intention pour le traitement du psoriasis en plaques chez l'adulte		
Aucune recommandation sur l'usage des agents biologiques en première intention de traitement	In case of severe disease, where a sufficient treatment success cannot be expected with the use of a conventional treatment, the initiation of a biologic with a first line label* is suggested as a first line treatment (weak recommendation for). *"First line label" refers to the therapeutic indication as approved by the European Medical Agency.	Aucune recommandation sur l'usage des agents biologiques en première intention de traitement
Recommandations en lien avec la place des agents biologiques par rapport aux immunosuppresseurs pour l'induction et le maintien de la rémission chez les adultes atteints de psoriasis en plaques		
R4 (↑↑) Offer biologic therapy to people with psoriasis requiring systemic therapy if methotrexate and ciclosporin have failed, are not tolerated or are contraindicated [see National Institute for Health and Care Excellence (NICE) guidelines CG153] and the psoriasis has a large impact on physical, psychological or social functioning [for example, Dermatology Life Quality Index (DLQI) or Children's DLQI > 10 or clinically relevant depressive or anxiety symptoms] and one or more of the following disease severity criteria apply: • the psoriasis is extensive [defined as body surface area (BSA) > 10% or Psoriasis Area and Severity Index (PASI) ≥ 10] • the psoriasis is severe at localized sites and associated with significant functional impairment and/or high levels of distress (for example nail disease or involvement of highimpact and difficult-to-treat sites such as the face, scalp, palms, soles, flexures and genitals). R5 (↑) Consider biologic therapy earlier in the treatment pathway (e.g. if methotrexate has failed, is not tolerated or is contraindicated) in people with psoriasis who fulfil the disease severity criteria and who also have active psoriatic arthritis (see the NICE	We recommend to take efficacy and safety (see Figure 6 /Cochrane Review and drug chapters), time until onset of treatment response, comorbidities (see decision grids, section Guidance for specific clinical and comorbid situations), and individual patient factors into account when choosing a systemic treatment for moderate or severe psoriasis. In addition, national regulations and reimbursement circumtances need to be taken into consideration and treatment algorithms should be developed on a national level (strong recommendation for). We recommend the initiation of systemic treatment in patients with moderate to severe (as defined in each country, see also section "Defining disease severity") psoriasis* (strong recommendation for). *UV therapy is not part of this guideline but it is recommended as an alternative induction therapy if suitable. For most patients who require systemic treatment, we recommend the initiation of 'conventional' systemic agents as first line treatment (strong recommendation for).	**1.5 Systemic therapy** 1.5.1.2 When offering systemic therapy, tailor the choice of agent and dosing schedule to the needs of the individual and include consideration of: • the person's age • disease phenotype, pattern of activity and previous treatment history • disease severity and impact • the presence of psoriatic arthritis (in consultation with a rheumatologist) • conception plans • comorbidities • the person's views. <u>1.5.3 Systemic biological therapy</u> The GDG did not review evidence for any aspect of the use of a first biological agent because guidance on this is already available in the existing NICE technology appraisals [36]. 1.5.3.2 If a person has both psoriasis and psoriatic arthritis, take into account both conditions before

