

Dokumentvorlage, Version vom 20.01.2011

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Sitagliptin (Januvia[®], Xelevia[®])

MSD SHARP & DOHME GmbH

Modul 2

Allgemeine Angaben zum Arzneimittel,
zugelassene Anwendungsgebiete

Stand: 26.03.2013

Inhaltsverzeichnis

	Seite
Tabellenverzeichnis	2
Abbildungsverzeichnis	3
Abkürzungsverzeichnis.....	4
2 Modul 2 – allgemeine Informationen	5
2.1 Allgemeine Angaben zum Arzneimittel	5
2.1.1 Administrative Angaben zum Arzneimittel	5
2.1.2 Angaben zum Wirkmechanismus des Arzneimittels.....	7
2.2 Zugelassene Anwendungsgebiete	14
2.2.1 Anwendungsgebiete, auf die sich das Dossier bezieht.....	15
2.2.2 Weitere in Deutschland zugelassene Anwendungsgebiete	17
2.2.3 Zulassungsstatus international.....	17
2.3 Beschreibung der Informationsbeschaffung für Modul 2.....	80
2.4 Referenzliste für Modul 2	81

Tabellenverzeichnis

	Seite
Tabelle 2-1: Allgemeine Angaben zum zu bewertenden Arzneimittel	5
Tabelle 2-2: Pharmazentralnummern und Zulassungsnummern für das zu bewertende Arzneimittel.....	6
Tabelle 2-3: Zugelassene Anwendungsgebiete, auf die sich das Dossier bezieht	16
Tabelle 2-4: Weitere in Deutschland zugelassene Anwendungsgebiete des zu bewertenden Arzneimittels	17
Tabelle 2-5: Zulassungsstatus international	19

Abbildungsverzeichnis

Seite

Es konnten keine Einträge für ein Abbildungsverzeichnis gefunden werden.

Abkürzungsverzeichnis

Abkürzung	Bedeutung
AGI	Alpha-Glucosidase-Hemmer
ATP	Adenosintriphosphat
BfArM	Bundesinstitut für Arzneimittel und Medizinprodukte
CHMP	Committee for Medicinal Products for Human Use
cyclo-AMP	Cyclisches Adenosinmonophosphat
ATC-Code	Anatomisch-Therapeutisch-Chemischer Code
DPP-4	Dipeptidyl-Peptidase 4
EMA	European Medicines Agency
GIP	Glukose-dependent insulinotropic Polypeptide
GLP-1	Glukagon-like-Peptide 1
HbA1c	Hämoglobin A1c
PPAR- γ	Peroxisome Proliferator activated Receptor- γ
PZN	Pharmazentralnummer

2 Modul 2 – allgemeine Informationen

Modul 2 enthält folgende Informationen:

- Allgemeine Angaben über das zu bewertende Arzneimittel (Abschnitt 2.1)
- Beschreibung der Anwendungsgebiete, für die das zu bewertende Arzneimittel zugelassen wurde (Abschnitt 0); dabei wird zwischen den Anwendungsgebieten, auf die sich das Dossier bezieht, und weiteren in Deutschland zugelassenen Anwendungsgebieten unterschieden. Darüber hinaus wird der internationale Zulassungsstatus für das zu bewertende Arzneimittel dargestellt.

Alle in den Abschnitten 2.1 und 0 getroffenen Aussagen sind zu begründen. Die Quellen (z. B. Publikationen), die für die Aussagen herangezogen werden, sind in Abschnitt 2.4 (Referenzliste) eindeutig zu benennen. Das Vorgehen zur Identifikation der Quellen ist im Abschnitt 2.3 (Beschreibung der Informationsbeschaffung) darzustellen.

Im Dokument verwendete Abkürzungen sind in das Abkürzungsverzeichnis aufzunehmen. Sofern Sie für Ihre Ausführungen Tabellen oder Abbildungen verwenden, sind diese im Tabellen- bzw. Abbildungsverzeichnis aufzuführen.

2.1 Allgemeine Angaben zum Arzneimittel

2.1.1 Administrative Angaben zum Arzneimittel

Geben Sie in Tabelle 2-1 den Namen des Wirkstoffs, den Markennamen und den ATC-Code für das zu bewertende Arzneimittel an.

Tabelle 2-1: Allgemeine Angaben zum zu bewertenden Arzneimittel

Wirkstoff:	Sitagliptin (als Sitagliptinphosphat 1 H₂O)
Markenname:	Januvia[®] 25 mg Filmtabletten Januvia[®] 50 mg Filmtabletten Januvia[®] 100 mg Filmtabletten Xelevia[®] 25 mg Filmtabletten Xelevia[®] 50 mg Filmtabletten Xelevia[®] 100 mg Filmtabletten
ATC-Code:	A10BH01 (Antidiabetika, Dipeptidyl-Peptidase 4 (DPP-4)-Inhibitoren)

Geben Sie in der nachfolgenden Tabelle 2-2 an, welche Pharmazentralnummern (PZN) und welche Zulassungsnummern dem zu bewertenden Arzneimittel zuzuordnen sind, und benennen

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

Sie dabei die zugehörige Wirkstärke und Packungsgröße. Fügen Sie für jede Pharmazentralnummer eine neue Zeile ein.

Tabelle 2-2: Pharmazentralnummern und Zulassungsnummern für das zu bewertende Arzneimittel

Januvia® 25 mg/50 mg/100 mg Filmtabletten

Pharmazentralnummer (PZN)	Zulassungsnummer	Wirkstärke	Packungsgröße
0814636	EU/1/07/383/002	25 mg	28 Filmtabletten
0814642	EU/1/07/383/005	25 mg	98 Filmtabletten
0814659	EU/1/07/383/002	25 mg	28 Filmtabletten (Klinikpackung)
0814665	EU/1/07/383/008	50 mg	28 Filmtabletten
0814671	EU/1/07/383/011	50 mg	98 Filmtabletten
0814731	EU/1/07/383/008	50 mg	28 Filmtabletten (Klinikpackung)
0814748	EU/1/07/383/014	100 mg	28 Filmtabletten
0817103	EU/1/07/383/017	100 mg	98 Filmtabletten
0817362	EU/1/07/383/014	100 mg	28 Filmtabletten (Klinikpackung)
Musterpackungen ("Unverkäufliches Muster" ohne PZN)	EU/1/07/383/007 EU/1/07/383/014	50 mg 100 mg	14 Filmtabletten 28 Filmtabletten

Xelevia® 25 mg/50 mg/ 100 mg Filmtabletten

Pharmazentralnummer (PZN)	Zulassungsnummer	Wirkstärke	Packungsgröße
9517673	EU/1/07/382/002	25 mg	28 Filmtabletten
9517696	EU/1/07/382/005	25 mg	98 Filmtabletten
9517704	EU/1/07/382/002	25 mg	28 Filmtabletten (Klinikpackung)
9517710	EU/1/07/382/008	50 mg	28 Filmtabletten
9517727	EU/1/07/382/011	50 mg	98 Filmtabletten
9517733	EU/1/07/382/008	50 mg	28 Filmtabletten (Klinikpackung)
4260525	EU/1/07/382/014	100 mg	28 Filmtabletten
4260531	EU/1/07/382/017	100 mg	98 Filmtabletten
4260548	EU/1/07/382/014	100 mg	28 Filmtabletten (Klinikpackung)
Musterpackungen ("Unverkäufliches Muster" ohne PZN)	EU/1/07/382/001	25 mg	14 Filmtabletten
	EU/1/07/382/007	50 mg	14 Filmtabletten
	EU/1/07/382/014	100 mg	28 Filmtabletten

2.1.2 Angaben zum Wirkmechanismus des Arzneimittels

Beschreiben Sie den Wirkmechanismus des zu bewertenden Arzneimittels. Begründen Sie Ihre Angaben unter Nennung der verwendeten Quellen.

Sitagliptin gehört zu einer Substanzklasse oraler Antidiabetika, den sog. Dipeptidyl-Peptidase 4 (DPP-4-)Inhibitoren, welche die Blutzuckerkontrolle bei Typ-2-Diabetikern dadurch verbessern, indem sie die Spiegel der aktiven Inkretinhormone erhöhen. Inkretinhormone, wie das Glukagon-like-Peptide 1 (GLP-1) und das Glukose-dependent insulinotropic Polypeptide (GIP), werden vom Darm über den Tag hinweg in die Blutbahn freigesetzt. Ihre Spiegel steigen als Reaktion auf eine Mahlzeit an. Die Inkretine sind Teil eines endogenen Systems, das bei der physiologischen Regulation der Glukosehomöostase eine Rolle spielt. Wenn die Blutglukosekonzentrationen erhöht sind, erhöhen GLP-1 und GIP die Insulinsynthese und –freisetzung aus den Beta-Zellen des Pankreas über intrazelluläre Signalwege unter Beteiligung von cyclo-AMP. In Tiermodellen zu Typ-2-Diabetes zeigte die Behandlung mit GLP-1 oder mit DPP-4-Inhibitoren eine Verbesserung der Sensibilität der Beta-Zellen gegenüber Glukose. Sie regte darüber hinaus die Insulinsynthese und –freisetzung an. Bei höheren Insulinspiegeln wird die Glukoseaufnahme in das Gewebe verstärkt. Zusätzlich senkt GLP-1 die Glukagonfreisetzung aus den Alpha-Zellen des Pankreas. Verringerte Glukagonkonzentrationen führen zusammen mit erhöhten Insulinspiegeln zu einer verminderten hepatischen Glukoseproduktion. Dies führt zur Senkung der Blutglukosespiegel.

