

Types of changes to be used in the national Variation form (structural numbers and texts), thematically arranged:

General information:

- Types of change are encoded by structural numbers (SKNo) for presentation in the AMIS data base. As a result thereof types of change will be presented in the database in German only and additionally it is impossible to modify a text assigned to an SKNo.
- A change pursuant to Section 29 sub-section 2a German Drug Law (Arzneimittelgesetz, AMG) comprises the entire chapter. This means that any change in the chapters "Therapeutic indications", "Posology" or "Method and duration of administration" requires approval, even the mere deletion of a general note or warning.
- The column "reason for change" states only why a change has been made. Therefore, add the changed sections themselves by listing the changes case by case and comparing them with their original versions in the present-proposed Table.
If none of the given reasons for change applies, additional reasons may be included in the cover letter or in the present-proposed Table .

* requires approval

Pharmaceutical Entrepreneur / Co-distributor / Manufacturer / Address

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0013	Marketing authorisation holder [Zulassungsinhaber]	
0026	Manufacturer/batch release * [Hersteller/Endfreigabe]	
0245	Other information and documents pursuant to Section 22 (4-6) (permission/authorisation) [sonstige Angaben und Unterlagen nach § 22 Abs.4-6 (Erlaubnis/Genehmigung)]	
0299	Co-distributor * [Mitvertreiber]	
0601	Active substance manufacturer * [Wirkstoffhersteller]	
1184	Manufacturing authorisation [Herstellungserlaubnis]	
1198	Import authorisation [Importerlaubnis]	
1208	Manufacturing site [Herstellungsstätte]	State only in combination with further SKNo (0026, 1417, 0601) since each manufacturing site is given a separate PNR (pharmaceutical company number).
1417	Manufacturer, other (not SKNo=0026) * [Hersteller, sonstige]	
1434	Company change (name, address) marketing authorisation holder (same legal entity) [Firmenänderung (Name, Anschrift) Zulassungsinhaber (gleiche jurist. Person)]	
1448	Company change (name, address) manufacturer (same legal entity) [Firmenänderung (Name, Anschrift) Hersteller (gleiche juristische Person)]	
1451	Company change (name, address) active substance manufacturer (same legal entity) [Firmenänderung (Name, Anschrift) Wirkstoffhersteller (gleiche jurist. Person)]	
1482	Company change (name, address) co-distributor (same legal entity) [Firmenänderung (Name, Anschrift) Mitvertreiber (gleiche juristische Person)]	
1643	Internet/email-address (as stated in the information texts pursuant to Section 22 (7) [Internet-e-mail-Adresse (als Angabe in den Informationstexten gem. § 22 Abs. 7)]	
1732	Manufacturer of an intermediate of the active substance	

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	[Zwischenproduktthersteller für Wirkstoff]	
2316	Company change (name, address) other manufacturer (same legal entity) [Firmenänderung (Name, Anschrift) sonstiger Hersteller (gleiche jurist. Person)]	
2765	Local representative [Örtlicher Vertreter]	
2779	Batch control testing site pursuant to Art. 51 of Directive 2001/83/EC [Prüfstätte gem. Art. 51 der Richtlinie 2001/83 (EC)]	
2806	Company change (name, address) local representative (same legal entity) [Firmenänderung (Name, Anschrift) Örtlicher Vertreter (gleiche juristische Person)]	

* All Co-distributors and manufacturers (including their function) have to be listed

Name of medicinal product

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0039	Name of medicinal product [Bezeichnung des Arzneimittels]	
1362	Name of medicinal product in other countries except Germany [Bezeichnung im Ausland]	

Informative Texts pursuant to Section 22 (7) AMG

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0041	Method and duration of administration * [Anwendungsart und –dauer]	For a new route of administration, state whether Art. 8 of the Paediatric Regulation applies.
0067	Effects [Wirkungen]	
0095	Posology / dosage * [Dosierung]	
0436	Change in legal status resulting from adoption of the medicinal product to existing legal regulations ruling the legal status of medicinal products [Änderung der Verkaufsabgrenzung durch Anpassung des Arzneimittels an bestehende gesetzliche Vorschriften zur Verkaufsabgrenzung]	

