Resolution
by the Federal Joint Committee
on an amendment to the Pharmaceutical Directive (AM-RL):
Appendix XII – Resolutions on the benefit assessment of pharmaceuticals with new active ingredients, in accordance with the German Social Code, Book Five (SGB V), section 35a
Apremilast

From 6 August 2015

In its session on 6 August 2015, the Federal Joint Committee resolved to amend the Pharmaceutical Directive (AM-RL), version published 18 December 2008/22 January 2009 (Federal Gazette, number 49a of 31 March 2009), last amended on 16 July 2015 (Federal Gazette, AT 1 October 2015 B2) as follows:

I.

Appendix XII shall be amended in alphabetical order to include the active ingredient apremilast:

Apremilast

Therapeutic indication:

Psoriatic arthritis

Otezla, alone or in combination with disease-modifying antirheumatic drugs (DMARDs), is indicated for the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior DMARD therapy (see section 5.1 of the product information).

Psoriasis

Otezla is indicated for the treatment of moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or psoralen and ultraviolet-A light (PUVA).

1. Additional benefit of the pharmaceutical over appropriate comparator

   a) Psoriatic arthritis

      Appropriate comparator:

      The appropriate comparator for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior DMARD therapy is:

      – TNF-alpha inhibitor (etanercept or adalimumab or infliximab or golimumab), if applicable in combination with methotrexate.

      Extent and probability of additional benefit over appropriate comparator:

      An additional benefit has not been proved.

   b) Plaque psoriasis

      Appropriate comparator:

      The appropriate comparator for the treatment of adult patients with moderate to severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or psoralen and ultraviolet-A light (PUVA) is.

      – Adalimumab or infliximab or ustekinumab

      Extent and probability of additional benefit over appropriate comparator:

      An additional benefit has not been proved.

2. Number of patients and criteria for defining patients eligible for treatment

   a) Psoriatic arthritis

      approx. 18,400 to 43,400 patients

   b) Plaque psoriasis

      approx. 32,400 to 97,100 patients

3. Requirements for quality-assured administration

The specifications outlined in the product information are to be followed. The European Medicines Agency (EMA), the European regulatory authority, provides the contents of the product information for Otezla® (active ingredient: apremilast) at the following public link (last accessed: 27 May 2015):

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003746/WC500182627.pdf

Treatment with apremilast must be initiated and monitored by physicians experienced in the treatment of patients with psoriasis or psoriatic arthritis.

If no therapeutic benefit is apparent in a patient after 24 weeks, treatment with apremilast should be reconsidered.

4. Costs of treatment

a) Psoriatic arthritis and b) plaque psoriasis

Duration of treatment:

Designation of therapy	Mode of treatment	Duration per treatment	Number of treatment days per patient per yea
Pharmaceutical evaluated			
Apremilast	2 x daily	ongoing	365
Methotrexate[1]	1 x weekly	ongoing	52
Appropriate comparator for the indication a) psoriatic arthritis			
Etanercept	2 x weekly 25 mg or 1 x weekly 50 mg	ongoing	104 or 52
Adalimumab	every 2nd week	ongoing	26
Infliximab	every 8 weeks	ongoing	6.5
Golimumab	1 x monthly	ongoing	12
Methotrexate[2]	1 x weekly	ongoing	52
Appropriate comparator for the indication b) plaque psoriasis			
Adalimumab	every 2nd week	ongoing	26
Infliximab	every 8 weeks	ongoing	6.5
Ustekinumab	every 12 weeks	ongoing	4.3

Consumption:

Designation of therapy	Strength (mg)	Dosage	Quantity per pack (pre-filled syringes [PFS]/ (coated) tablets [(C)tab]/vials [V])	Average annual consumption (pre-filled syringes [PFS]/(coated) tablets [(C)tab])
Pharmaceutical evaluated				
Apremilast	30 mg[3]	60 mg/day	168 Ctab	730 Ctab
Methotrexate[1]	7.5 – 15 mg	7.5 – 30 mg	30 tab	52 – 104 tab
Appropriate comparator for the indication a) psoriatic arthritis				
Etanercept	25 mg	2 x weekly 25 mg	24 PFS	104 PFS
	50 mg	1 x weekly 50 mg	12 PFS	52 PFS
Adalimumab	40 mg	40 mg	6 PFS	26 PFS
Infliximab	100 mg/vial	5 mg/kg BW	5 V	26 V[4]
Golimumab	50 mg	50 mg	3 PFS	12 PFS
Methotrexate	7.5 – 15 mg	7.5 – 30 mg	30 tab	52 – 104 tab
Appropriate comparator for the indication b) plaque psoriasis				
Adalimumab	40 mg	40 mg	6 PFS	26 PFS

[1] Only for the indication psoriatic arthritis. Methotrexate is named as an example of the combination of disease-modifying antirheumatic drugs (DMARDs).

[2] MTX only in combination with infliximab or golimumab, if indicated

[3] Other dosages available: starter pack with 4 x 10 mg, 4 x 20 mg, 19 x 30 mg apremilast

[4] Based on a body weight of 76.3 kg (microcensus 2013)

Designation of therapy	Strength (mg)	Dosage	Quantity per pack (pre-filled syringes [PFS]/ (coated) tablets [(C)tab]/vials [V])	Average annual consumption (pre-filled syringes [PFS]/(coated) tablets [(C)tab])
Infliximab	100 mg/vial	5 mg/kg BW	5 V	26 V[4]
Ustekinumab	45 mg	45 mg	1 PFS	4.3 PFS

Costs:

Cost of pharmaceutical:

Designation of therapy	Cost (pharmacy retail price)	Cost after legally mandated rebates
Pharmaceutical evaluated		
Apremilast	€4,080.34	€3,848.81 [€1.77[5]; €229.76[6]]
Methotrexat 7.5 mg[1]	€33.42[7]	€29.88 [€1.77[5]; €1.77[6]]
Methotrexat 10 mg[1]	€41.29[7]	€37.12 [€1.77[5]; €2.40[6]]
Methotrexat 15 mg[1]	€57.45[7]	€52.00 [€1.77[5]; €3.68[6]]
Appropriate comparator for the indication a) psoriatic arthritis		
Etanercept 25 mg	€5,231.36	€4,934.10 [€1.77[5]; €295.49[6]]
Etanercept 50 mg	€5,231.36	€4,934.10 [€1.77[5]; €295.49[6]]
Adalimumab	€5,231.36	€4,934.10 [€1.77[5]; €295.49[6]]
Infliximab	€3,506.19	€3,335.59 [€1.77[5]; €168.83[6]]
Golimumab	€5,308.97	€5,007.28 [€1.77[5]; €299.76[6]]
Methotrexate 7.5 mg	€33.42[7]	€29.88 [€1.77[5]; €1.77[6]]
Methotrexate 10 mg	€41.29[7]	€37.12 [€1.77[5]; €2.40[6]]
Methotrexate 15 mg	€57.45[7]	€52.00 [€1.77[5]; €3.68[6]]
Appropriate comparator for the indication b) plaque psoriasis		
Adalimumab	€5,231.36	€4,934.10 [€1.77[5]; €295.49[6]]
Infliximab	€3,506.19	€3,335.59 [€1.77[5]; €168.83[6]]
Ustekinumab	€5,021.41	€4,736.14 [€1.77[5]; €283.50[6]]

"Lauer-Taxe", effective: 15 June 2015

[5] Rebate in accordance with SGB V, section 130

[6] Rebate in accordance with SGB V, section 130a

[7] Reference price

Costs for additional, necessary statutory health insurance (SHI) benefits:

Designation of therapy	Designation of service	Number	Cost per unit	Cost per patient per year
Appropriate comparator				
Adalimumab Etanercept Golimumab Infliximab Ustekinumab	Quantitative test for in vitro interferon-gamma discharge after ex vivo stimulation with antigen (at least ESAT-6 and CFP-10) specifically for mycobacterium tuberculosis complex (except BCG) (fee schedule item [GOP] 32670)	1	€58.00	€58.00
Adalimumab Etanercept Golimumab Infliximab	HBs antigen (GOP 32781)	1	€5.50	€5.50
	anti-HBs antibodies (GOP 32617)[8]	1	€5.50	€5.50
	anti-HBc antibodies (GOP 32614)	1	€5.90	€5.90
	HBV DNA (GOP 32823)[9]	1	€89.50	€89.50

Annual treatment costs:

Designation of therapy	Annual treatment costs per patient
Pharmaceutical evaluated	
Apremilast	€16,724.00
Apremilast if applicable in combination with DMARD (e.g. MTX)[1]	€16,775.79 – €16,904.27
Appropriate comparator for the indication a) Psoriatic arthritis	
Etanercept or adalimumab or infliximab or golimumab	€17,345.07 – €21,381.10
Etanercept or adalimumab or infliximab, if applicable in combination with MTX or golimumab if applicable in combination with MTX	€17,396.86 – €21,381.10[10]
Additional necessary SHI benefits	€69.40 – €164.40
Appropriate comparator for the indication b) Plaque psoriasis	
Adalimumab or infliximab or ustekinumab	€17,345.07 – €21,381.10
Additional necessary SHI benefits	€69.40 – €164.40

Other SHI expense items:

Surcharge for the production of a parenteral solution[11]

Designation of therapy	Cost per unit	Number per cycle	Number per patient per year	Cost per patient per year
Appropriate comparator				
Infliximab	maximum €81.00	1	6.5	maximum €526.50

[8] Only if HBs antigen-negative and anti-HBc antibody-positive.

[9] Invoicing for GOP 32823 possible before or during antiviral therapy with interferon and/or nucleic acid analogues.

[10] The range results from the costs for infliximab + 7.5 mg MTX (lower range) and and etanercept or adalimumab (upper range). According to the product information, there is an explicit recommendation for combination therapy with MTX only for infliximab and golimumab.

[11] The "Hilfstaxe" (a pricing contract for substances and formulations made with substances) has not been used in its entirety to calculate the costs because it (1) is negotiated flexibly, (2) is not representative for the provision of care due to the large number of invoicing modes for cytostatics, largely non-public contracts, which are not bound by the "Hilfstaxe", and (3) may not include all relevant substances at any one time, and for these reasons is unsuitable for a standardized cost overview. In contrast, the publicly accessible pharmacy retail price shown in the listing services in accordance with SGB V, section 131, paragraph 4 is a suitable basis for a standardized calculation.

According to the “Hilfstaxe” (effective: 5th supplementary agreement on the pricing contract for substances and formulations made with substances, from 10 December 2014), surcharges of maximum €81 apply per application-ready preparation to parenteral preparations containing cytostatics. This amount can be lowered in contracts. These additional extra costs are not added to the pharmacy retail price; they follow the calculation regulations set forth in the “Hilfstaxe”. The costs shown are based on the pharmacy retail price and the maximum surcharge for production, and thus only approximate the actual treatment costs. Not shown are e.g. discounts on the pharmacy retail price of the active ingredient, invoicing of waste, calculation of the application vessels or carrier solutions, or differing labour costs according to the regulations in appendix 3 of the “Hilfstaxe”.

II.

This resolution takes effect on the day of its publication in the internet on the website of the Federal Joint Committee on 6 August 2015.

The justification for this resolution will be published on the websites of the Federal Joint Committee at www.g-ba.de.

Berlin, 6 August 2015

The Federal Joint Committee in
accordance with SGB V,
section 91

The Chair
Prof. Hecken