Die Wirkungen von GLP-1 und GIP sind glukoseabhängig, so dass bei niedrigen Blutglukosespiegeln weder eine Stimulation der Insulinfreisetzung noch die Unterdrückung der Glukagonfreisetzung durch GLP-1 beobachtet werden. Sowohl für GLP-1 als auch GIP gilt, dass bei Glukoseanstieg über den Normalwert die Insulinfreisetzung verstärkt angeregt wird. GLP-1 beeinträchtigt zudem die normale Glukagonreaktion auf Hypoglykämien nicht. Die Aktivität von GLP-1 und GIP wird durch das Enzym DPP-4 begrenzt, welches die Inkretine rasch zu inaktiven Produkten abbaut. Sitagliptin verhindert den durch DPP-4 bedingten Abbau der Inkretine und erhöht dadurch die Plasmakonzentrationen der aktiven Formen von GLP-1 und GIP. Indem Sitagliptin die Spiegel aktiver Inkretine erhöht, steigert es die Insulinfreisetzung und senkt die Glukagonspiegel jeweils glukoseabhängig. Bei Typ-2-Diabetikern mit Hyperglykämie führen diese Veränderungen der Insulin- und Glukagonspiegel zu einer Reduzierung des Hämoglobin A1c (HbA1c) und niedrigeren Nüchtern- und postprandialen Blutzuckerwerten. Der glukoseabhängige Wirkmechanismus von Sitagliptin unterscheidet sich von dem der Sulfonylharnstoffe, welche glukoseunabhängig wirken. Dies bedeutet, dass unter Gabe von Sulfonylharnstoffen auch bei niedrigen Glukosespiegeln die Insulinfreisetzung erhöht wird, was bei Typ-2-Diabetikern und gesunden Personen zu Hypoglykämien führen kann (Fachinformation Januvia[®], Fachinformation Xelevia[®]).

Es ist an dieser Stelle zu betonen, dass Sitagliptin kein intrinsisches Hypoglykämierisiko besitzt. Dies erklärt sich durch den oben beschriebenen, innovativen Wirkmechanismus. Dieser gewährleistet, dass eine Insulinausschüttung stets an die Anwesenheit von Glukose gebunden ist und daher nur als Antwort auf die Aufnahme von Glukose in die Betazellen erfolgt. Da somit direkt auf einen Anstieg der Blutzuckerkonzentrationen reagiert wird, besteht im Gegensatz zu anderen insulinotropen Therapien (z.B. mit Sulfonylharnstoffen) kein erhöhtes Hypoglykämierisiko. In klinischen Studien zu Sitagliptin als Monotherapie und als Teil einer Kombinationstherapie mit Arzneimitteln, von denen es nicht bekannt ist, dass sie zu Hypoglykämien führen (d.h. Metformin und/oder ein PPAR γ -Agonist) war die Häufigkeit der unter Sitagliptin berichteten Hypoglykämien ähnlich der unter Plazebo. (Fachinformation Januvia[®], Fachinformation Xelevia[®]).

Beschreiben Sie, ob und inwieweit sich der Wirkmechanismus des zu bewertenden Arzneimittels vom Wirkmechanismus anderer bereits in Deutschland zugelassener Arzneimittel unterscheidet. Differenzieren Sie dabei zwischen verschiedenen Anwendungsgebieten, für die das zu bewertende Arzneimittel zugelassen ist. Begründen Sie Ihre Angaben unter Nennung der verwendeten Quellen.

Zunächst werden an dieser Stelle kurz verschiedene Vertreter der DPP-4-Inhibitoren beschrieben, anschließend werden die Wirkmechanismen weiterer in Deutschland zur Therapie des Diabetes mellitus Typ 2 zugelassener Arzneimittelklassen (Metformin,

Sulfonylharnstoffe und Glinide, Alpha-Glucosidase-Hemmer, Glitazone, GLP-1-Mimetika, Inhibitoren des Natrium-Glukose-Cotransporters 2 sowie Insulin) vorgestellt.

Sitagliptin und andere DPP-4-Inhibitoren

Die in Deutschland im zentralen Zulassungsverfahren zugelassenen DPP-4-Hemmer sind Sitagliptin, Vildagliptin, Saxagliptin und Linagliptin. Ein weiterer Wirkstoff, Alogliptin, befindet sich zum Zeitpunkt der Dossiererstellung noch im Zulassungsverfahren der European Medicines Agency (European Medicines Agency: Medicines under Evaluation, 2012). Die Wirkmechanismen von Vildagliptin, Saxagliptin sowie Linagliptin entsprechen prinzipiell dem oben beschriebenen von Sitagliptin. Alle Substanzen sind reversible kompetitive Hemmstoffe, welche eine hohe Affinität zum Enzym Dipeptidyl-Peptidase 4 zeigen.

Sitagliptin zeichnet sich hierbei durch die hoch selektive ca. 97% Hemmung (Alba et al., 2009) des Enzyms Dipeptidyl-Peptidase-4 (DPP-4) aus. Folglich handelt es sich bei Sitagliptin um einen hoch spezifischen Inhibitor der DPP-4, der auf verwandte Dipeptidyl-Peptidasen (z. B. DPP-8 und DPP-9) bei physiologischen Dosierungen keinen toxischen Effekt gezeigt hat (Lyseng-Williamson, 2007). Sitagliptin wird nur ca. zu 20% über den Cytochrom P450 Metabolismus (CYP3A4 unter Zuhilfenahme von CYP2C8) verstoffwechselt. In-vitro-Daten legen allerdings nahe, dass Sitagliptin CYP450-Isoenzyme weder hemmt noch induziert (Fachinformation Januvia[®] bzw. Xelvia[®]).

Die Metabolisierung von Sitagliptin spielt eine untergeordnete Rolle, es wird größtenteils unverändert ausgeschieden. Für Risikopatienten mit mäßiger und schwerer Nierenfunktionsstörung bis zu einer Nierenerkrankung im Endstadium (Dialyse) stehen bei Sitagliptin geringere Dosierungsstärken zur Verfügung, deren Sicherheit und Wirksamkeit ausreichend belegt sind. (Fachinformation Januvia[®] bzw. Xelvia[®]).

Metformin

Das Biguanid Metformin verbessert die glykämische Kontrolle ohne Stimulation der Insulinsekretion und ohne Gefahr der Hypoglykämie bzw. Gewichtszunahme (Jacob, 2011). Metformin bewirkt eine Senkung sowohl des basalen als auch des postprandialen Blutzuckerspiegels, welche auf folgende Mechanismen zurückgeführt wird:

(1) Senkung der Glukoseproduktion in der Leber durch Hemmung der Glukoneogenese und der Glykogenolyse. (2) Erhöhung der Insulinempfindlichkeit in der Muskulatur und damit Verbesserung der peripheren Glukoseaufnahme und -verwertung. (3) Verzögerung der intestinalen Glukoseresorption (Fachinformation Glucophage[®]).

Zu o. g. Mechanismen tragen die Erhöhung der Transportkapazität von allen bis jetzt bekannten membranständigen Transportproteinen für Glukose (GLUTs) sowie eine

Stimulation der intrazellulären Glykogensynthese bei. Zusätzlich wurde eine günstige Wirkung auf den Fettstoffwechsel durch eine Senkung des Gesamtcholesterins, des LDL- des LDL-Cholesterins und der Triglyzeride nachgewiesen (Fachinformation Glucophage®).

Sulfonylharnstoffe und Glinide

Sulfonylharnstoffe

Sulfonylharnstoffe wirken sowohl bei Stoffwechselgesunden als auch bei Patienten mit einem nicht insulinabhängigen Diabetes mellitus blutzuckersenkend. Dieser Effekt entsteht durch eine Steigerung der Insulinsekretion aus den Beta-Zellen des Pankreas. Dabei regulieren Sulfonylharnstoffe die Insulinsekretion durch Hemmung ATP-gesteuerter Kaliumkanäle in der Betazellmembran. Die dadurch verursachte Depolarisation der Beta-Zelle führt nach anschließendem Kalziumeinstrom zu einer exozytotischen Insulinfreisetzung. Im Gegensatz zu DPP-4-Hemmern wird dabei die Insulinsekretion unabhängig von der Glukosekonzentration im Blut stimuliert (Gallwitz et al., 2011).

Bei den Sulfonylharnstoffen wird im Wesentlichen zwischen Derivaten der sogenannten 1. Generation und 2. Generation unterschieden. Sulfonylharnstoffe der 1. Generation (Tolbutamid, Carbutamid) wiesen unerwünschte bzw. verbesserungswürdige Eigenschaften auf, etwa eine bakteriostatische Restwirkung von Carbutamid oder die erforderlichen hohen Dosen im Gramm-Bereich (Tolbutamid). Die weitere Entwicklung der Sulfonylharnstoffe führte zu sehr viel potenteren Substanzen. Die Vertreter der 2. Generation wirken u.a. aufgrund von Molekülmodifizierungen bereits im Milligramm-Bereich (Tagesdosis). Heute werden weltweit fast ausschließlich Sulfonylharnstoffe der 2. Generation verordnet. Hierzu zählen u.a. insbesondere Glibenclamid, Glimperid und Glipizid.

