RMACEUTICAL FORM solution for injection in pre-filled syri solution for injection in pre-filled per

rapeutic Indications

e rheumatoid arthritis in adults

be given as monotherapy in case of intolerance to methohexate or used teatment with methotexate is inappropriate. been shown to reduce the rate of progression of pint damage as y X-ray and to improve physical function, when given in combina thortexate. Appendix all justices ideating at the product of the position of a confidence of the position of the position

Ankylosing spondylifis/ASI Humira is indicated for the treatment of adults with severe active ankylic spondylifis who have had an inadequate response to conventional therapy

are in dicated for the treatment of moderate to severe chronic plaque asis in adult patients who failed to respond to or who have a contraind to, or are infolerant to other systemic therapy including cyclosporine observance ID MA.

At the continuent should be inflated and superised by specialist physicians cod in the dispricial and sustment of conditions for which Humita is oper training in hysician such rise. Against may suffered with Humita sport training in hysician such rise against and make with Humita sport such and the superised and medical follow-or suppliciant desiments for its approprised and medical follow-or professional such as the superised and medical follow-or superised superised and superised and superised superised and superised and superised superised superised and superised superise

Planmissid white The accumissid about of harm's for said in galactin, with insurantical grafters. The accuminated down of them for the said and particular state in the continuous specific. Methods should be continuous specific. Methods should be continuous specific. Methods should be continuous specific and should be shoul

in in need for dose interruption, for instance before surgery or if a nocurs. suggest that re-instruduction of Humina after discontinuation for per resulted in the same magnitudes of clinical response and office as before dose interruption.

controls
did dose of Humina for patients with antiquising spondigitis, axial
without nadiographic evidence of AS and for patients with proord gradient many administrated way of their week is a single
insour injection.

I will injection, we indicate that suggest that the clinical insports
of within 12 weeks of teathmark. Continued thratpy wholed be
leaded in a patient on expending within the time practice.

nmended dose of Humira for adult patients is an initial dose of 80 red auboutaneously, followed by 40 mg subcutaneously given e sk starting one week after the initial dose. Continued therapy bey should be casefully reconsidered in a patient not responding wi

commended in-finise includes down openine for add patients with most commended in-finish includes an expension of the commended of the projectors in finishing. In the commended of the projectors in finishing in the commended of the projectors in finishing includes an expension of the commended of the commended

nce guidelines.

ho desperance discrease in their response may benefit from an bit desperacy for 40 mg Humina every week.
ho have not responded by Wieek 4 may benefit from continued
respy through Week 12. Confinued threspy should be carefully
patient not responding within this time period.

Understand collection and invariance induction does regimen for sold galaxies with mode or and to seem of contract of collection of the seem of the collection of the collect

content belowith. Arthrill from 2 to 17 years of page credit Calcate Arthrill from 2 to 17 years of page rolled Calcate Arthrill from 2 to 17 years of page years of 1 years of 2 arthrill from 2 arthrill from 2 years on see up to a year of 2 to 19 years of 2 arthrill from 2 years of 2 ar



robn's disease cations a 40 kg, sended Harriai induction does regimen for paediatric subjects with followed by 40 mg; at Week 0 Stolewed by 40 mg; at Week 2. In a need for a more regist response to therapy, the regimen 600 mg of all for the consonable dupit, 80 mg at Week 2 can be used, senses that the risk for adverse events may be higher with use of duction dose.

or induction treatment, the recommended dose is 40 mg every other week subcutameous injection. Some abjects who experience insufficient re-rise may benefit from an increase in dissing frequency to 40 mg Humita by week.

Humita of brappy should be carefully considered in a subject not responding to its no relivent use of 14 kinsta in whitehers.

nod of administration aira is administered by subo ided in the package leaflet.

ontraindications ypersensitivity to the active substance or to any of the excipients. Active tuber closels or other severe infactions such as sepsie, and opportunistic infactions loderate to severe heart failure (NYHA class III/N).

week been ground on which been ground or common to are recognized by the common to are recognized by the common to the common to

cies are available Neys, there was no indi-anicity. Preclinical data or

y-into the serum of infants born to womer nancy. Consequently, these infants may

e at increased risk for infection. Administration of live vaccines to infants ex-ceed to adalimumab in utero is not recommended for 5 months following the nother's list artistics main injection divino recommency.

on. an immunoglobulins are excreted in milk, wo ast five months after the last Humira treatmer

of child bearing potential. Contraception in makes and females of childbearing potential are strongly recommended to use adequate option to prevent pregnancy and continue its use for at least five months last Humina treatment.

week as the description of the control of the contr

times taking k-limits and 5 fit for control hauled patients.