* requires approval

0581	Therapeutic indications (extension) * [Anwendungsgebiete (mit neuen Indikationen)]	Additional documents according to Section 22 subsection 3c are required for assessment of environmental risks or plausible reason for a waiver quoting SKNR 2631. State whether Art. 8 of the Paediatric Regulation applies
1119	Deletion of therapeutic indications * [Reduktion der Anwendungsgebiete]	
1331	Non-official part of package leaflet [nicht amtlicher Teil der Packungsbeilage]	
1763	Editorial change [redaktionelle Änderung]	Only changes in orthography and punctuation.
2021	Change in ATC code [Änderung des ATC-Codes (Anh. 1 Nr. 6 d. EG-VO 1084/2003)]	
2659	Change in legal status resulting from a change in the legal regulation ruling the legal status of medicinal products [Änderung der Verkaufsabgrenzung aufgrund der Änderung gesetzlicher Vorschriften zur Verkaufsabgrenzung]	
2693	Adaptation to 14 th amendment of AMG [Anpassung an 14. AMG-Novelle]	Confirm in cover letter that it is exclusively a change in the sequence of text paragraphs <u>without changes in content</u> ; no highlighting is necessary then.
2823	Omission of particulars pursuant to Section 11a (1e) AMG (patent law) [Wegfall von Angaben entsprechend § 11a Abs. 1e AMG (Patentschutz)]	List the categories of change (e.g. 1119, 0095) and attach Table of Comparison. It is treated as a obligatory notification of variation.
2837	Addition of omitted particulars pursuant to Section 11a (1e) (patent law) [Wiederaufnahme von gem. § 11a Abs. 1e AMG entfallenen Angaben]	
3352	Other variations of primary packaging pursuant to Section 10 AMG not requiring approval [sonstige nicht zustimmungspflichtige Änderungen des Behältnis gemäß § 10 AMG]	Take these SKNos only for changes for which no other SKNo is available. The SKNos mentioned here do not cover changes in such sections as side effects, warnings, contraindications, interactions, pregnancy and lactation, overdosage and effects!
3366	Other variations to outer packaging pursuant to Section 10 AMG not requiring approval [sonstige nicht zustimmungspflichtige Änderungen der äußeren Umhüllung gemäß § 10 AMG]	
3370	Other variations to the package leaflet pursuant to Section 11 AMG not requiring approval [sonstige nicht zustimmungspflichtige Änderungen der Gebrauchsinformation gemäß § 11 AMG]	

* requires approval

3383	Other variations to the expert information pursuant to Section 11a AMG not requiring approval [sonstige nicht zustimmungspflichtige Änderungen der Fachinformation gemäß § 11a AMG]	
3410	Therapeutic indications (without additional indications) * [Anwendungsgebiete (ohne neue Indikationen)]	
3784	Pharmacodynamic properties [Pharmakodynamische Eigenschaften]	
3798	Pharmacokinetic properties [Pharmakokinetische Eigenschaften]	
3808	Preclinical safety data [Präklinische Daten zur Sicherheit]	
3811	Incompatibilities [Inkompatibilitäten]	

Risk information in the informative texts

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0128	Warning / precautions for use [Warnhinweise / Vorsichtsmaßnahmen]	
1479	Information about overdose, skipped taking of medication or discontinuation [Hinweise bei Überdosierung, unterlassene Einnahme oder Absetzen]	
1571	Pregnancy and lactation [Schwangerschaft/Stillzeit]	
2419	Contraindications (with restrictions of contraindications)* [Gegenanzeigen (mit Einschränkungen von Gegenanzeigen)]	
2422	Side effects (with restrictions of contraindications)* [Nebenwirkungen (mit Einschränkungen von Nebenwirkungen)]	
2436	Interactions (with restrictions of contraindications)* [Wechselwirkungen (mit Einschränkungen von Wechselwirkungen)]	
2556	Side effects (without restrictions of contraindications) [Nebenwirkungen (ohne Einschränkungen von Nebenwirkungen)]	
2573	Contraindications (without restrictions of contraindications)	

* requires approval

	[Gegenanzeigen (ohne Einschränkungen von Gegenanzeigen)]	
2587	Interactions (without restrictions of contraindications) [Wechselwirkungen mit anderen Mitteln (ohne Einschränkungen von Wechselwirkungen)]	
2796	Information on resistance situation [Angaben zur Resistenzsituation]	

Informative text concerned by a change applied for (additional information)

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0319	Expert information (SPC) pursuant to Section 11a AMG [Fachinformation gemäß § 11a AMG]	Only in combination with other SKNRs, shows implications of changes for SPC.
1002	Package leaflet (PIL) pursuant to Section 11 AMG [Gebrauchsinformation gemäß § 11 AMG]	Only in combination with other SKNRs; shows implications of changes for PIL.
1064	Primary packaging pursuant to Section 10 AMG [Behältnis gemäß § 10 AMG]	Only in combination with other SKNRs; shows implications of changes for the labelling of containers.
1078	Outer packaging pursuant to Section 10 AMG [Äußere Umhüllung gemäß § 10 AMG]	Only in combination with other SKNR; shows implications of changes for the labelling of outer packaging.