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
musculoskeletal conditions overview)8 or who have psoriasis that is persistent, i.e. that relapses rapidly (defined as > 50% baseline disease severity within 3 months of completion of any treatment) off a therapy that cannot be continued in the long term (e.g. narrowband ultraviolet B and ciclosporin).	We recommend the initiation of a biologic if conventional systemic agents were inadequate in response, are contraindicated or not tolerated (strong recommendation for). We suggest to use apremilast if an oral treatment is desired and "conventional" systemic agents were inadequate in response or if they are contraindicated or not tolerated (weak recommendation for). *Strong consensus, 100% agreement, evidence and consensus-based recommendations.*	initiating or making changes to biological therapy and manage their treatment in consultation with a rheumatologist (see also the NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis[37], ustekinumab for treating active psoriatic arthritis[38], certolizumab pegol and secukinumab for treating active psoriatic arthritis after inadequate response to DMARDs[37] and golimumab for the treatment of psoriatic arthritis [37], and the NICE guideline on spondyloarthritis in over 16s). <u>Adalimumab for the treatment of adults with psoriasis [TA146].</u> 1.1 Adalimumab is recommended as a treatment option for adults with plaque psoriasis for whom anti-tumour necrosis factor (TNF) treatment is being considered and when the following criteria are both met. • The disease is severe as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10. • The psoriasis has not responded to standard systemic therapies including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation); or the person is intolerant of, or has a contraindication to, these treatments. 1.2 Adalimumab should be discontinued in people whose psoriasis has not responded adequately at 16 weeks. An adequate response is defined as either: • a 75% reduction in the PASI score (PASI 75) from when treatment started, or • a 50% reduction in the PASI score (PASI 50) and a five-point reduction in DLQI from start of treatment. <u>Etanercept and efalizumab for the treatment of adults with psoriasis [TA103]</u>

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
		1.1 Etanercept, within its licensed indications, administered at a dose not exceeding 25 mg twice weekly is recommended for the treatment of adults with plaque psoriasis only when the following criteria are met. • The disease is severe as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10. • The psoriasis has failed to respond to standard systemic therapies including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation); or the person is intolerant to, or has a contraindication to, these treatments. 1.2 Etanercept treatment should be discontinued in patients whose psoriasis has not responded adequately at 12 weeks. Further treatment cycles are not recommended in these patients. An adequate response is defined as either: • a 75% reduction in the PASI score from when treatment started (PASI 75) or • a 50% reduction in the PASI score (PASI 50) and a five-point reduction in DLQI from when treatment started. <u>Infliximab for the treatment of adults with psoriasis [TA134]</u> 1.1 Infliximab, within its licensed indications, is recommended as a treatment option for adults with plaque psoriasis only when the following criteria are met. • The disease is very severe as defined by a total Psoriasis Area Severity Index (PASI) of 20 or more and a Dermatology Life Quality Index (DLQI) of more than 18. • The psoriasis has failed to respond to standard systemic therapies such as

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
		ciclosporin, methotrexate or PUVA (psoralen and long-wave ultraviolet radiation), or the person is intolerant to or has a contraindication to these treatments. 1.2 Infliximab treatment should be continued beyond 10 weeks only in people whose psoriasis has shown an adequate response to treatment within 10 weeks. An adequate response is defined as either: • a 75% reduction in the PASI score from when treatment started (PASI 75) or • a 50% reduction in the PASI score (PASI 50) and a five-point reduction in the DLQI from when treatment started. <u>Certolizumab pegol for treating moderate to severe plaque psoriasis [TA574]</u> 1.1 Certolizumab pegol is recommended as an option for treating plaque psoriasis in adults, only if: • the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and • the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and • the lowest maintenance dosage of certolizumab pegol is used (200 mg every 2 weeks) after the loading dosage and • the company provides the drug according to the commercial arrangement. <u>Ixekizumab for treating moderate to severe plaque psoriasis [TA442]</u> 1.1 Ixekizumab is recommended as an option for treating plaque psoriasis in adults, only if:

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
		• the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 • the disease has not responded to standard systemic therapies, for example, ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation), or these treatments are contraindicated or the person cannot tolerate them, and • the company provides the drug with the discount agreed in the patient access scheme. 1.2 Stop ixekizumab treatment at 12 weeks if the psoriasis has not responded adequately. An adequate response is defined as: • a 75% reduction in the PASI score (PASI 75) from when treatment started or • a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started. <u>Secukinumab for treating moderate to severe plaque psoriasis [TA350]</u> 1.1 Secukinumab is recommended, within its marketing authorisation, as an option for treating adults with plaque psoriasis only when: • the disease is severe, as defined by a total Psoriasis Area Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 • the disease has failed to respond to standard systemic therapies, for example, ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation), or these treatments are contraindicated or the person cannot tolerate them