Generals of the saltest parties and fit for control hauled patients.

The road corrowsly appointed adverse sections are infections (putch as reaching the patients), the patients of the patient

and type to those seen in auth prolifers.

This billowing list of advisors reactions is based on experience for and on postmission good processing and on postmissions of an aid oscipalised by system and on postmissions growthers are all as displayed by system and on postmissions of the system and aid displayed by system and an aid of the system and aid of the system aid of the system and aid of the system aid of the system aid of the system and aid of the system aid of

	Under	Table 2 irable Effects
System Organ Class	Frequency	Adverse Reaction
Infections and	Vary common	respiratory tract infections (including low-
infestations"	.,	respiratory tract infections (including low- er and upper respiratory tract infection, pneumonia, sinusitis, pharyngitis, naso- shoungitis and neumonia bosnou sint
	Common	pharyngitis and pneumonia herpes viral
	Common	systemic infections (including sepsis, candidiasis and influenza), intestinal
		infections (including gastroenteritis viral), skin and soft tissue infections (including
		paronychia, cellulitis, impetigo, necrotising fasciltis and herpes zosteri.
		ear infections, oral infections (including homes simpley and homes and tooth
		infections), reproductive tract infections (including wild paging) myrotic infec-
		tion),urinary tract infactions (including
	Lincommon	phayright and pneumonia hispase vital yeather infection (including sepais, candidates and influence), intentional infection (including sepais), particular and including particular and particular and including including particular and infection (including particular), and infection (including infections, and infections (including infections, and infections (including infections, and infections including infections, and infections including infections, and infections infections, including infections, in any infections, particularly infections, particularity and infections, particularity infect
	Uncommon	meurological infections (including viral meningilis), opportunistic infections and tuberoulosis (including coccidicidomyco- sis, histoplasmosis and mycobactarium avium compiles infection), bacterial infec- tions, eye infections, diverticultis ⁽¹⁾
		tuberculosis (including coccidioidomyco- sis, histoplasmosis and mycobacterium
		avium complex infection), bacterial infec- tions, eye infections, diverticulitis?
Neoplasms be- nign, malignant and unspecified	Common	skin cancer excluding melanoma (includ- ing basal cell carcinoma and squamous
and unspecified	Uncommon	cell carcinoma), benign neoplasm
(including cysts and polyps)*	Uncommon	cell carcinoma), benign neoplasm lymphoma", solid organ neoplasm (including breast cancer, lung neoplasm and thyroid neoplasm), melanoma"
	Rare	leukaemia"
	Not Known	hepatospienic T-cell lymphoma ¹ , Merkel
		hepatospienic T-cell lymphoma ¹ , Merkel cell carcinoma (neuroendocrine carcino- ma of the skin) ¹ leucopaenia (including neutropaenia and
Blood and the lymphatic sys- tem disorders*	Wary Common	leucopaenia (including neutropaenia and agranulocytosis), anaemia
	Common	leucocytosis, thrombocytopaenia
	Rare	idiopathic thrombocytopaenic purpura Pancytopaenia
Immune system disorders*	Common	hypersensitivity, allergies (including
	Uncommon	seasonal allergy) sarcoidosis ¹
	Rare	anaphylaxis ¹⁾
Metabolism and nutrition disorders	Wary common Common	lipids increased
		hypokalaemia, uric acid increased, blood sodium abnormal, hypocalcaemia, hyperglycaemia, hypophosphataemia, deburkation
	_	dehydration mood alterations (including depression),
Psychiatric disorders	Common	arxiety, insomnia
Nevous system disorders*	Very common	Headache paraesthesias (including hypoaesthesia).
	COMMON	migraine, nerve root compression
	Uncommon	cerebrovescular accident ¹ , tremor, neuropathy
	Rare	neuropathy multiple sclerosis, demyelinating disorder (e.g. optic neuritis, Guillain-Barré syn- droma) ¹
	Common	drome) 10
Eye disorders		itis,
Ear and labo	Uncommon	eye swelling, diplopia Vertigo
Ear and laby- rinth disorders	Uncommon	deafness, tinnitus
Cardiac disorders*	Common Uncommon	tachycardia myocardial infarction ¹ , arrhythmia, con-
		gestive heart failure
Vascular disorders	Rare Common	cardiac arest hypertension, flushing, haematoma
	Uncommon	
Respiratory, thoracic and	Common	sion, thrombophiabitis asthma, dyspnosa, cough