Reason for change (additional information)

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0220	Fulfilment of specific conditions resulting from a national graduated plan in Pharmacovigilance [Erfüllung von Stufenplanauflagen]	Please do not state further changes. Check if the BfArM website has published information for pharmaceutical companies about a graduated plan procedure (<i>Stufenplanverfahren</i>) that is to be complied with – if so, submit the relevant data sheet.

* requires approval

0477	Adoption of BfArM core texts for PIL and SPC [Anpassung an Mustergebrauchs-/fachinformation]	Please do not state further changes. Submit the declaration to adoption the BfArM core texts . Please look out for special instructions. Adoption of core PIL/SPC is not possible for parallel import authorisations.
1211	Fulfilment of conditions [Auflagenerfüllung]	Use only for requirements resulting from a renewal procedure. Do not include further changes in this notification.
1794	National implementation of changes resulting from an MRP with Germany as RMS [nationale Anpassung nach MRP mit Deutschland als RMS]	
1972	Implementation of referral [Anpassung an Referral]	
2734	Adaptation to speciality list [Anpassung an die Besonderheitenliste]	
3589	Variation in preparation of a MRP with Germany as RMS [Änderungen zur Vorbereitung eines MRP mit Deutschland als RMS]	Use only for the authorisation which is actually destined for MRP. Do not use for harmonisation of other authorisations with an EU authorisation (if an EU procedure is intended please point out in the cover letter or in the Table of Comparison).
3722	Adaptation to Art. 45/46-Procedure [Anpassung an Art. 45/46-Verfahren]	Additional submission of the national Variation form .
3753	Adaptation of package leaflet to results of a readability test pursuant to Section 22 (7) AMG [Umsetzung der Ergebnisse von Bewertungen der Packungsbeilage gem. § 22 (7) AMG]	Assign structural numbers to the changed paragraphs to show the categories the changes belong to.

Shelf-life / stability

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0512	Method of preservation, storage conditions pursuant to Section 22 (1) 14 [Art der Haltbarmachung, Art der Aufbewahrung [§ 22(1)14]]	
0716	Prolongation of shelf-life of medicinal product [Verlängerung der Haltbarkeit des Arzneimittels]	

* requires approval

0731	Shelf-life after reconstitution or dilution [Haltbarkeitsdauer nach Rekonstituierung oder Verdünnung]	
0744	Storage conditions [Lagerbedingungen]	
1393	Results of stability testing for active substance [Ergebnisse von Haltbarkeitsuntersuchungen zum Wirkstoff]	
1746	Retest period of active substance [Retest-Periode des Wirkstoffs]	
1883	Results of stability testing of finished product (Section 22 (1) 14) without change in shelf-life [Ergebnisse von Haltbarkeitsversuchen des Arzneimittels [§ 22(1)14] (Ohne Änderung der Dauer der Haltbarkeit)]	
3215	Reduction of shelf-life of finished product [Verkürzung der Haltbarkeit des Arzneimittels]	
3277	Shelf-life after first opening, reduction [Dauer der Haltbarkeit nach 1. Öffnen, Verkürzung]	
3280	Shelf-life after first opening, extension [Dauer der Haltbarkeit nach 1. Öffnen, Verlängerung]	
3294	Shelf-life after reconstitution or dilution, reduction [Haltbarkeitsdauer nach Rekonstituierung oder Verdünnung, Verkürzung]	
3304	Shelf-life after reconstitution of dilution, extension [Haltbarkeitsdauer nach Rekonstituierung oder Verdünnung, Verlängerung]	

Composition/Pharmaceutical form

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0054	Excipients (qualitative and quantitative) * [Sonstige Bestandteile nach Art und Menge]	
0306	Active substances * [Wirkstoffe]	
0321	Active constituents (excluding medicinal active substances)* * [Wirksame, aber nicht arzneilich wirksame Bestandteile]	
0334	Pharmaceutical form (comparable)*	State whether Art. 8 of the Paediatric Regulation