Für Glibenclamid sind sowohl die Hemmung der Glukagonfreisetzung aus den Alpha-Zellen des Pankreas als auch weitere extrapankreatische Wirkungen beschrieben (Vermehrung der Insulinrezeptoren, Zunahme der Insulinempfindlichkeit peripherer Gewebe (Fachinformation Glibenclamid STADA, 2010). Extrapankreatische Wirkungen sind auch z. B. für Glimperid beschrieben. So soll z. B. eine Verbesserung der Insulinempfindlichkeit des peripheren Gewebes u. a. durch eine Erhöhung der Anzahl der aktiven Glukosetransportmoleküle in den Plasmamembranen der Muskel- und Fettzellen erreicht werden. Weitere direkte Wirkungen auf den Glukosestoffwechsel in Leber-, Fett- und Muskelzellen wurden beschrieben (Fachinformation Amaryl®).

Der molekularbiologische Wirkmechanismus aller antidiabetischen Sulfonylharnstoff Derivate ist grundsätzlich identisch und bewirkt eine Insulinausschüttung, die glukose-unabhängig ist. Dies ist ein wesentliches Unterscheidungsmerkmal zum Wirkmechanismus der DPP-4-Inhibitoren, die wie zuvor beschrieben eine optimierte Insulinsekretion bewirken, die an die Glukoseaufnahme in die Betazellen gebunden ist. Somit besitzt Sitagliptin im Gegensatz zu Sulfonylharnstoffen kein intrinsisches Hypoglykämierisiko. Für die

Sulfonylharnstoffe Glibenclamid, Glimepirid und Glipizid kann auf der Basis der biopharmazeutischen und pharmakokinetischen Eigenschaften sowie der publizierten Informationen zur systemischen Exposition/Bioverfügbarkeit der entsprechenden, diese Sulfonylharnstoffe enthaltenden Fertigarzneimittel davon ausgegangen werden, dass bei der klinischen Anwendung vergleichbare Effekte resultieren (Blume, 2012). Auch anhand von verfügbaren klinischen Studien sind die drei genannten Sulfonylharnstoffe vergleichbar (Nauck, 2012).

Das erhöhte Risiko für kardiovaskuläre Ereignisse in Zusammenhang mit der Anwendung von Sulfonylharnstoffen wird insbesondere in Modul 4B dieses Dossiers ausführlich diskutiert.

Sulfonylharnstoff-Analoga (Repaglinid, Nateglinid)

Glinide (Nateglinid und Repaglinid) sind orale Sekretagoga mit schnellem Wirkungseintritt und kurzer Wirkdauer. Sie unterscheiden sich chemisch von den Sulfonylharnstoffen, verfügen jedoch über den gleichen Wirkmechanismus: sowohl Nateglinid als auch Repaglinid schließen ATP-abhängige Kaliumkanäle der Betazellmembran. Dies führt zu einer Depolarisation der Betazellen und zu einer Öffnung der Kalziumkanäle. Der hieraus resultierende Kalziumeinstrom erhöht die Insulinsekretion. (Fachinformation Repaglinid AL; Fachinformation Starlix®).

Glinide sind durch ihre kürzere Wirkung hauptsächlich zur postprandialen Glukosesenkung geeignet (Mutschler et al., 2008).

Insulin-Sensitizer (Glitazone)

Die Thiazolidindione Pioglitazon und Rosiglitazon bewirken eine Verringerung der Insulinresistenz. Diese Wirkung scheint über eine Aktivierung spezifischer Kernrezeptoren (Peroxisome Proliferator activated Receptor- γ (PPAR- γ)) vermittelt zu werden. Dies wiederum führt zu einer vermehrten Expression und Translokation von Glukosetransportmolekülen und so zu einer erhöhten Insulinsensitivität von Leber-, Fett- und Skelettmuskelzellen (Mutschler et al., 2008).

Darüber hinaus konnte gezeigt werden, dass Pioglitazon die Glukoseproduktion in der Leber reduziert. Die Nüchtern- und postprandiale Blutzuckerkontrolle von Patienten mit Diabetes mellitus Typ 2 wird verbessert. Diese verbesserte Blutzuckerkontrolle geht mit einer Senkung sowohl der Nüchtern- als auch der postprandialen Plasma-Insulinkonzentrationen einher (Fachinformation Actos[®]).

Die Insulinsekretion wird nicht beeinflusst, Hypoglykämien werden daher in der Monotherapie nicht beobachtet (Jacob & Rosak, 2011).

Rosiglitazon wurde im November 2010 aufgrund eines negativen Nutzen-Risiko-Verhältnisses europaweit vom Markt genommen (Bundesinstitut für Arzneimittel und Medizinprodukte: Rosiglitazon, 2010)

Der CHMP empfiehlt die Behandlung mit Pioglitazon aufgrund des mit dessen Anwendung im Zusammenhang stehendem geringfügig erhöhten Risikos für das Auftreten von Blasenkrebs und/oder Herzinsuffizienz nicht als Erstlinienbehandlung und nur nach sorgfältiger Abwägung des Nutzen-Risiko-Profiles (Bundesinstitut für Arzneimittel und Medizinprodukte: Pioglitazon, 2012).

Alpha-Glucosidase-Hemmer (AGI)

Alpha-Glucosidase-Hemmer hemmen die Aufspaltung von Di-, Oligo- und Polysacchariden in Monosaccharide im Darm. Dies führt dosisabhängig zu einer Verzögerung der Verdauung der erwähnten Kohlenhydrate. Dadurch wird insbesondere die aus Kohlenhydraten stammende Glukose langsamer frei und langsamer ins Blut aufgenommen. Auf diese Weise vermindern Alpha-Glucosidase-Hemmer den Blutzuckerspiegel nach den Mahlzeiten.

Durch die Verminderung des Blutzuckerspiegels nach den Mahlzeiten entlastet Acarbose auch die Betazellen des Pankreas, eine kompensatorische postprandiale Hyperinsulinämie wird so vermieden. Unter der Behandlung mit Acarbose nehmen die Werte der Nüchternblutglukose und des glykosylierten Hämoglobin (HbA1c) deutlich ab (Fachinformation Glucobay[®]). Ähnliche Effekte werden ebenfalls für Miglitol beschrieben (Fachinformation Diastabol[®]).

GLP-1-Mimetika

In Deutschland bisher zugelassene GLP1-Mimetika sind Exenatide und Liraglutid, die zur Behandlung des Typ 2 Diabetes mellitus in Kombination mit anderen Antidiabetika angezeigt sind. (Matthaei et al., 2009). Ein weiteres GLP-1-Mimetikum, Lixisenatide, befindet sich derzeit im Zulassungsverfahren der European Medicines Agency (European Medicines Agency: Medicines under Evaluation, 2012).

GLP-1-Mimetika sind Peptide, die an den Rezeptor für das Inkretin Glukagon-Like-Peptide-1 binden und diesen aktivieren. Dabei wird durch cAMP-gesteuerte intrazelluläre Signalkaskaden in den Betazellen des Pankreas - glukoseabhängig - die Sekretion von Insulin erhöht. Bei sinkender Blutzuckerkonzentration geht daher auch die Insulinsekretion zurück (Fachinformation Byetta®). Gleichzeitig wird - ebenfalls glukoseabhängig - durch eine Hemmung der Glukagonsekretion die Glukoseabgabe der Leber reduziert. Exenatide beeinträchtigt jedoch nicht die normale Glukagonwirkung und die Wirkung anderer Hormone als Reaktion auf eine Hypoglykämie. Eine Verlangsamung der Entleerung des Magens und somit indirekt eine Verringerung der Aufnahmegeschwindigkeit von Glukose wird ebenfalls beschrieben (Fachinformation Byetta®).

Inhibitoren des Natrium-Glukose Cotransporters 2 (SGLT-2)

Die Arzneimittelklasse der SGLT-2 Inhibitoren senkt den Blutzuckerspiegel über eine Hemmung des renalen Natrium-Glukose Cotransporters 2 (SGLT-2). SGLT-2 ist der Haupttransporter, der für die Reabsorption von Glukose aus dem glomerulären Filtrat zurück in den Kreislauf verantwortlich ist. Dabei führt die Hemmung der renalen Rückresorption von Glukose zu einer Erhöhung der Glukoseausscheidung über die Nieren und infolgedessen zu einer Senkung sowohl der Nüchtern- als auch der postprandialen Plasma-Glukosespiegel (Fachinformation Forxiga®).

Der erste SGLT2- Inhibitor (Dapagliflozin) wurde im November 2012 für die Monotherapie bei Metforminunverträglichkeit sowie in Kombination mit Insulin und anderen glukosesenkenden Arzneimitteln zugelassen (European Commission: Community Register of medicinal products, 2012)

Dapagliflozin behindert nicht die normale endogene Glukoseproduktion als Reaktion auf eine Hypoglykämie und wirkt unabhängig von der Insulinsekretion und Insulinwirkung. (Fachinformation Forxiga®).