thoracic and mediastinal disorders*	Common Uncommon	asthma, dyspnosa, cough pulmonary embolism ¹ , interstitial lung disease, chronic obstructive pulmonary
disorders*		disease, pneumonitis, pleural effusion ¹ pulmonary fibrosis ¹
Gastrointestinal disorders	Rare Very common	pulmonary fibrosis ¹⁾ abdominal pain, nausea and vomiting
	Common	Gl haemonhage, dyspepsia, gas- troesophageal reflux disease, sicca
		troesophageal reflux disease, sicca syndrome
	Uncommon	pancreatitis, dysphagia, face cedema
Hepato-biliary disorders*	Wary common	intestinal perforation ¹⁾ elevated liver enzymes
	Uncommon	cholecystitis and cholelithiasis, hepatic
	Rare	steatosis, blirubin increased Hepatitis, reactivation of hepatitis B ¹ ,
	Not known	autoimmune hepatitis ¹
Skin and subcu- taneous tissue	Very common Common	rash (including exfoliative rash)
disorders	Common	worsening or new onset of psoriasus (in- cluding paimplantar pustular psoriasis) ¹ , urticaria, bruising (including purpura),
		urticaria, bruising (including purpura), dermatitis (including eczema), onycho- clasis, hyperhydrosis, alopecia ¹ , pruritus
	Uncommon	clasis, hyperhydrosis, alopecia ¹ , pruritus night sweats, scar
	Rare	erythema multiforme ¹ , Stevens-Johnson syndrome ¹ , angioedema ¹ , cutaneous
		vasoults1
	Not known	worsening of symptoms of dermatomy- ositis?
Musculoskeletal and connective tissue disorders	Very common	musculoskeletal pain
tissue disorders		
tissue disorders	Common	muscle spasms (including blood creatine phosphokinase increased)
tissue disorders	Common	muscle spasms (including blood creatine phosphokinase increased) rhabdomyolysis, systemic lupus erythe- matisus
	Common Uncommon Rare	Iupus-like syndrome ¹
Renal and urinary	Uncommon Rare Common	Iupus-like syndrome ¹
Renal and urinary disorders	Uncommon Rare Common Uncommon	matosus lupus-like syndrome ¹¹ renal impairment Haematuria, nocturia
Renal and urinary disorders	Uncommon Rare Common	Iupus-like syndrome ¹
Renal and urinary disorders Reproductive system and breast disorders	Uncommon Rare Common Uncommon	matosus in tupus-like syndrome ¹ / renal impairment Heamaturia, nocturia erectile dysfunction
Renal and urinary disorders Reproductive system and breast disorders	Common Uncommon Fare Common Uncommon Uncommon Uncommon Uncommon	milatosis. Ispus-lika syndrome? Israal Impairment Hisematuria, nocturia erectile dysfunction Injection site reaction (including injection site arythema)
Renal and urhary disorders Reproductive system and breast disorders General disor- dissipation site conditions*	Common Uncommon Rare Common Uncommon Uncommon	maticaus syndrome? lapus-like syndrome? eraal impairment Haematuria, nocturia erectile dystunction injection site reaction (including injection site eriphama) cheat pain, ooderna, pyeede?
Renal and urinary disorders Reproductive system and breast disorders	Common Uncommon Bare Common Uncommon Uncommon Uncommon Uncommon Common	maticaus syndrome? lapus-like syndrome? eraal impairment Haematuria, nocturia erectile dystunction injection site reaction (including injection site eriphama) cheat pain, ooderna, pyeede?
Renal and urhary disorders Reproductive system and breast disorders General disor- dissipation site conditions*	Common Uncommon Bare Common Uncommon Uncommon Uncommon Uncommon Common	maticaus syndrome? lapus-like syndrome? eraal impairment Haematuria, nocturia erectile dystunction injection site reaction (including injection site eriphama) cheat pain, ooderna, pyeede?
Renal and urhary disorders Reproductive system and breast disorders General disor- dissipation site conditions*	Common Uncommon Bare Common Uncommon Uncommon Uncommon Uncommon Common	maticaus syndrome? lapus-like syndrome? eraal impairment Haematuria, nocturia erectile dystunction injection site reaction (including injection site eriphama) cheat pain, ooderna, pyeede?
Renal and urinary discorders Reproductive system and breast disorders General disor- ders and admin- istration site conditions* Investigations*	Common Uncommon Bare Common Uncommon Uncommon Uncommon Uncommon Common	maticus a syndrome?* sonal impalment Haematuria, nocturia erectile dystunction injection site reaction (including injection site arythmens) cheat pain, codema, pyleola?
Renal and urhary disorders Reproductive system and breast disorders General disor- dissipation site conditions*	Common Uncommon Hare Common Uncommon Uncommon Uncommon Uncommon Uncommon Common Common Common	Traditional Springers of the Springers o