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
		• the company provides secukinumab with the discount agreed in the patient access scheme. 1.2 Secukinumab treatment should be stopped in people whose psoriasis has not responded adequately at 12 weeks. Further treatment cycles are not recommended in these people. An adequate response is defined as either: • a 75% reduction in the PASI score from when treatment started (PASI 75) or • a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in DLQI from when treatment started. <u>Brodalumab for treating moderate to severe plaque psoriasis [TA511]</u> Brodalumab is recommended as an option for treating plaque psoriasis in adults, only if: • the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and • the disease has not responded to other systemic therapies, including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet A radiation), or these options are contraindicated or not tolerated and • the company provides the drug with the discount agreed in the patient access scheme. <u>Ustekinumab for the treatment of adults with moderate to severe psoriasis [TA180]</u> 1.1 Ustekinumab is recommended as a treatment option for adults with plaque psoriasis when the following criteria are met.

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
		• The disease is severe, as defined by a total Psoriasis Area Severity Index (PASI) score of 10 or more and a Dermatology Life Quality Index (DLQI) score of more than 10. • The psoriasis has not responded to standard systemic therapies, including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet radiation), or the person is intolerant of or has a contraindication to these treatments. 1.2Ustekinumab treatment should be stopped in people whose psoriasis has not responded adequately by 16 weeks after starting treatment. An adequate response is defined as either: • a 75% reduction in the PASI score (PASI 75) from when treatment started or • a 50% reduction in the PASI score (PASI 50) and a 5-point reduction in the DLQI score from when treatment started. <u>Guselkumab for treating moderate to severe plaque psoriasis [TA521]</u> 1.1 Guselkumab is recommended as an option for treating plaque psoriasis in adults, only if: • the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and • the disease has not responded to other systemic therapies, including ciclosporin, methotrexate and PUVA (psoralen and long-wave ultraviolet A radiation), or these options are contraindicated or not tolerated and • the company provides the drug according to the commercial arrangement.

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
		Risankizumab for treating moderate to severe plaque psoriasis [TA596] Risankizumab is recommended as an option for treating plaque psoriasis in adults, only if: • the disease is severe, as defined by a total Psoriasis Area and Severity Index (PASI) of 10 or more and a Dermatology Life Quality Index (DLQI) of more than 10 and • the disease has not responded to other systemic treatments, including ciclosporin, methotrexate and phototherapy, or these options are contraindicated or not tolerated and • the company provides the drug according to the commercial arrangement.
Recommandations en lien avec l'usage des agents de rémission systémiques conventionnels pour le traitement du psoriasis en plaques		
R4 (strong recommendation for) : Offer biologic therapy to people with psoriasis requiring systemic therapy if methotrexate and ciclosporin have failed, are not tolerated or are contraindicated [see National Institute for Health and Care Excellence (NICE) guidelines CG153] and the psoriasis has a large impact on physical, psychological or social functioning [for example, Dermatology Life Quality Index (DLQI) or Children's DLQI > 10 or clinically relevant depressive or anxiety symptoms] and one or more of the following disease severity criteria apply: • the psoriasis is extensive [defined as body surface area (BSA) > 10% or Psoriasis Area and Severity Index (PASI) ≥ 10] • the psoriasis is severe at localized sites and associated with significant functional impairment and/or high levels of distress (for example nail disease or involvement of high-impact and difficult-to-treat sites such as the	We recommend to take efficacy and safety (see Figure 6 /Cochrane Review and drug chapters), time until onset of treatment response, comorbidities (see decision grids, section Guidance for specific clinical and comorbid situations), and individual patient factors into account when choosing a systemic treatment for moderate or severe psoriasis. In addition, national regulations and reimbursement circumtances need to be taken into consideration and treatment algorithms should be developed on a national level (strong recommendation for). We recommend the initiation of systemic treatment in patients with moderate to severe (as defined in each country, see also section "Defining disease severity") psoriasis* (strong recommendation for). *UV therapy is not part of this guideline but it is recommended as an alternative induction therapy if suitable. For most patients who require systemic treatment, we recommend the initiation of 'conventional' systemic	**1.5 Systemic therapy** 1.5.1 General recommendations 1.5.1.2 When offering systemic therapy, tailor the choice of agent and dosing schedule to the needs of the individual and include consideration of: • the person's age • disease phenotype, pattern of activity and previous treatment history • disease severity and impact • the presence of psoriatic arthritis (in consultation with a rheumatologist) • conception plans • comorbidities • the person's views. 1.5.2 Systemic non-biological therapy