Insulin

Insulin, das wichtigste Hormon zur Aufrechterhaltung der Glukosehomöostase, wird in den Betazellen der Langerhansinseln des Pankreas synthetisiert. Dabei handelt sich um ein über eine Disulfidbrücke verknüpfte, aus zwei Aminosäureketten bestehendes Proteohormon. An den Zielzellen der peripheren Organe (Leber, Muskulatur, Fettgewebe, Niere) entfaltet Insulin seine Wirkung über den Insulinrezeptor mit tyrosinkinase-aktivierten nachgeschalteten Signalkaskaden (Bretzel, 2011). Insulin fördert die Glukoseaufnahme in peripheren Geweben und supprimiert auch die hepatische Glukoseproduktion, die die basale Hyperglykämie bei Typ-2-Diabetikern unterhält. Weiterhin korrigiert Insulin andere Stoffwechselstörungen, wie z. B. erhöhte Lipolyse. Insulin hat auch einen günstigen Effekt auf den Fettstoffwechsel und das Gerinnungssystem.

Entsprechend ihrem Wirkprofil stehen heute nahezu ausschließlich gentechnisch hergestellte Insuline zur Verfügung. Prinzipiell werden schnell wirkendes Insulin (Analog- und Humaninsulin), intermediär wirkendes Insulin (Humaninsulin), intermediär wirkendes kombiniert mit schnell wirkendem Insulin (sog. Mischinsulin; Analog- und Humaninsulin), sowie lang wirkendes Insulin (Analog- und Humaninsulin) voneinander unterschieden (Rote Liste[®], 2012).

Der Einsatz der verschiedenen Therapieregime (konventionell, intensiviert konventionell, Kombinationstherapie mit oralen Antidiabetika, Insulinpumpentherapie) erfolgt leitliniengerecht aufgrund individueller Bedürfnisse und orientiert sich dabei an der Stoffwechselsituation des Patienten. Sie erfordert i. d. R. eine intensive Schulung des Patienten durch speziell ausgebildetes Fachpersonal (Matthaei et al., 2009).

Zusammenfassung der Wirkmechanismen

Antidiabetika führen über unterschiedliche Mechanismen zu einer Blutzuckersenkung:

a) Erhöhung der Insulinsensitivität (Metformin, Glitazone), b) Steigerung der Insulinsekretion (Sulfonylharnstoffe, Glinide), c) Verzögerung der Glukoseresorption über Hemmung des Abbaus von Di-, Oligo- und Polysacchariden (Alpha-Glucosidase-Hemmer), d) Erhöhung der aktiven Inkretinhormone GLP-1 und GIP durch die Verhinderung des Abbaus durch Hemmung der Dipeptidyl-Peptidase 4 (DPP-4-Inhibitoren) oder durch die Gabe langlebiger GLP-1-Mimetika, die eine glukoseabhängige Insulinsekretion fördern und gleichzeitig die Glukagonsekretion hemmen oder e) Hemmung des renalen Natrium-Glukose Cotransporters 2 (SGLT2), die über die Hemmung der renalen Rückresorption von Glukose zu einer verstärkten Glukoseausscheidung führt.

Der DPP-4-Inhibitor Sitagliptin führt zu einer effizienten Verbesserung der Glukosehomöostase (Reduktion der Nüchtern- und postprandialen Blutzuckerwerte und des HbA_{1c}). Dabei wird der Blutzuckerspiegel physiologisch über das Inkretinsystem kontrolliert. Somit kommt es zu einer bedarfsgerechten Insulinausschüttung im Anschluss an eine Nahrungsaufnahme ohne ein erhöhtes Hypoglykämierisiko.

2.2 Zugelassene Anwendungsgebiete

2.2.1 Anwendungsgebiete, auf die sich das Dossier bezieht

Benennen Sie in der nachfolgenden Tabelle 2-3 die Anwendungsgebiete, auf die sich das vorliegende Dossier bezieht. Geben Sie hierzu den Wortlaut der Fachinformation an. Sofern im Abschnitt „Anwendungsgebiete“ der Fachinformation Verweise enthalten sind, führen Sie auch den Wortlaut an, auf den verwiesen wird. Fügen Sie für jedes Anwendungsgebiet eine neue Zeile ein, und vergeben Sie eine Kodierung (fortlaufende Bezeichnung von „A“ bis „Z“) [Anmerkung: Diese Kodierung ist für die übrigen Module des Dossiers entsprechend zu verwenden].

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

Tabelle 2-3: Zugelassene Anwendungsgebiete, auf die sich das Dossier bezieht

Anwendungsgebiet (Wortlaut der Fachinformation inkl. Wortlaut bei Verweisen)	Datum der Zulassungserteilung	Kodierung im Dossier^a
Als Monotherapie bei Patienten, bei denen Diät und Bewegung allein den Blutzucker nicht ausreichend senken und für die Metformin aufgrund von Gegenanzeigen oder Unverträglichkeit nicht geeignet ist.	29.07.2009	A
Als orale Zweifachtherapie in Kombination mit Metformin, wenn Diät und Bewegung plus eine Monotherapie mit Metformin den Blutzucker nicht ausreichend senken.	21.03.2007	B
Als orale Zweifachtherapie in Kombination mit einem Sulfonylharnstoff, wenn Diät und Bewegung plus eine Monotherapie mit einem Sulfonylharnstoff in der höchsten vertragenen Dosis den Blutzucker nicht ausreichend senken und wenn Metformin aufgrund von Gegenanzeigen oder Unverträglichkeit nicht geeignet ist.	19.12. 2007	C
Als orale Zweifachtherapie in Kombination mit einem Peroxisomal Proliferator activated Receptor gamma(PPAR γ)-Agonisten (d. h. einem Thiazolidin), wenn die Anwendung eines PPAR γ -Agonisten angebracht ist und Diät und Bewegung plus Monotherapie mit einem PPAR γ -Agonisten den Blutzucker nicht ausreichend senken.	21.03.2007	entfällt – siehe Protokoll der G-BA Beratung vom 20.08.2012 ^b
Als orale Dreifachtherapie in Kombination mit einem Sulfonylharnstoff und Metformin, wenn Diät und Bewegung plus eine Zweifachtherapie mit diesen Wirkstoffen den Blutzucker nicht ausreichend senken.	19.12. 2007	D
Als orale Dreifachtherapie in Kombination mit einem PPAR γ -Agonisten und Metformin, wenn die Anwendung eines PPAR γ -Agonisten angebracht ist und Diät und Bewegung plus eine Zweifachtherapie mit diesen Wirkstoffen den Blutzucker nicht ausreichend senken.	02.06.2009	entfällt – siehe Protokoll der G-BA Beratung vom 20.08.2012 ^b
Zusätzlich zu Insulin (mit oder ohne Metformin), wenn Diät und Bewegung sowie eine stabile Insulindosis den Blutzucker nicht ausreichend senken.	09.11.2009	E

a: Fortlaufende Angabe „A“ bis „Z“.

b: Gemeinsamer Bundesausschuss (G-BA). Finale Niederschrift zum Beratungsgespräch gemäß § 8 Abs. 1 AM-NutzenV. Beratungsanforderung Nr.: 2012-B-028. 2012 (22. Oktober 2012).

Benennen Sie die den Angaben in Tabelle 2-3 zugrunde gelegten Quellen.

BERLIN-CHEMIE 2012. Fachinformation Xelevia.

GEMEINSAMER BUNDESAUSSCHUSS 2012. Finale Niederschrift zum Beratungsgespräch gemäß § 8 Abs. 1 AM-NutzenV. Beratungsanforderung Nr.: 2012-B-028. 2012 (22. Oktober 2012).

MSD SHARP&DOHME 2012. Fachinformation Januvia.

2.2.2 Weitere in Deutschland zugelassene Anwendungsgebiete

Falls es sich um ein Dossier zu einem neuen Anwendungsgebiet eines bereits zugelassenen Arzneimittels handelt, benennen Sie in der nachfolgenden Tabelle 2-4 die weiteren in Deutschland zugelassenen Anwendungsgebiete des zu bewertenden Arzneimittels. Geben Sie hierzu den Wortlaut der Fachinformation an; sofern im Abschnitt „Anwendungsgebiete“ der Fachinformation Verweise enthalten sind, führen Sie auch den Wortlaut an, auf den verwiesen wird. Fügen Sie dabei für jedes Anwendungsgebiet eine neue Zeile ein. Falls es kein weiteres zugelassenes Anwendungsgebiet gibt oder es sich nicht um ein Dossier zu einem neuen Anwendungsgebiet eines bereits zugelassenen Arzneimittels handelt, fügen Sie in der ersten Zeile unter „Anwendungsgebiet“ „kein weiteres Anwendungsgebiet“ ein.

Tabelle 2-4: Weitere in Deutschland zugelassene Anwendungsgebiete des zu bewertenden Arzneimittels

Anwendungsgebiet (Wortlaut der Fachinformation inkl. Wortlaut bei Verweisen)	Datum der Zulassungserteilung
Nicht zutreffend	

Benennen Sie die den Angaben in Tabelle 2-4 zugrunde gelegten Quellen. Falls es kein weiteres zugelassenes Anwendungsgebiet gibt oder es sich nicht um ein Dossier zu einem neuen Anwendungsgebiet eines bereits zugelassenen Arzneimittels handelt, geben Sie „nicht zutreffend“ an.