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	[Darreichungsform (vergleichbare)]	applies.
0423	Reference quantity [Bezugsmenge]	
0538	Change in colouring system [Farbstoffänderung (Anh. 1 Nr. 34 d. EG-VO 1084/2003)]	
0553	Change in flavouring system [Geschmackstoffänderung (Anh. 1 Nr. 34 d. EG-VO 1084/2003)]	
0566	Change in weight of capsule shells or coating weight of tablets [Gewichtsänderung von Kapselhüllen oder Überzugschicht von Tbl.]	
1095	Short term for method and route of administration [Kurzbezeichnung der Art der Anwendung]	
1105	Name of pharmaceutical form [Bezeichnung der Darreichungsform]	
1167	Declaration [Deklaration]	Change in the designation of ingredients in the information texts.
1729	Change in excipient from animal to plant origin [Hilfsstoffänderung - tierischer auf pflanzlichen Ursprung]	
2018	Declaration of active substance pursuant to Section 10-11a AMG [Wirkstoffbezeichnung (§§ 10-11a AMG)]	
3349	Adjuvants * [Adjuvantien]	

* complete composition of finished product (present and proposed) has to be stated

Pack size / Container

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0102	Pack size [Packungsgröße] * *	For national variations (Section 29 AMG), change of pack sizes for products authorised in MR or DC procedures: you may only apply for pack sizes to be marketed in DE if they are already authorised for the EU. Pack sizes available in DE are encoded in the AMIS database as original packs (OP), hospital pack (KP) or nonmarketable

* requires approval

		sample pack (UM), pack sizes available in the EU are encoded as SPCOP. Changes to SPCOP are to be applied for pursuant to Variation Regulation 1234/2008.
0579	Change in immediate packaging material [Primärverpackungsänderung]	
0805	Test procedure for immediate packaging [Prüfverfahren für Primärverpackung]	
0818	Test procedure for measuring or administration device [Prüfverfahren für Applikator / Messvorrichtung]	
0833	Application aid / Applicator [Applikationshilfe / Applikator]	
0846	Change in shape of container [Behältnisformänderung (Anh. 1 Nr. 36 d. EG-VO 1084/2003)]	
1376	Measuring device (e.g. measuring cup, measuring spoon) [Messvorrichtung (z.B. Messbecher, Messlöffel)]	
2035	Specification of primary packaging [Spezifikation der Primärverpackung]	

* All pack sizes (present and proposed) have to be mentioned

Manufacturing / Test procedure / Specification / Analytics

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0070	Virus validation of manufacturing process [Virusvalidierung des Herstellungsverfahrens]	
0171	Information about manufacturing process of medicinal product [Angaben über die Herstellung des Arzneimittels]	
0197	Control methods [Kontrollmethoden]	
0614	Active substance manufacturing process [Wirkstoffherstellungsverfahren]	
0627	Batch size of active substance [Wirkstoff (Chargengröße)]	
0642	Active substance specification	

* requires approval

	[Wirkstoffspezifikation]	
0655	Minor change in the manufacture of finished product [Arzneimittelherstellung, kleinere Änderung]	
0668	Batch size of finished product [Fertigprodukt (Chargengröße)]	
0683	Specification of finished product [Arzneimittelspezifikation]	
0696	Change in synthesis or recovery of a non-pharmacopeial excipient [Hilfsstoffherstellung (nicht von Arzneibuchmonographie abgedeckt)]	
0703	Specification of an excipient [Hilfsstoffspezifikation]	
0757	Test procedure of active substance [Wirkstoffprüfverfahren]	
0772	Test procedure of medicinal product [Arzneimittelprüfverfahren]	
0785	Change to comply with an update of the relevant monograph of the Ph. Eur. [Erfüllung von Bestimmungen bei Ph. Eur.-Änderung]	
0798	Test procedure for an excipient [Hilfsstoffprüfverfahren]	
0859	Imprint, form, bossing of tablet or capsule [Aufdruck, Form, Prägung von Tbl oder Kps]	
0861	Dimension of tablet, capsule, suppository, pessary (without quantitative change) [Abmessung von Tbl, Kps, Supp, Pessar (ohne quantitative Änd.)]	
1955	Certificate of Suitability (CEP)	
1969	Resumption of manufacture/marketing of TSE-relevant medicinal product [Wiederaufnahme von Herstellung/Inverkehrbringen von TSE-relevanten AM]	
2049	Supplier of packaging components [Lieferant von Packungsteilen]	
2244	Certificate of Suitability (CEP) - (TSE, active substance) [Certificate of Suitability (CEP) - (TSE, Wirkstoff)]	
2258	Certificate of Suitability (CEP) - (TSE, excipient) [Certificate of Suitability (CEP) - (TSE, Hilfsstoff)]	
2261	Dosing accuracy [Dosiergenauigkeit]	