site reactions votal controlled trials in adults and children, mind developed injection site reactions (eryth pain or swelling), compared to 7.6% of pa

factions. We plotted controlled thate in adults and children, the rate of infaction was the plotted controlled that in adults and children, the rate of infaction was 55 per patient year in the Human treated patients and 1.45 per patient year the placetor and cathe control feated points. The infactions consisted pri-arily reacceptancy (St., upper respiratory tract effection, and unkney tract infac-ration. In Adolt patients control and on Human that the infaction reaction. Amen trace in patients and COS per patient, year in placeto and achies control — teated efforts.

"waldative duudes with Humina, service, "we ethodors, which coosund rainly have been sponted, seports of buberoulosis fredding miles, and ender pulmony to make opportunistic inflactions (a). balannyosis, coolidatio-ror eshapitumosy literatumosis, balannyosis, coolidatio-to eshapitumosy literatumosis, balannyosis, coolidatio-to eshapitumosy literatumosis, balannyosis, coolidatio-beruchosis coosuned within the first sight months after inflation of my inflact inculsions con of tatert disease.

Whenever any effect reconductions or shared disease.

Management and particular shared shared disease.

Management and particular shared share

The site (67% conflares interval) of furphrones was 0.7 (0.2, 1.0, per 1.000 colorist years arrows frames beauting inferiors and 1.5 (0.4, 5.8) per Vision contenting conflared formers of these bids and opegang and colorist and operations of the conflared formers of the set of opegang and colorist and the set of the per 1.5 (a.5) and the conflared formers of the colorist and contents in approximately for 1.000 performers of the colorist performers of

isonato-bilary exercis r controlled Phase 3 trials of Humina in patients with rheumatoid arthritis sociatic arthritis with a control period duration ranging from 4 to 104 we LT elevations ₈ 3 x UIN occurred in 3.7% of Humina-treated patients. 4% of control-leaded patients.

As a state of the state of the

iting toxicity was observed during clinical trials. The highest dose ad has been multiple intravenous doses of 10 mg/kg, which is ap-15 times the recommended riveo.

PRAFMACULTURION.

Pharmacodynamic properties
Machanism of action
Adalmunab binds specifically to TNF and neutralizes the bi
TNF by blooking its infranction with the p65 and p75 cell aurit
Adalmunab also modulates biological responses that are in
by TNF, michaling anarage in the foliace of adression moloculalackcyte intigration (EJAM-1, VCMM-1, and iCAM-1 with an II r regulated onsible for

The second secon

when existence of miscond heating is admirrated heating plates.

Harmoniciating Opportunia

Segretary and plates and properties

Segretary and plates and

Following the administration of 24 mg/m² (up to a maximum of 40 mg sub-cutaneously every other week to patients with polyarticular juvenile (dispatitic arthritis (JM) who were 4 to 17 years the mean trough steady-state (value measured from West 20 to 48 jearum admirrumbic concentration was 5 till = 5.5 ligylim; (1029 c) Huntina monorharapy and 10.9 a 5.2 µg/m; (47.7% c)/ with concentration and inclinations.