Nicht zutreffend.

2.2.3 Zulassungsstatus international

Geben Sie in der nachfolgenden Tabelle 2-5 die Ihnen bekannten internationalen Zulassungen für das zu bewertende Arzneimittel an. Unterscheiden Sie dabei zwischen verschiedenen Anwendungsgebieten. Geben Sie für jedes Anwendungsgebiet den Wortlaut aus der jeweiligen

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

Produktinformation in deutscher Sprache an (ggf. als Übersetzung). Falls das jeweilige Anwendungsgebiet mit einem der Anwendungsgebiete, auf die sich das Dossier bezieht, ganz oder teilweise identisch ist, dann geben Sie die Kodierung für das betreffende Anwendungsgebiet an (siehe Tabelle 2-3). Fügen Sie für jedes Land und für jedes Anwendungsgebiet eine neue Zeile ein. Falls es keine weiteren Zulassungen international gibt oder Ihnen solche nicht bekannt sind, geben Sie in der ersten Zeile unter „Land“ „nicht zutreffend“ an.

Tabelle 2-5: Zulassungsstatus international

Land	Zugelassenes Anwendungsgebiet (Wortlaut der Produktinformation, ggf. Übersetzung)	Datum der Zulassungs-erteilung	Bezug zu Anwendungs-gebieten, auf die sich das Dossier bezieht ^a
Albania	<p>For patients with type 2 diabetes mellitus, Januvia is indicated:</p> <ul style="list-style-type: none"> - to improve glycaemic control in combination with metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - to improve glycaemic control in combination with a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - to improve glycaemic control in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>For patients with type 2 diabetes mellitus in whom use of a PPARγ agonist (i.e. a thiazolidinedione) is appropriate, Januvia is indicated: in combination with the PPARγ agonist when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control</p>	11-Sep-09	B C D
Argentina	<p><u>Monotherapy</u> JANUVIA is indicated as adjuvant of diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with metformin when diet and exercise plus the single agent do not provide adequate glycaemic control.</p> <p><u>Combination with sulphonylurea</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with a sulphonylurea when diet and exercise plus the single</p>	18-Apr-07	A B C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>agent do not provide adequate glycemic control.</p> <p><u>Combination with an agonist PPARγ</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with PPARγ agonist (eg, thiazolidinediones) when diet and exercise plus the single agent do not provide adequate glycemic control.</p> <p><u>Combination with metformin and sulfonylurea</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and sulphonylurea when dual therapy with these agents plus diet and exercise do not provide adequate glycemic control</p> <p><u>Combination with metformin and a PPAR agonist</u> JANUVIA is indicated in combination with a PPAR agonist and metformin when PPAR agonist use is appropriate and in cases where diet and exercise plus dual therapy with these agents may not provide adequate glycemic control.</p> <p><u>Combination with insulin</u> JANUVIA is also indicated as adjunctive therapy to insulin (with or without metformin) in cases where diet and exercise plus a stable dose of insulin, do not provide adequate glycemic control.</p>			D
				E
Armenia	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and</p>	12-Apr-11		A
				B
				C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ-agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ-agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ-agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		D
			E
Aruba	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and</p>	8-Feb-07	B C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>exercise, does not provide adequate glyceemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glyceemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glyceemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glyceemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glyceemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glyceemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glyceemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glyceemic control in combination with insulin (with or without metformin).</p>		<p>D</p> <p>E</p>
<p>Australia</p>	<p>For the treatment of diabetes mellitus type 2 in persons 18 years of age and older who have failed dietary measures and exercise as dual combination therapy with metformin, or with a sulfonylurea, or with a thiazolidinedione where the use of a thiazolidinedione is considered appropriate</p>	<p>21-Dec-07</p>	<p>B,C</p>
<p>Azerbaijan</p>	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glyceemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glyceemic control in combination with</p>	<p>25-May-11</p>	<p>A</p> <p>B</p>

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		<p>C</p> <p>D</p> <p>E</p>
Bahamas	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with</p>	17-Oct-06	B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		C
			D
			E
Bahrain	<p><u>Monotherapy & Combination Therapy</u> Januvia is indicated as adjunct to diet & exercise to improve glycemic control in adults with type 2 diabetes mellitus.</p> <p><u>Combination Therapy</u> Januvia is indicated in patients with type 2 diabetes mellitus to improve</p>	22-Nov-07	A
			B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	glycemic control in combination with metformin or a PPAR γ agonist(e.g. thiazolidinediones)when the single agent alone, with diet & exercise, does not provide adequate glycemic control.		
Barbados	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p>	12-Oct-07	B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin)</p>		E
Belarus	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ-agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ-agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate</p>	28-Sep-10	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
Bermuda	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate</p>	19-Oct-07	B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	glycemic control. <u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).		E
Bolivia	As monotherapy adjunct to diet and exercise in patients with type II diabetes mellitus. In combination with metformin or a PPAR agonist when diet and exercise along with monotherapy does not provide adequate glycemic control	13-Dec-07	A; B
Bosnia/Herzegovina	For patients with type 2 diabetes mellitus, JANUVIA is indicated to improve glycaemic control: <u>as monotherapy</u> - in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <u>as dual oral therapy in combination with</u> - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator-activated receptor gamma (PPAR γ) agonist (i.e. a thiazolidinedione) when use of a PPAR γ agonist is appropriate and when diet and exercise plus the PPAR γ agonist alone do not provide adequate glycaemic control. <u>as triple oral therapy in combination with</u> - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPAR γ agonist and metformin when use of a PPAR γ agonist is	11-Mar-11	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control.</p> <p>JANUVIA is also indicated as add on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.</p>		E
Brazil	<p>Monotherapy: JANUVIA® is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p>Combination with metformin: JANUVIA® is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with a Sulfonylurea JANUVIA® is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with a PPARγ agonist JANUVIA® is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with Metformin and a Sulfonylurea JANUVIA® is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control</p> <p>Combination with Metformin and a PPARγ agonist JANUVIA® is indicated in patients with type 2 diabetes mellitus to improve glycemic control in</p>	27-Nov-06	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with Insulin</p> <p>JANUVIA® is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
Canada	<p><u>Monotherapy</u></p> <p>JANUVIA® (sitagliptin) is indicated as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus and for whom metformin is inappropriate due to contraindications or intolerance.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA® is indicated in combination with metformin in adult patients with type 2 diabetes mellitus to improve glycemic control when diet and exercise, plus metformin do not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u></p> <p>JANUVIA® is indicated in combination with metformin and a sulfonylurea in adult patients with type 2 diabetes mellitus to improve glycemic control when diet and exercise, and dual therapy with these agents, do not provide adequate glycemic control</p>	14-Dec-07	A B D
Cayman Islands	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and</p>	19-Oct-06	B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		<p>C</p> <p>D</p> <p>E</p>
Chile	JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	10-Jul-07	N/A
China	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p>	<p>29-Sep-09</p> <p>15-Jan-10</p>	A

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

Colombia	<p><u>Monotherapy</u> As complement of the diet and the exercise to improve the control of the blood sugar in the patients with diabetes mellitus Type 2.</p> <p><u>Combined Treatment</u> It is indicated also for diabetes mellitus 2 patients to improve the control of the blood sugar in combination with the metformin or an agonist of the PPARγ (for example the thiazolidinediona) when the diet and the exercise along one only agent does not provide a suitable control glycemic.</p>	11-May-07	A B
Costa Rica	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p>	6-Feb-08	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p><u>Combination with Metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin)</p>		E
Croatia	<p>For patients with type 2 diabetes mellitus, JANUVIA is indicated:</p> <ul style="list-style-type: none"> - to improve glycaemic control in combination with metformin alone when diet and exercise plus metformin alone do not provide adequate glycaemic control. - to improve glycaemic control in combination with a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - to improve glycaemic control in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>For patients with type 2 diabetes mellitus in whom use of a PPARγ agonist (i.e. a thiazolidinedione) is appropriate, JANUVIA is indicated: in combination with the PPARγ agonist when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control.</p>	2-Jul-08	B C D
Curacao	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with</p>	20-Jul-11	B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin)</p>		C
			D
			E
Dominican Republic	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve</p>	28-Dec-07	A
			B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).t</p>		C
			D
			E
Ecuador	<p><u>Monootherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p>	22-Feb-07	A
			B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with PPARγ Agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e. thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ Agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		<p>C</p> <p>D</p> <p>E</p>
Egypt	Januvia is a member of a class of medicines you take by mouth called DPP-4 inhibitors (dipeptidyl peptidase-4 inhibitors) that lowers blood sugar levels in patients with	19-Mar-09	