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2292	TSE/ information on application safety [TSE/Anwendungssicherheit (Angaben zur Anwendungssicherheit)]	
2614	Treatment with ionizing radiation * [Behandlung mit ionisierenden Strahlen]	
2628	Manufacturing process using genetic engineering * [Gentechnologisches Herstellungsverfahren]	
2676	Divisibility of tablets [Teilbarkeit der Tabletten]	
3263	Supplier of an excipient [Hilfsstofflieferant]	
3736	Parametric release [Parametrische Freigabe]	This SKNR is used for the introduction of the parametric release procedure and for all changes related to it. It applies to changes to an already existing parametric release procedure as well. For additional changes use the appropriate SKNRs.

Documents / Documentation

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0204	Information and documents about analytical testing [Angaben und Unterlagen zur analytischen Prüfung]	
0217	Information and documents about pharmacological, toxicological testing [Angaben und Unterlagen zur pharmakologischen, toxikologischen Prüfung]	
0232	Information and documents about clinical testing [Angaben und Unterlagen zur klinischen Prüfung]	
0273	Information and documents pursuant to Section 24 (Expert statement) [Angaben und Unterlagen nach § 24 AMG (Sachverständigungsgutachten)]	
1359	Active substance Master file [Drug Master File]	
1554	Bioavailability, bioequivalence [Bioverfügbarkeit, Bioäquivalenz (BV)]	
2539	Information and documents pursuant to Section 24a AMG	

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	[Angaben und Unterlagen nach § 24a AMG]	
2542	Information and documents pursuant to Section 25b AMG [Angaben und Unterlagen nach § 25b AMG]	
2631	Documents about evaluation of possible environmental risks [Unterlagen über die Bewertung möglicher Umweltrisiken]	
2645	Readability test of package leaflet pursuant to Section 22 (7) AMG [Ergebnisse von Bewertungen der Packungsbeilage gem. § 22 (7) AMG]	

Pharmacovigilance

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
2484	Information incl. prohibitions and restrictions with influence on benefit/risk assessment [Informationen incl. Verbote und Beschränkungen mit Einfluss auf die Nutzen/Risiko-Bewertung]	
2511	Pharmacovigilance/risk management system [Pharmakovigilanz-/Risikomanagement-System]	
2525	Evidence of access to a qualified person pursuant to Section 63a AMG [Nachweis über qualifizierte Person nach Par. 63a AMG]	

Parallel import

SKNo	Type of change [German term as presented in the Database]	Explanatory remarks
0408	Parallel import source contra (additional) [Parallelimportländer (zusätzlich)]	
1081	Adoption of imported medicinal product to PIL/SPC of reference medicinal product [Anpassung von ParImp-AM an GI/FI der Bezugszul.]	This SKNR is used for the PILs and SPCs fully harmonised (1:1) with the texts of the reference authorisation. If in the process of harmonisation, different formulations are used for indications the numbers 3410 or 0581 or 1119 should be used in

* requires approval

		addition to 1081. In the case of further specific parallel import deviations from the formulations in the reference authorisation, identify them by the respective structural numbers, for example in the storage specification.
1496	Import declaration (name, distributor, MA number in import country) [Importversicherung (Bezeichnung, Vertreiber, ZNR)]	
1804	MA number of reference medicinal product [Bezugszulassungsnummer von ParImp-AM]	
1924	Parallel import source country, deletion [Parallelimportland/-länder, Wegfall]	
3250	MA number of imported medicinal product in source country (changed or added) [Zulassungsnummer für Parallelimport im Herkunftsstaat (geändert oder ergänzt)]	
3469	Name of medicinal product in source country of parallel import [Bezeichnung im Importland]	

2453	Other changes [Sonstige Änderungen]	
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