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
face, scalp, palms, soles, flexures and genitals).	agents as first line treatment (strong recommendation for). In case of severe disease, where a sufficient treatment success cannot be expected with the use of a conventional treatment, the initiation of a biologic with a first line label* is suggested as a first line treatment (weak recommendation for). *"First line label" refers to the therapeutic indication as approved by the European Medical Agency. We recommend the initiation of a biologic if conventional systemic agents were inadequate in response, are contraindicated or not tolerated (strong recommendation for). We suggest to use apremilast if an oral treatment is desired and "conventional" systemic agents were inadequate in response or if they are contraindicated or not tolerated (weak recommendation for). *Strong consensus, 100% agreement, evidence and consensus-based recommendations.*	1.5.2.1 Offer systemic non-biological therapy to people with any type of psoriasis if: it cannot be controlled with topical therapy and it has a significant impact on physical, psychological or social wellbeing and one or more of the following apply: • psoriasis is extensive (for example, more than 10% of body surface area affected or a PASI score of more than 10) or • psoriasis is localised and associated with significant functional impairment and/or high levels of distress (for example severe nail disease or involvement at high-impact sites) or • phototherapy has been ineffective, cannot be used or has resulted in rapid relapse (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months). 1.5.2.2 Offer methotrexate [34] as the first choice of systemic agent for people with psoriasis who fulfil the criteria for systemic therapy (see previous recommendation 1.5.2.1) except in the circumstances described in recommendations 1.5.2.4 and 1.5.2.12. 1.5.2.3 In people with both active psoriatic arthritis and any type of psoriasis that fulfils the criteria for systemic therapy (see recommendation 1.5.2.1) consider the choice of systemic agent in consultation with a rheumatologist. 1.5.2.4 Offer ciclosporin [35] as the first choice of systemic agent for people who fulfil the criteria for systemic therapy (see recommendation 1.5.2.1) and who: • need rapid or short-term disease control (for example a psoriasis flare) or • have palmoplantar pustulosis or

BAD 2020 [Smith *et al.*, 2020]	EuroGuiDerm 2020/2021 [Nast *et al.*, 2021; Nast *et al.*, 2020]	NICE CG153 2017 [NICE, 2017]
		• are considering conception (both men and women) and systemic therapy cannot be avoided. 1.5.2.5 Consider changing from methotrexate to ciclosporin (or vice-versa) when response to the first-choice systemic treatment is inadequate. 1.5.2.6 Consider acitretin[32] for adults, and in exceptional cases only for children and young people, in the following circumstances: • if methotrexate and ciclosporin are not appropriate or have failed or • for people with pustular forms of psoriasis. 1.5.2.12 When considering the risks and benefits of treating any type of psoriasis with methotrexate, be aware that methotrexate can cause a clinically significant rise in transaminases and that long-term therapy may be associated with liver fibrosis (see recommendations 1.5.2.13 to 1.5.2.16).