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>type 2 diabetes mellitus. Type 2 diabetes is also called non-insulin-dependent diabetes mellitus, or NIDDM.</p> <p>Januvia helps to improve the levels of insulin after a meal and decreases the amount of sugar made by the body. It is unlikely to cause low blood sugar because it does not work when your blood sugar is low. However, when Januvia is used in combination with a sulphonylurea medicine or with insulin, low blood sugar (hypoglycaemia) can occur.</p> <p>Januvia to help lower your blood sugar, which is too high because of your type 2 diabetes. Januvia can be used alone or in combination with certain other medicines (insulin, metformin, sulphonylureas, or glitazones) that lower blood sugar, which you may already be taking for your diabetes together with a food and exercise plan.</p>		A; E; B, C;
El Salvador	<p><u>Monotherapy</u></p> <p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a</u></p>	18-Apr-07	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p><u>Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
<p>European Union:</p> <p>Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom</p>	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> - in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic 	21-Mar-07	A B C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>control.</p> <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.</p>		<p>D</p> <p>E</p>
Ethiopia	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> • in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> • metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. • a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. • a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control. <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> • a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. • a PPARγ agonist and metformin when use of a PPARγ agonist is 	xx.11.2012	<p>A</p> <p>B</p> <p>C</p> <p>D</p>

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.		E
Ghana	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> - in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control. <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.</p>	02-Apr-12	A B C D E
Georgia	<u>Monotherapy</u>	29-Dec-08	A

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ-agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ-agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		<p>B</p> <p>C</p> <p>D</p> <p>E</p>
--	---	--	-------------------------------------

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

Guatemala	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with</p>	27-Feb-07	<p>A</p> <p>B</p> <p>C</p> <p>D</p> <p>E</p>
-----------	---	-----------	--

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	insulin (with or without metformin)		
Honduras	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct</p>	28-Mar-07	A B C D E

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).		
Hong Kong	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the maximal tolerated dose of a single agent alone, with diet and exercise, does not provide adequate glycemic control and when metformin is inappropriate due to contraindications or intolerance.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate</p>	9-Nov-07	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
Iceland	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> - in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control. <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus</p>	10-Apr-07	<p>A</p> <p>B</p> <p>C</p> <p>D</p> <p>E</p>

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	stable dose of insulin do not provide adequate glycaemic control		
India	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and PPARγ agonist</u> JANUVIA is indicated in combination with metformin and a PPARγ agonist as an adjunct to diet and exercise in adult patients with type 2 diabetes mellitus who are inadequately controlled on combination therapy with metformin and a PPARγ agonist.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in combination with insulin, alone or in combination</p>	31-Oct-07	A B C D E

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	with metformin.		
Indonesia	<p><u>Monotherapy</u></p> <p>JANUVIA1 is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin or PPARγ agonist</u></p> <p>Januvia is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with Metformin or a PPARγ agonist (i.e. thiazolidinediones) when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and Sulfonylurea</u></p> <p>Januvia is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agent, with diet and exercise, does not provide adequate glycemic control.</p>	19-Dec-07	A B C
Iraq	To be determined: approved by fast track IDL so the label is not finalized yet	27-Sep-11	N/A
Israel	<p>INDICATIONS AND USAGE</p> <p>Monotherapy and Combination Therapy</p> <p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.</p> <p>Important Limitations of Use</p> <p>JANUVIA should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.</p> <p>JANUVIA has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using JANUVIA.</p>	30-Mar-08	N/A
Jamaica	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p>	Jamaica	B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		C
			D
			E
Japan	<p>Type 2 diabetes mellitus</p> <p>Sitagliptin should be used only in patients who do not sufficiently respond to any one of the following treatments.</p>	16-Oct-09	

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>1. Dietary therapy and/or exercise therapy only</p> <p>2. Use of sulfonylureas in addition to dietary therapy and/or exercise therapy</p> <p>3. Use of thiazolidinediones in addition to dietary therapy and/or exercise therapy</p> <p>4. Use of biguanides in addition to dietary therapy and/or exercise therapy</p> <p>5. Use of α-glucosidase inhibitors in addition to dietary therapy and/or exercise therapy</p> <p>6. Use of insulin in addition to dietary therapy and/or exercise therapy</p>		A C B E
Jordan	JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	31-Dec-08	N/A
Kazakhstan	Type 2 diabetes mellitus as monotherapy as adjunct to exercise and diet in case of inefficiency; Type 2 diabetes mellitus in combined therapy	13-Jan-10	N/A
Korea	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus (type 2 diabetes).</p> <p>JANUVIA is indicated for:</p> <ol style="list-style-type: none"> 1. Monotherapy. 2. Initial combination therapy with metformin. 3. Dual combination therapy with metformin or sulfonylurea or thiazolidinediones or insulin when the single agent alone does not provide adequate glycemic control. 4. Triple Combination therapy with metformin and sulfonylurea or metformin and thiazolidinediones or Metformin and insulin when dual therapy with these agents does not provide adequate glycemic control. 	21-Sep-07	A B B,C; E D
Kuwait	<p><u>Monotherapy & Combination Therapy</u></p> <p>Januvia is indicated as adjunct to diet & exercise to improve glycemic control in adults with type 2 diabetes mellitus.</p> <p><u>Combination Therapy</u></p> <p>Januvia is indicated in patients with type 2 diabetes mellitus to improve</p>	2-May-07	A B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	glycemic control in combination with metformin or a PPAR γ agonist(e.g. thiazolidinediones)when the single agent alone, with diet & exercise, does not provide adequate glycemic control.		
Lebanon	JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus	28-Nov-08	N/A
Macau	<p>Monotherapy</p> <p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p>Combination with Metformin</p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with a Sulfonylurea</p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the maximal tolerated dose of a single agent alone, with diet and exercise, does not provide adequate glycemic control and when metformin is inappropriate due to contraindications or intolerance.</p> <p>Combination with a PPAR agonist</p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPAR agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with Metformin and a Sulfonylurea</p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with</p>	19-Mar-07	<p>A</p> <p>B</p> <p>C</p> <p>D</p>

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with Metformin and a PPARγ agonist JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with Insulin JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
Macedonia	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> • in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> • metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. • a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. • a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control. 	22-July-09	A B C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> • a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. • a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.</p>		<p>D</p> <p>E</p>
Malaysia	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control. Initial combination therapy or maintenance of combination therapy may not be appropriate for all patients. These management options are left to the discretion of the health care provider.</p> <p><u>Combination with a sulphonylurea</u> Januvia is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulphonylurea when treatment with maximal tolerated dose of sulphonylurea alone, with diet and exercise, does not provide adequate glycemic control and when metformin is inappropriate due to contraindications or intolerance.</p> <p><u>Combination with metformin and a sulphonylurea</u> Januvia is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with</p>	21-Jun-07	<p>A</p> <p>B</p> <p>C</p> <p>D</p>

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>metformin and a sulphonylurea when dual therapy with these two agents and with diet and exercise does not provide adequate glycemc control.</p> <p><u>Combination with a peroxisome proliferator-activated receptor gamma (PPARγ) agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemc control in combination with a PPARγ agonist (i.e. thiazolidinediones) when diet and exercise, plus the single agent do not provide adequate glycemc control.</p> <p><u>Combination with metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemc control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemc control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemc control in combination with insulin (with or without metformin).</p>		E
Mali	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> - in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator- 	19-Nov-11	A B C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control.</p> <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.</p>		D
			E
Mauritius	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> - in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not 	29-Nov-11	A
			B
			C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>provide adequate glycaemic control.</p> <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.</p>		D
			E
Mexico	<p><u>Monotherapy</u></p> <p>JANUVIA is indicated as a complementary treatment to diet and exercise in diabetes type 2 to improve glycaemia.</p> <p><u>Combination with Metformin</u></p> <p>For patients with Diabetes type 2 to improve the control of glycemia in combination with metformin as initial treatment or when the control of glycemia is not reached with only one of these substances.</p> <p><u>Combination with SU</u></p> <p>For patients with diabetes mellitus type 2 to improve the control of glycemia in combination with SU when the treatment with only one of these actives does not bring an adequate control.</p> <p><u>Combination with an Agonist of PPARγ</u></p> <p>for patients with diabetes mellitus type 2 to improve the control of glycemia in combination with agonists of PPARγ (i.e. thiazolidinediones) when the treatment with only one of these actives do not control adequately the glycemia.</p> <p><u>Combination with Metformin and SU</u></p> <p>for patients with diabetes mellitus type 2 to improve the control of glycemia in combination with metformin and SU when dual treatment with these</p>	4-Aug-06	A
			B
			C
			D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>actives do not control adequately.</p> <p><u>Combination with Metformin and an Agonist of PPARγ</u></p> <p>for patients with type 2 diabetes mellitus to improve the control of glycemia in triple combination when dual treatment do not offer adequate control of glycemia.</p> <p><u>Combination with Insulin</u></p> <p>for patients with diabetes type 2 for the control of glycemia in patients under insulin (with or without metformin).</p>		E
Moldova	<p><u>Monotherapy</u></p> <p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ-agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ-agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a</u></p>	01-Aug-11	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p><u>PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
Montenegro	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> • in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> • metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. • a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. • a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control. <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> • a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. • a PPARγ agonist and metformin when use of a PPARγ agonist is 	24-Jul-07	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control.</p> <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.?</p>		E
Marocco	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p>as monotherapy</p> <ul style="list-style-type: none"> - in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p>as dual oral therapy in combination with</p> <ul style="list-style-type: none"> - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control. <p>as triple oral therapy in combination with</p> <ul style="list-style-type: none"> - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to</p>	17-Oct-07	<p>A</p> <p>B</p> <p>C</p> <p>D</p> <p>E</p>