In patients with JIA who were 2 -<4 years old or aged 4 and <15 kg dosed with Humira 24 mg/m2, the mean tough ste addiminants oncontrations was 6.0 a 6.1 µg/m1 (1016; CV) H apy and 7.9 a 5.6 µg/m1 (71.2% CV) with concomitant methot

asy and 7.9 at 56 giptiff CT-9% CV yield concomitant methodisades. In platfest with possible, the man itsubuly element body concentration was 5 spirit. All registrations, the control platfest with possible production of the platfest with Control to displatfest and control to displatfest with Control to displatfest and Control to displatfest and Control to displatfest and control to displatfest and concentration of approximately 6.5 spirit analysis in existent period. Askide Control to displatfest and c

more done of 40 mg Herma overy dres medic.

Proposition support, monitoring to source CI, the open likely staff summer interface to the source CI, the open likely staff summer interface to see see 1500 mg of 1000 mg of 1000 mg of 1000 mg. The Marke CI support seed to 1000 mg of 1000 mg of 1000 mg of 1000 mg. The Marke CI support seed to 1000 mg of 10

In patients with ulcerative collis, a loading dose of 160 mg Humira or 0 followed by 80 mg Humira or West? achieves serum adalmumsh concentrations of approximately 12 µg/ml during the induction period steady-state trough levels of approximately 8 µg/ml were observed in collist patients who received a maintenance dose of 40 mg Humira eve ordite patients who received a maintenance dose of 40 mg Humira eve 10 period of 10 period period

Elimination
Population phermacolininatio analysis with data from over 1,300 RA patients invasied a fored toward higher apparent disarrance of adalimumab with increasing
body weight. After adaptement for weight officences, gender and gas apparent
to have a minimal effect on adalimumab clearance. The serum levels of free
adalimumah print bound to artification number affection, AAA were observed
to be lower in patients with measurable AAA. Humira has not been studied in
patients with hepatic or renal impairmation.

Hepatic or renal impairment

review are not been studied in patients with health or renal impairment. Precibition lastly but Precibition and the Precibit and the Precibition and the Precibition and the Precibit and the Precibition and the Precibit and the Precibit and the Precibition a

List of Exciplents
Mannick, Cliffa acid monohydrate, Sodium citrate, Sodium dihydrogen phos-phate dhydrate
Discollam phosphate dhydrate, Sodium chloride, Polysorbate 80, Sodium Water for Injections

Incompatibilities
In the absence of compatibility studies, this medicinal promised with other medicinal products.

Special precautions for storage Store in a retrigerator (2°C = 8°C). Do not freeze Keep the syringe in the outer carton. Keep the pen in the outer carton.

ow supplied umins 40 mg solution for injection in single-use pre-filled sylinge (type I glass) th a plunger stopper (promobuty) rubber) and a needle with a needle shield semoplastic elestrome) for palsert use:

Passion Co.

**Jone Blood Sydney G. Der statells outbriefy with 1 alcohol pad in a bletste.

**2 pre-Blied sydneyse (D. Ber statells excluding, aceh with 1 alcohol pad, in a bletste.

**2 pre-Blied sydneyse (D. Ber statells excluding, aceh with 1 alcohol pad, in a bletste.

**4 pre-Blied sydneyse (D. Ber statells excluding, aceh with 1 alcohol pad, in a bletste.

**6 pre-Blied sydneyse (D. Ber statells excluding, aceh with 1 alcohol pad, in a bletste.

**North all pads sides may be marketsten.

Not as place, some may be manufactured.

Herman All my soldnoth for injection in single-uses pure-filled pain for patient use containing a post-filled synthey. This synthey filled the pain is made from typic and the patient of the patient of the manufactured of the manufactured of the manufactured of the manufactured of the patient of the manufactured of the patient of the patie

Special precedings for disposal and other handling. Humina 40 mg solution for injection does not contain preservatives. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

local requirements.

Manufacturer
See outer pack

Marketing Authorisation Holder
AbbVis Deutschiland GmibH and Co. R
Loudwigshafen, Germany

Date of Revision of the Text
September 2013