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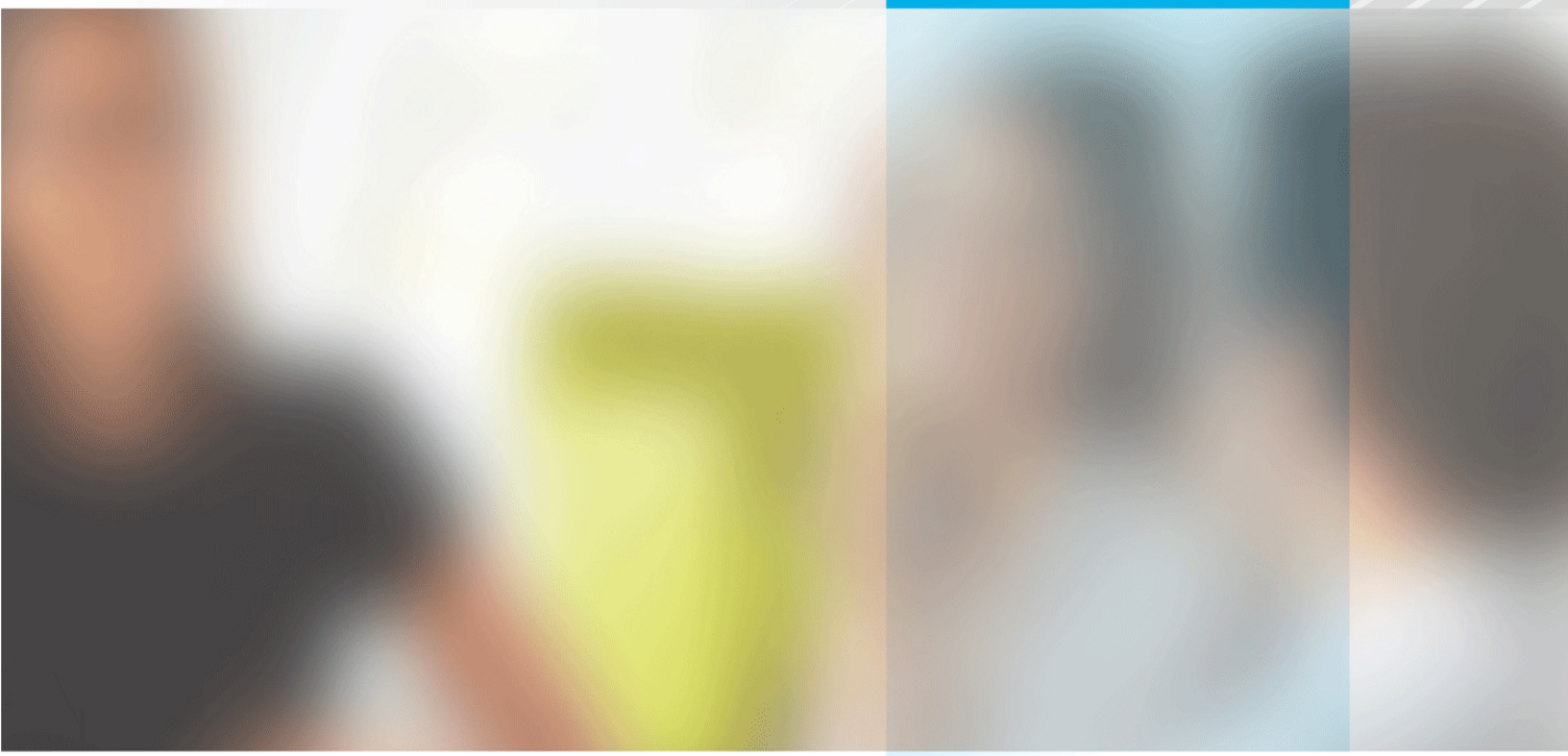

Siège social

2535, boulevard Laurier, 5e étage
Québec (Québec) G1V 4M3
418 643-1339

Bureau de Montréal

2021, avenue Union, 12e étage, bureau 1200
Montréal (Québec) H3A 2S9
514 873-2563
inesss.qc.ca

Institut national d'excellence en santé et en services sociaux
Québec