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.		
Namibia	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> - in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> - •metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPAR agonist alone do not provide adequate glycaemic control. <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control</p>	21-Jan-10	A B C D E
New Zealand	<u>Monotherapy</u>	28-Feb-08	A

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with metformin as initial therapy or when diet and exercise, plus the single agent do not provide adequate glycaemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycaemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycaemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycaemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycaemic control.</p>		B C D
Nicaragua	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p>	2-Apr-07	A

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		<p>B</p> <p>C</p> <p>D</p> <p>E</p>
Norway	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <p>- in patients inadequately controlled</p>	21-Mar-07	A

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance.</p> <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control. <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. - a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.</p>		<p>B</p> <p>C</p> <p>D</p> <p>E</p>
Oman	<p><u>Monotherapy & Combination Therapy</u> Januvia is indicated as adjunct to diet & exercise to improve glycaemic control in adults with type 2 diabetes mellitus.</p> <p><u>Combination Therapy</u> Januvia is indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with</p>	26-Feb-11	<p>A</p> <p>B</p>

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	metformin or a PPAR γ agonist(e.g. thiazolidinediones)when the single agent alone, with diet & exercise, does not provide adequate glycemic control.		
Pakistan	<u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus. <u>Combination Therapy</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin or a PPAR γ agonist (e.g., thiazolidinedione) when diet and exercise, plus the single agent do not provide adequate glycemic control.	7-Oct-09	A B
Panama	<u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus. <u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control. <u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control. <u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPAR γ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control. <u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with	23-Apr-10	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
Paraguay	<p><u>Monotherapy</u></p> <p>JANUVIA is indicated as adjuvant of diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with metformin</u></p> <p>JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin when diet and exercise plus the single agent do not provide adequate glycemic control.</p> <p><u>Combination with sulfonylurea</u></p> <p>JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulphonylurea when diet and exercise plus the single agent do not provide adequate glycemic control.</p> <p><u>Combination with an agonist PPARγ</u></p> <p>JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with PPARγ agonist (e.g. thiazolidinediones) when diet and exercise plus the single agent do not provide adequate glycemic control.</p> <p><u>Combination with metformin and sulfonylurea</u></p> <p>JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in</p>	04-Feb-11	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	combination with metformin and sulfonylurea when dual therapy with these agents plus diet and exercise do not provide adequate glycemic control		
Peru	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination Therapy</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve the glycaemic control in combination with metformin or an PPARγ agonist (for example, thiazolidiona) when diet and exercises, along with an only agent, does not provide a proper glycemic control.</p>	19-Oct-06	A B
Philippines	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve</p>	26-Feb-07	A B C D

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
Puerto Rico	JANUVIA® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	23-Oct-06	N/A
Qatar	<p><u>Monotherapy & Combination Therapy</u></p> <p>Januvia is indicated as adjunct to diet & exercise to improve glycemic control in adults with type 2 diabetes mellitus.</p> <p><u>Combination Therapy</u></p> <p>Januvia is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin or a PPARγ agonist(e.g. thiazolidinediones)when the single agent alone, with diet & exercise, does not provide adequate glycemic control</p>	19-Mar-09	A B
Russia	<p><u>Monotherapy</u></p> <p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with</p>	15-Oct-07	A B C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>			D
				E
Saudia Arabia	<p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p><u>as monotherapy</u></p> <ul style="list-style-type: none"> • in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p><u>as dual oral therapy in combination with</u></p> <ul style="list-style-type: none"> • metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. • a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. • a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and 	18-May-12		A
				B
				C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control.</p> <p><u>as triple oral therapy in combination with</u></p> <ul style="list-style-type: none"> • a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. • a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.</p>		<p>D</p> <p>E</p>
Serbia	<p>4.1 Therapeutic indications</p> <p>For patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p>as monotherapy</p> <ul style="list-style-type: none"> • in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p>as dual oral therapy in combination with</p> <ul style="list-style-type: none"> • metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. • a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. • a PPARγ agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control. <p>as triple oral therapy in combination with</p> <ul style="list-style-type: none"> • a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide 	24-Dec-07	<p>A</p> <p>B</p> <p>C</p> <p>D</p>

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>adequate glycaemic control.</p> <ul style="list-style-type: none"> • a PPARγ agonist and metformin when use of a PPARγ agonist is appropriate and when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. <p>Januvia is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dosage of insulin do not provide adequate glycaemic control.</p>		E
Singapore	<p><u>Monotherapy</u></p> <p>JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (e.g., thiazolidinediones) when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is also indicated as add-on to insulin (with or without metformin)</p>	23-Apr-07	A B C D E

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.		
South Africa	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycaemic control in adult patients with type 2 diabetes mellitus.</p> <p><u>Combination Therapy</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycaemic control in combination with metformin or a PPARα agonist (e.g., thiazolidinedione) when diet and exercise, plus the single agent do not provide adequate glycaemic control. The combination of sitagliptin and sulphonylureas has not been adequately studied.</p>	Nov 2012	A B
Sri-Lanka	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control</p>	07-Sep-11	A B
Switzerland	<p>Type 2 diabetes mellitus If the blood Glukose level is insufficiently controlled by diet and exercise</p> <ul style="list-style-type: none"> - as monotherapy - in combination with metformin or a sulfonylurea in patients where no adequate glycemic control is achieved with metformin or any other oral antidiabetic agent. - in combination with metformin and a sulfonylurea when therapy with these two agents does not provide adequate glycemic control. <p>If the blood Glukose level is insufficiently controlled by diet and exercise and insulin in combination with insulin (with or without metformin).</p>	18-Apr-07	A B, C D E
Taiwan	Type 2 diabetes mellitus	13-Jul-07	N/A

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u></p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
Tunisia	<p>For adult patients with type 2 diabetes mellitus, Januvia is indicated to improve glycaemic control:</p> <p>as monotherapy</p> <ul style="list-style-type: none"> • in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. <p>as dual oral therapy in combination with</p> <ul style="list-style-type: none"> • metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. • a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. • a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control.. 	28-Dec-11	A B C
Turkey	<p>Sitagliptin is indicated in patients with Type II diabetes</p> <ul style="list-style-type: none"> - to improve glycaemic control in combination with metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control, - to improve glycaemic control in combination with a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to 	31-Jan-08	B C

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>contraindication or intolerance,</p> <ul style="list-style-type: none"> - to improve glycaemic control in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control, - Sitagliptin is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control. 		<p>D</p> <p>E</p>
Turkmenistan	<p>Monotherapy JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p>Combination with Metformin JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with a Sulphonylurea JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulphonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with a PPARγ-agonist JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ-agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with Metformin and a Sulphonylurea JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulphonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with Metformin and a PPARγ agonist</p>	17-Feb-12	<p>A</p> <p>B</p> <p>C</p> <p>D</p>

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p>Combination with Insulin</p> <p>JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		E
Ukraine	<p>As monotherapy: in patients inadequately controlled by diet and exercise alone.</p> <p>As oral therapy in combination with:</p> <ul style="list-style-type: none"> - metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control. - a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance. - a peroxisome proliferator-activated receptor gamma (PPARγ) agonist (i.e. a thiazolidinedione) when use of a PPARγ agonist is appropriate and when diet and exercise plus the PPARγ agonist alone do not provide adequate glycaemic control. - a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control. 	16-Apr-09	A B C D
United Arab Emirates	<p><u>Monotherapy & Combination Therapy</u></p> <p>Januvia is indicated as adjunct to diet & exercise to improve glycemic control in adults with type 2 diabetes mellitus.</p> <p><u>Combination Therapy</u></p> <p>Januvia is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin or a PPARγ agonist(e.g. thiazolidinediones)when the single</p>	17-Jan-07	A B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	agent alone, with diet & exercise, does not provide adequate glycemic control.		
United States	JANUVIA® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.	16-Oct-06	N/A
Uruguay	<p><u>Monotherapy</u> JANUVIA is indicated as adjuvant of diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with metformin</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin when diet and exercise plus the single agent do not provide adequate glycemic control.</p> <p><u>Combination with sulfonylurea</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulphonylurea when diet and exercise plus the single agent do not provide adequate glycemic control.</p> <p><u>Combination with an agonist PPARγ</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with PPARγ agonist (e.g. thiazolidinediones) when diet and exercise plus the single agent do not provide adequate glycemic control.</p> <p><u>Combination with metformin and sulfonylurea</u> JANUVIA is also indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and sulfonylurea when dual therapy with these agents plus diet and exercise do not provide adequate glycemic control.</p>	6-Dec-07	A B C D
Uzbekistan	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with</p>	07-May-10	A B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p>type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ-agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ-agonist (i.e., thiazolidinediones) as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Insulin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control in combination with insulin (with or without metformin).</p>		C
			D
			E
Venezuela	Treatment of Diabetes mellitus type 2 in combination with Metformin or Pioglitazone, when it is used on diet and with exercise, and when other therapies do not provide adequate glycemic control.	21-Jun-07	B

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

Vietnam	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p> <p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p>	15-Feb-11	A B C D
Vietnam	<p><u>Monotherapy</u> JANUVIA is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus.</p>	15-Feb-11	A

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

	<p><u>Combination with Metformin</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin as initial therapy or when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a sulfonylurea when treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with a PPARγ agonist (i.e., thiazolidinediones) as initial therapy when the single agent alone, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a Sulfonylurea</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a sulfonylurea when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p> <p><u>Combination with Metformin and a PPARγ agonist</u> JANUVIA is indicated in patients with type 2 diabetes mellitus to improve glycemic control in combination with metformin and a PPARγ agonist (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.</p>		<p>B</p> <p>C</p> <p>D</p>
<p>a: Angabe der Kodierung analog Tabelle 2-4; falls keine Überschneidung mit einem der Anwendungsgebiete, auf die sich das Dossier bezieht, besteht, ist „kein Bezug“ anzugeben.</p>			

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

Benennen Sie die den Angaben in Tabelle 2-5 zugrunde gelegten Quellen. Falls es keine weiteren Zulassungen international gibt oder Ihnen solche nicht bekannt sind, geben Sie „nicht zutreffend“ an.

Die Information bzgl. des internationalen Zulassungsstatus entstammt einer firmeninternen Datenbasis der amerikanischen Mutterfirma Merck & Co, Inc., Whitehouse Station, USA (Merck intern Databases, 2012). Der Stand des internationalen Zulassungsstatus ist Oktober 2012.

2.3 Beschreibung der Informationsbeschaffung für Modul 2

Erläutern Sie an dieser Stelle das Vorgehen zur Identifikation der im Abschnitt 2.1 und im Abschnitt 0 genannten Quellen (Informationsbeschaffung). Sofern erforderlich, können Sie zur Beschreibung der Informationsbeschaffung weitere Quellen benennen.

Die allgemeinen Angaben zum Arzneimittel, wie administrative Angaben, Angaben zum Wirkmechanismus des Arzneimittels und zu den Anwendungsgebieten, auf die sich das Dossier bezieht, wurden der Fachinformation von Januvia[®] bzw. Xelevia[®] entnommen bzw. entstammen der Informationsstelle für Arzneispezialitäten - IFA GmbH (Angaben zu den PZNs).

Die Informationen zur Zulassung der DPP-4-Inhibitoren und andere Produkte wurden den Angaben auf dem Community Register der Europäischen Kommission (http://ec.europa.eu/health/documents/community-register/html/index_en.htm), die Angaben zum laufenden Zulassungsverfahren von Alogliptin und Lixisenatide den Internetseite der European Medicines Agency (http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/document_listing/document_listing_000349.jsp&mid=WC0b01ac05805083eb) entnommen.

Die Informationen zur Beschreibung der Wirkmechanismen bzw. der Unterschiede im Wirkmechanismus von DPP4-Hemmern und anderer in Deutschland bereits zugelassener Antidiabetika wurden der Evidenzbasierten Leitlinie der Deutschen Diabetes-Gesellschaft (Matthaei et al., 2009), zwei aktuellen und umfangreichen Lehrbüchern zu Diabetes bzw. Pharmakologie und Toxikologie (Bretzel, 2011; Mutschler et al., 2008), sowie den Fachinformationen der entsprechenden Arzneimittel (siehe Kap. 2.4) entnommen.

Der internationale Zulassungsstatus von Januvia entstammt einer firmeninternen Datenbasis der amerikanischen Mutterfirma Merck & Co, Inc., Whitehouse Station, USA (Merck intern Databases, 2012).

2.4 Referenzliste für Modul 2

Benennen Sie nachfolgend alle Quellen (z. B. Publikationen), die Sie in den vorhergehenden Abschnitten angegeben haben. Verwenden Sie hierzu einen allgemein gebräuchlichen Zitierstil (z. B. Vancouver oder Harvard).

1. 2012. Rote Liste, Rote Liste Service GmbH.
2. ALBA, M., SHENG, D., GUAN, Y., WILLIAMS-HERMAN, D., LARSON, P., SACHS, J. R., THORNBERRY, N., HERMAN, G., KAUFMAN, K. D. & GOLDSTEIN, B. J. 2009. Sitagliptin 100 mg daily effect on DPP-4 inhibition and compound-specific glyceimic improvement. *Curr Med Res Opin*, 25, 2507-14.
3. ALIUD 2009. Fachinformation Repaglinid AL. www.fachinfo.de.
4. BAYER VITAL 2011. Fachinformation Glucobay. www.fachinfo.de.
5. BERLIN-CHEMIE 2012. Fachinformation Xelevia. www.fachinfo.de.
6. BLUME, H. H. 2012. Gutachten: Vergleich der Sulfonylharnstoffe Glibenclamid, Glimpepid und Glipizid aus pharmakologischer Sicht [unveröffentlicher Report].
7. BRETZEL, R. G. 2011. Behandlung mit Insulin, Thieme Verlag.
8. BRISTOL-MYERS SQUIBB 2012. Fachinformation Forxiga. http://ec.europa.eu/health/documents/community-register/html/index_en.htm.
9. BUNDESINSTITUT FÜR ARZNEIMITTEL UND MEDIZINPRODUKTE. 2010. Rosiglitazon: Das BfArM ordnet Vertriebseinstellung an [Online]. <http://www.bfarm.de/DE/BfArM/Presse/mitteil2010/pm11-2010.html>: Bundesinstitut für Arzneimittel und Medizinprodukte. [Accessed 28.11.2012 2012].
10. BUNDESINSTITUT FÜR ARZNEIMITTEL UND MEDIZINPRODUKTE. 2012. Pioglitazon (Actos®, Competact®, Tandemact®): Leitfaden für die Verordnung und das Risikomanagement [Online]. <http://www.bfarm.de/DE/Pharmakovigilanz/risikoinfo/2012/RI-pioglitazon.html>: Bundesinstitut für Arzneimittel und Medizinprodukte. [Accessed 28.11.2012 2012].
11. EUROPEAN COMMISSION. 2012. Community Register of medicinal products [Online]. http://ec.europa.eu/health/documents/community-register/html/index_en.htm: European Commission. [Accessed 28.11.2012 2012].
12. EUROPEAN MEDICINES AGENCY. 2012. Medicines under evaluation [Online]. http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/document_listing/docum

Allgemeine Angaben zum Arzneimittel, zugelassene Anwendungsgebiete

ent_listing_000349.jsp&mid=WC0b01ac05805083eb: European Medicines Agency.
[Accessed 28.11.2012 2012].

13. GALLWITZ, B., JOOST, H.-G. & MATTHAEI, S. 2011. Insulinotrope orale Antidiabetika und inkretinbasierte Therapieformen, Thieme Verlag.
14. GEMEINSAMER BUNDESAUSSCHUSS 2012. Niederschrift zum Beratungsgespräch gemäß § 8 Abs. 1 AM-NutzenV. Beratungsanforderung Nr.: 2012-B-028. 2012 (22. Oktober 2012).
15. JACOB, S. & ROSAK, C. 2011. Nicht beta-zytotrop wirkende orale Antidiabetika, Thieme Verlag.
16. LILLY DEUTSCHLAND 2012. Fachinformation Byetta. www.fachinfo.de.
17. LYSENG-WILLIAMSON, K. A. 2007. Sitagliptin. *Drugs*, 67, 587-597.
18. MATTHAEI, S., BIERWIRTH, R., FRITSCHKE, A., GALLWITZ, B., HÄRING, H. U., JOOST, H. G., KELLERER, M., KLOOS, C., KUNT, T., NAUCK, M., SCHERNTHANER, G., SIEGEL, E. & THIENEL, F. 2009. Medikamentöse antihyperglykämische Therapie des Diabetes mellitus Typ2. *Diabetologie und Stoffwechsel*, 4, 32-64.
19. MERCK SERONO 2010. Fachinformation Glucophage. www.fachinfo.de.
20. MSD SHARP&DOHME 2012. Fachinformation Januvia. www.fachinfo.de.
21. MUTSCHLER, E., GEISLINGER, G., KROEMER, H. K. & SCHÄFER-KORTING, M. 2008. Mutschler Arzneimittelwirkungen: Lehrbuch der Pharmakologie und Toxikologie, Wissenschaftl. Verlagsgesellschaft mbH Stuttgart.
22. NAUCK, M. 2012. Wissenschaftliches Gutachten zur Frage "Möglicherweise unterschiedlicher klinischer Konsequenzen einer Behandlung mit den Sulfonylharnstoffen Glibenclamid (Glyburide) und Glipizid(e) in der Behandlung des Typ 2-Diabetes" [unveröffentlicht].
23. NOVARTIS PHARMA 2011. Fachinformation Starlix. www.fachinfo.de.
24. SANOFI-AVENTIS 2010. Fachinformation Diastabol. www.fachinfo.de.
25. SANOFI-AVENTIS 2011. Fachinformation Amaryl. www.fachinfo.de.
26. STADAPHARM 2010. Fachinformation Glibenclamid STADA. www.fachinfo.de.
27. TAKEDA PHARMA 2011. Fachinformation Actos. www.fachinfo.de.